

Enzymatic Promiscuity

A Thesis
Presented to
The Division of Mathematics and Natural Sciences
Reed College

In Partial Fulfillment
of the Requirements for the Degree
Bachelor of Arts

Nelly Selim

May 2016

Approved for the Division
(Mathematics)

Francisco Barona Gomez

Acknowledgements

I want to thank a few people.

Preface

This is an example of a thesis setup to use the reed thesis document class.

Table of Contents

Background	1
0.1 Introduction	2
0.1.1 Relacion del pangenoma con la promiscuidad enzimatica . . .	4
0.1.2 Expansion y contextos genomicos como herramienta de anotacion funcional	4
0.1.3 Modelos bioinformaticos de promiscuidad	5
0.1.4 Promiscuidad in vitro y promiscuidad in vivo	6
0.1.5 El papel de la dinamica molecular en la promiscuidad	7
0.1.6 Modelo biologico diversidad de Actinobacteria	7
0.1.7 Modelo metabolico biosintesis de aminoacidos.	8
0.2 Antecedentes	8
0.2.1 Modelo biologico	9
0.2.2 Subsistemas metabolicos	9
0.2.3 Contexto y vecindades genomicas	9
0.2.4 Metodos bioinformaticos	10
0.2.5 Evomining	10
0.2.6 Caracterizacion in vivo	11
0.2.7 Caracterizacion bioquimica in vitro.	11
0.2.8 Modelado de dinamica molecular	11
0.3 Objetivo General	12
0.4 Objetivos particulares	12
0.5 Estrategias	13
0.5.1 La promiscuidad en familias enzimaticas.	13
Obtener informacion genomica del phylum Actinobacteria. . .	13
Promiscuidad in vitro dentro de miembros de una familia promiscua de enzimas.	13
Seleccionar miembros homologos de la familia de enzimas. . .	13
Determinar posibles correlaciones entre los datos producidos..	14
0.5.2 Desarrollar una metodologia para la deteccion in vivo de promiscuidad enzimatica.	14
Crear cepas geneticamente modificadas con variantes funcionales no nativas de PriA y enzimas asociadas.	14
0.6 Metodologia	15
0.6.1 La promiscuidad en familias enzimaticas.	15

Actinobacteria genomic	15
Annotation	15
Genomic DB phylogeny	15
0.6.2 Identificar cambios en la vecindad genómica en familias selectas de enzimas de metabolismo central.	16
Organizar y presentar los datos en una plataforma.	17
0.6.3 Promiscuidad in vitro	18
Datos cinéticos:	18
Dinámica molecular	18
0.6.4 Promiscuidad in vivo	18
0.6.5 Consideraciones	19
Chapter 1: EvoMining	23
1.1 Introduction	23
1.2 Gen families expansions on genomes	23
1.2.1 Pangenomes	23
1.3 EvoMining	23
1.4 Pangenome	24
1.5 EvoMining Implementation	24
1.6 EvoMining Databases	25
Genome DB	26
Phylogeny	26
Central DB	27
1.7 Data Bases	27
1.7.1 Central pathways	27
1.7.2 Genome Dynamics	28
Natural Products DB	28
1.7.3 AntisMASH optional DB	29
1.7.4 Otras estrategias para los clusters Argon context Idea	29
1.8 Argonne	29
1.8.1 Inline code	32
1.9 Recomendaciones de Luis	32
1.10 CORASON: Other genome Mining tools context-based	33
1.11 CORe Analysis of Syntenic Orthologs to prioritize Natural Product-Biosynthetic Gene Cluster	33
1.12 Loading and exploring data	35
Chapter 2: PriA Family	39
2.1 Methods	40
2.2 Chemistry 101: Symbols	155
2.2.1 Typesetting reactions	157
2.2.2 Other examples of reactions	157
2.3 Physics	157
2.4 Biology	158

Chapter 3: Archaea EvoMining Results	161
3.1 Tables	162
3.1.1 Expansions BoxPlot by metabolic family	163
3.1.2 Expansions BoxPlot by metabolic family by phylum	164
3.2 Central pathway expansions	175
3.3 Genome Size correlations	176
3.3.1 Correlation between genome size and AntiSMASH products .	176
3.3.2 Correlation between genome size and Central pathway expansions	178
3.4 Natural products	182
3.4.1 Natural products recruitments from EvoMining heatplot . .	182
3.5 Archaeas AntiSMASH	184
3.5.1 AntisSMASH vs Central Expansions	186
3.6 Selected trees from EvoMining	189
3.7	190
3.8 Bibliographies	190
3.9 Anything else?	191
Chapter 4: Actinobacteria EvoMining Results	193
4.1 Tables	193
4.1.1 Expansions BoxPlot by metabolic family	194
4.2 Central pathway expansions	196
4.3 Genome Size correlations	200
4.3.1 Correlation between genome size and AntiSMASH products .	200
4.3.2 Correlation between genome size and Central pathway expansions	202
4.4 Natural products	206
4.4.1 Natural products recruitments from EvoMining heatplot . .	206
4.5 Actinos AntiSMASH	208
4.5.1 AntisSMASH vs Central Expansions	210
4.6 Selected trees from EvoMining	213
Chapter 5: Cyanobacteria EvoMining Results	215
5.1 Tables	215
5.1.1 Expansions BoxPlot by metabolic family	216
5.2 Central pathway expansions	218
5.3 Genome Size correlations	219
5.3.1 Correlation between genome size and AntiSMASH products .	219
5.3.2 Correlation between genome size and Central pathway expansions	221
5.4 Natural products	225
5.4.1 Natural products recruitments from EvoMining heatplot . .	225
5.5 Cyanobacterias AntiSMASH	227
5.5.1 AntisSMASH vs Central Expansions	229
5.6 Selected trees from EvoMining	232
Conclusion	237
More info	237

Appendix A: The First Appendix	239
In the main Rmd file:	239
In :	239
Appendix B: The Second Appendix, Open source code on this document	241
B.1 R markdown	241
B.2 Docker	241
B.3 Git	242
B.4 Connect GitHub and DockerHub	242
B.5 Additional resources	242
References	245

List of Tables

1.1	Maximum Delays by Airline	36
2.1	Substrates	40
2.2	Enzymes docking	153
3.1	Families on Archaeabacteria	162
4.1	Correlation of Inheritance Factors for Parents and Child	193
5.1	Families on Cyanobacteria	215

List of Figures

2.1	Heat Plot PriA Streptomyces vs other substrates	156
2.2	Heat Plot TrpF Streptomyces vs other substrates	156
2.3	Combustion of glucose	157
3.1	Expansions Boxplot	163
3.2	Archaeas Heatplot	175
3.3	Correlation between Archaeas genome size and antismash Natural products detection colored by Order	176
3.4	Correlation between Archaeas genome size and antismash Natural products detection grided by Order	177
3.5	Correlation between Archaeas genome size and central pathway expansions	178
3.6	Correlation between Archaeas genome size and central pathway expansions grided by order	179
3.7	Correlation between Archaeas Genome size vs Total central pathway expansion coloured by metabolic Family	180
3.8	Archaeas Recruitmens on central families coloured by kingdom	182
3.9	Archaeas Recruitmens on central families coloured by taxonomy	183
3.10	Archaeas Diversity	184
3.11	Archaeas Smash Taxonomical Diversity	185
3.12	Correlation between Archaeas central pathway expansions and anti-smash Natural products detection	186
3.13	Correlation between Archaeas central pathway expansions and anti-smash Natural products detection	187
3.14	Archaeas Natural products by family	188
3.15	Phosphoribosyl isomerase A EvoMiningtree	189
3.16	Phosphoribosyl isomerase other EvoMiningtree	189
3.17	Phosphoribosyl anthranilate isomerase EvoMiningtree	189
4.1	Expansions Boxplot	195
4.2	Actinobacterial Heatplot	197
4.3	Streptomyces Genomes expansions on PGA Aminoacids HeatPlot	199
4.4	Correlation between Actinos genome size and antismash Natural products detection colored by Order	200

4.5	Correlation between Actinos genome size and antismash Natural products detection grided by Order	201
4.6	Correlation between Actinos genome size and central pathway expansions	202
4.7	Correlation between Actinos genome size and central pathway expansions grided by order	203
4.8	Correlation between Actinos Genome size vs Total central pathway expansion coloured by metabolic Family	204
4.9	Actinos Recruitmens on central families coloured by kingdom	206
4.10	Actinos Recruitmens on central families coloured by taxonomy	207
4.11	Actinos Diversity	208
4.12	Actinos Smash Taxonomical Diversity	209
4.13	Correlation between Actinos central pathway expansions and antismash Natural products detection	210
4.14	Correlation between Actinos central pathway expnasions and antismash Natural products detection	211
4.15	Actinos Natural products by family	212
4.16	Enolase EvoMiningtree	213
4.17	Phosphoribosyl isomerase EvoMiningtree	213
4.18	Phosphoribosyl isomerase A EvoMiningtree	213
4.19	phosphoshikimate carboxyvinyltransferase EvoMiningtree	214
5.1	Expansions Boxplot	217
5.2	Cyanobacterial Heatplot	218
5.3	Correlation between genome size and antismash Natural products detection colored by Order	219
5.4	Correlation between genome size and antismash Natural products detection grided by Order	220
5.5	Correlation between genome size and central pathway expansions	221
5.6	Correlation between genome size and central pathway expansions grided by order	222
5.7	Correlation between Genome size vs Total central pathway expansion coloured by metabolic Family	223
5.8	Recruitmens on central families coloured by kingdom	225
5.9	Recruitmens on central families coloured by taxonomy	226
5.10	Diversity	227
5.11	Smash	228
5.12	Correlation between central pathway axpnasions and antismash Natural products detection	229
5.13	Correlation between central pathway axpnasions and antismash Natural products detection	230
5.14	Natural products by family	231
5.15	Phosphoribosyl isomerase EvoMiningtree	232
5.16	Phosphoglycerate dehydrogenase EvoMiningtree	232
5.17	Phosphoserine aminotransferase EvoMiningtree	232

5.18	Triosephosphate isomerase EvoMiningtree	233
5.19	glyceraldehyde3phosphate dehydrogenase EvoMiningtree	233
5.20	phosphoglycerate kinase EvoMiningtree	233
5.21	phosphoglycerate mutaseEvoMiningtree	234
5.22	enolase EvoMiningtree	234
5.23	Pyruvate kinase EvoMiningtree	234
5.24	Aspartate transaminase EvoMiningtree	235
5.25	Asparagine synthase EvoMiningtree	235
5.26	Aspartate kinase EvoMiningtree	235
5.27	Aspartate semialdehyde dehydrogenase EvoMiningtree	236
5.28	Homoserine dehydrogenase EvoMiningtree	236

Abstract

The preface pretty much says it all.

Second paragraph of abstract starts here.

Dedication

You can have a dedication here if you wish.

Background

Enzymes catalyze chemical reactions transforming substrates into products. During 20th century enzymes were perceived as highly specific catalysts, nevertheless this perception changed with the discovery that they can . This ability to catalyze several chemical functions is known as enzyme promiscuity. *Escherichia coli* contains at least 404 promiscuous enzymes. La relevancia de la promiscuidad radica tanto en su papel como mecanismo de evolución de la función enzimática, así como en la necesidad de su detección para la corrección de modelos de flujo metabólico y la determinación de efectos secundarios en drogas farmacológicas. A pesar de su frecuencia e importancia aún se está en el proceso de entender las causas y las características observables de la promiscuidad enzimática.

Para estudiar la promiscuidad esta propuesta discierne entre dos problemas. El primero es el de ubicar cuáles familias tienen enzimas promiscuas, al que llamaremos problema de las familias. El segundo es el de los miembros: una vez identificada una familia promiscua, cómo distinguir entre sus miembros enzimas con distinto nivel de promiscuidad. Se ha intentado identificar enzimas promiscuas, a nivel de secuencia, sin pasar por experimentación mediante aprendizaje maquinaria. Estos enfoques son incapaces de identificar una familia promiscua si no se conoce previamente al menos un miembro promiscuo de ella. Por otra parte, en el problema de los miembros se presentan dificultades cuando la identidad de secuencia es alta, e.g. en la familia PriA-HisA se sabe que la enzima HisA de *E. coli* no es promiscua, pero PriA de *Streptomyces coelicolor* sí lo es.

Para mejorar nuestro entendimiento del fenómeno, además de la comparación de secuencias es necesario integrar otros elementos de análisis. Se debe notar que es prácticamente imposible decir que una enzima no es promiscua ya que para ello se deberían haber descartado todos los posibles sustratos. Sin embargo, para el estudio de cambios en promiscuidad se han detectado como elementos relevantes a los cambios en vecindad genómica, los cambios en flexibilidad durante la dinámica molecular, la pérdida de genes centrales, y finalmente a las expansiones genéticas dentro de un grupo taxonómico. Estos elementos tienen en común que reflejan un cambio en alguna propiedad genómica o biofísica, de lo que se deriva que el buscar cambios en la promiscuidad de una enzima resulta más factible que la búsqueda intrínseca de promiscuidad, a lo que aspiran los métodos basados en comparaciones de secuencias.

Evomining es una plataforma bioinformatica pensada para la busqueda de expansiones de familias genicas de metabolismo central. Desarrollarla en combinacion con algoritmos de busqueda de cambios en la vecindad genomica la haran una plataforma ideal para abordar el problema de las familias, proporcionando una solucion a la dificultad de no tener conocimiento previo de un miembro promiscuo en la familia investigada. Respecto al problema de los miembros, se propone explorar variaciones en vecindad genomica, flujo genico y dinamica molecular, como candidatos a reflejar la variacion en promiscuidad. Finalmente, he detectado que a pesar de que pruebas *in vivo* son mas sensibles a niveles bajos de promiscuidad que mediciones *in vitro*, esta ultima suele ser la unica estudiada. *In vivo*, la metabolomica aplicada en genes biosinteticos de productos naturales ha ayudado en la identificacion de sustratos, por lo que esta tecnica podria ayudar a revelar el nuevo sustrato de una enzima en la que se sospecha ganancia de promiscuidad. En resumen, el objetivo de mi trabajo sera abordar los dos problemas de promiscuidad considerando la diferenciacion *in vitro* e *in vivo* tomando como modelo biologico el phylum Actinobacteria, un grupo de bacterias reconocido por su diversidad metabolica donde se ha probado la existencia de promiscuidad enzimatica.

0.1 Introduction

Para estudiar la promiscuidad es necesario contar con una definicion, algunos autores emplean el termino promiscuidad para describir actividades enzimaticas distintas a la funcion principal [4] otros lo ven como una actividad secundaria fortuita [5] que pudo aparecer de forma accidental o inducida artificialmente [6]. Otros mas, cuando una enzima puede operar sobre un amplio rango de sustratos, prefieren llamarla multiespecifica [4]. A la accion de realizar distintas funciones cataliticas, ya sea al catalizar varias reacciones quimicas o bien una misma reaccion en sustratos diferentes se le conoce como promiscuidad enzimatica [7]. Existen varios tipos de promiscuidad enzimatica.

Por sustrato cuando la reaccion es la misma pero se lleva a cabo en distintos sustratos ejemplo la familia PriA [8] y la familia de betalactamasas [9]

Catalitica cuando la enzima utiliza diferentes mecanismos de reaccion y/o residuos cataliticos, e.g. la quimotripsina puede catalizar reacciones de amidasa y fosfotriesterasa en un mismo sitio activo. [7] Por condiciones del entorno, cuando la enzima cambia su conformacion dependiendo de las condiciones quimicas y fisicas presentes como pH, temperatura, solventes organicos y salinidad e.g. algunas lipasas pueden actuar como sintetizadoras de esteres en lugar de hidrolasas en presencia de solventes organicos [6].

Este trabajo se enfocara a la promiscuidad por sustrato, entendiendo asi que la enzima es capaz de catalizar la misma reaccion quimica en al menos dos sustratos. La promiscuidad por sustrato es importante en terminos evolutivos, por ejemplo la enzyme commission number (EC) separa las enzimas en clases, a cada enzima se

asignan 4 digitos, los tres primeros corresponden a la reaccion y el ultimo al sustrato; el mayor numero de sustratos (4306 clases) que de reacciones quimicas (234 en el tercer nivel) sugiere que la mayor variacion evolutiva se da a nivel de sustrato y no de reaccion [11]. Otra evidencia de la importancia de la multiespecificidad por sustrato esta en el descubrimiento de las superfamilias, enzimas mecanistica y estructuralmente relacionadas que divergen en su afinidad por sustrato [12]

Si bien existen familias de enzimas con alta especificidad por sustrato, otras familias como el citocromo P450 [14] y las beta lactamasas [16] son promiscuas. Es posible que la vision previa de alta especificidad se deba a que las primeras rutas metabolicas estudiadas pertenecen al metabolismo central, donde la especificidad puede haber sido favorecida por presiones de seleccion [17]. Esta vision ha cambiado debido al conocimiento de mas enzimas con multifuncionalidad [18], sin afectar la eficiencia catalitica por la funcion primaria [19]. En 1976 el interes por la promiscuidad comenzó por su influencia en la evolucion de la funcion enzimática[20], las aproximaciones variaron desde la aparicion de la sintesis funcional [22], cuando la disponibilidad de genomas permitio la combinacion de analisis filogeneticos con tecnicas de biologia molecular, bioquimica y biofisica (Fig 1). En 2003 la biofisica de las proteinas entra en escena al postularse que la diversidad conformacional durante la dinamica molecular debe incidir en la aceptacion de distintos sustratos. Recientemente se ha investigado su papel en efectos secundarios en drogas farmacologicas [23]. Entre 2005 y 2010 se avanza del estudio de una sola familia enzimática hacia el interes por propiedades globales, por ejemplo dado un genoma se investiga la distribucion de familias promiscuas en subsistemas metabolicos. En estos años, surge el desarrollo de indices que reflejen las caracteristicas bioquimicas de enzimas promiscuas. En 2010, comienzan los intentos por desarrollar un metodo computacional de predicción de promiscuidad. Desde 2012 a la fecha, a la par que las aproximaciones bioinformaticas se multiplican, se desarrollan investigaciones de aspectos biofisicos, bioquimicos y evolutivos de enzimas promiscuas reafirmando que todos estos aspectos estan relacionados al fenomeno. En las siguientes secciones se describiran trabajos importantes sobre la relacion que guarda la promiscuidad con expansiones genomicas y flexibilidad molecular. Ademas se hablara sobre analisis bioquimicos y metabolicos para la descripcion del fenomeno.

TeX or L^AT_EX

###Funcion biologica de la promiscuidad enzimática

¿Por que existe la promiscuidad enzimática? Se tiene evidencia de dos papeles biologicos: el primero proporcionar robustez a la red metabolica de un organismo mediante redundancia de reacciones de otras enzimas; el segundo permitir plasticidad evolutiva, es decir materia prima para la adaptacion a variaciones ambientales [19] mediante la adquisicion de nuevas funciones quimicas. Respecto a la robustez, se probó que sobreexpresar enzimas promiscuas puede rescatar perdidas genicas [30]. De 104 knockout sencillos de genes esenciales para *E. coli* K-12, 20% de las auxotrofias pudieron ser suprimidas por la sobreexpresión de plasmidos que contenian enzimas promiscuas. Otro ejemplo que aporta a la robustez es PriA, enzima de la ruta de histidina que realiza en la ruta del triptofano la reaccion E.C. 5.3.1.24 [8]. En cuanto a la plasticidad se propone que para que la promiscuidad pueda dar origen a la aparicion de nuevas

funciones la actividad promiscua debe proveer una ventaja fisiologica inmediata para poder ser seleccionada positivamente, ademas una vez que una funcion promiscua se vuelva relevante se debe poder mejorar mediante pocas mutaciones derivando en el intercambio entre la actividad promiscua y la principal[4].

Aun cuando el producto de la promiscuidad genera metabolitos que no se integran al metabolismo central de la celula, su efecto es positivo ya que estos metabolitos podrian colaborar a la adaptacion al entorno participando por ejemplo en una relacion de simbiosis o de competencia con otros organismos. Este tipo de metabolitos, por lo general, no son dañinos [31] y pueden servir como bloques de construccion para vias metabolicas nuevas [34]. La respuesta inmediata de adaptacion de un organismo podria ser una consecuencia de su grado de promiscuidad.

0.1.1 Relacion del pangenoma con la promiscuidad enzimatica

El core genome de un grupo taxonomico es el conjunto de secuencias codificantes presentes en todos los organismos del grupo. En el Dominio Bacteria el core esta estimado entre 200 y 300 secuencias [37]. Dada su conservacion el core genome puede utilizarse para trazar mejores relaciones filogeneticas que las obtenidas con el uso exclusivo de marcadores como la subunidad 16s del RNA ribosomal o el gen rpoB. El pangenoma es el conjunto complemento del core genome, es decir todas aquellas secuencias que estan ausentes de uno o mas organismos del grupo y por lo tanto no son necesarias para todos, sino solo posiblemente para el organismo que las posee. Como en el pangenoma la presion de seleccion esta relajada respecto al core-genome [17] es el conjunto donde la plasticidad genomica tiene facilidades para desarrollarse.

Esta idea puede restringirse a subsistemas metabolicos para identificar genes cuyas enzimas estan en proceso de cambio de funcion quimica, por ejemplo, en este trabajo se encontro que el gen *trpF* esta presente en solo 49 de 290 genomas analizados del genero Streptomyces por lo que se encuentra en el pangenoma de triptofano de este genero taxonomico, posiblemente adquiriendo una nueva funcion [34]. Para evitar problemas tecnicos del calculo del pangenoma existen otros modelos de medicion de variabilidad del genomica entre especies bacterianas [38].

0.1.2 Expansion y contextos genomicos como herramienta de anotacion funcional

La diversidad enzimática existente es el resultado de un proceso de expansion, mutacion y seleccion que se ha desarrollado durante el transcurso de la historia evolutiva [4]. Existe evidencia de que cierto grado de promiscuidad o divergencia funcional precede a la duplicacion genica [40]. Por este motivo detectar expansiones ya sea duplicaciones o transferencias horizontales [41], puede ser un buen punto de partida para determinar

divergencia funcional y promiscuidad. No todas las expansiones denotan cambio de funcion enzimatica, algunas pueden ser meros accidentes, sin embargo dado que la funcion de una enzima suele estar relacionada con sus vecinos [42], una expansion en una vecindad genomica diferente de la tradicional sera un referente de adquisicion de una nueva funcion y entonces un indicador de existencia previa de promiscuidad.

La funcion de una enzima es un concepto jerarquico, dependiente de la filogenia de un organismo [46]. Para sistematizar el estudio de contextos y vecindades genomicas se desarrollo Search Tool for the Retrieval of Interacting Genes/Proteins STRING [47], que cuenta con una anotacion de ortologia jerarquica y consistente, realizada en 2000 organismos en cuyo marco interacciones de proteinas con implicaciones funcionales son predichas tanto de novo por informacion genomica de co-ocurrencia como por mineria de datos en articulos publicados. STRING es una base de datos, y como tal no permite agregar nuevos genomas para su analisis. Sus 2000 organismos incluyen especies tanto bacterianas como eucariotas. Al existir tanta diversidad, los genomas disponibles para un genero o clase especificos son escasos, p. g. de los mas de 300 genomas disponibles de Streptomyces solo 24 estan incluidos.

Para resolver la baja cobertura de STRING hacia ciertos grupos taxonomicos se pueden desarrollar scripts de vecindad genomica utilizando RAST (Rapid Annotation using Subsystem Technology); un servicio interactivo de anotacion automatica de genomas de bacterias y arqueas [48] donde la funcion de cada gen se asigna de acuerdo a conocimiento previo de subsecuencias de organismos cercanos filogeneticamente, cuando es posible se incluye en un subsistema metabolico. Estamos en una era de explosion de datos genomicos, proximamente se espera contar con millones de genomas bacterianos incluso provenientes de bacterias no cultivables, por ello los algoritmos deben ser constantemente optimizados a los nuevos volumenes de datos [50]. Ante esta expectativa seria muy util desarrollar algoritmos de analisis genomico que sean de codigo libre o al menos interactivos para que cada laboratorio pueda personalizarlos para sus propios genomas.

Finalmente, no solo la vecindad genomica inmediata puede ser utilizada como distinutivo en la busqueda de promiscuidad, diferencias en el contexto genomico en genes relacionados con una enzima promiscua, sin importar su ubicacion dentro del genoma tambien pueden ser relevantes para la perdida o ganancia de funcion quimica [51], (Juarez Vazquez et al 2015).

0.1.3 Modelos bioinformaticos de promiscuidad

Con el fin de reducir la inversion en el proceso de experimentacion, se han implementado en los ultimos años algoritmos computacionales para predecir promiscuidad enzimatica [52]. Estos procedimientos cuentan con un conjunto de aprendizaje, unos descriptores del conjunto, una fase de ajuste de parametros y finalmente una prediccion. En 2010, Carbonell propone un algoritmo de soporte vectorial basado en subsecuencias de distinto tamaño que llama huellas moleculares. En este trabajo aplicado sobre 500,000

proteinas reportadas en la enciclopedia de Kyoto de genes y genomas (KEGG) se reporta 85% de exito en detección de enzimas promiscuas anotadas en KEGG. En 2012, Cheng compara los métodos de random forest y soporte vectorial en 6799 proteínas provenientes de la base de datos Universal Protein Resource (UniProt). Las enzimas son descritas con subsecuencias de aminoácidos incorporando además características biofísicas como polaridad. Se utiliza como grupo de control a familias de enzimas donde nunca se ha reportado una enzima promiscua.

Un aspecto no considerado en estos métodos es que hay familias de enzimas con alta identidad de secuencia entre sus miembros, con cambios bruscos en promiscuidad, debidos por ejemplo a la dinámica genómica [51], lo que dificulta que considerar solo la secuencia lleve a buenos predictores de promiscuidad. Cuando se obtiene una predicción positiva utilizando los modelos existentes, lo que significa es que dada esa secuencia, en su familia se conoce previamente un elemento promiscuo y que además sus subsecuencias de cierto tamaño son suficientemente similares. Estos enfoques no pueden predecir de novo, en familias donde la promiscuidad no ha sido previamente detectada experimentalmente, pues no consideran aspectos evolutivos ni mecanísticos de las enzimas.

Otra limitante a los enfoques descritos es que mezclan en su conjunto de entrenamiento fenómenos distintos de promiscuidad. Cheng p. g. incluye enzimas moonlight que si bien poseen funciones adicionales a la catalización, son distantes a las enzimas promiscuas [5]. Además en ambos casos mezclan en el mismo conjunto enzimas bacterianas y eucariotas, con lo que si existía una huella basada en secuencia entonces esta puede diluirse por la gran distancia taxonómica entre estos grupos (Tabla 1).

0.1.4 Promiscuidad *in vitro* y promiscuidad *in vivo*

La ganancia de promiscuidad no solo puede entenderse como la capacidad de convertir más sustratos [52], sino también como la mejora de la capacidad catalítica respecto a ellos. El I-index [15], está definido como un rango de valores entre 0 y 1 que tiende a 1 entre más parecida sea la actividad de la enzima sobre distintos sustratos, la capacidad catalítica es medida en términos del cociente de Michaelis - Menten $\frac{K_{cat}}{K_m}$. El índice ha sido utilizado para predecir la afinidad por sustrato del citocromo P450 [25]. Una limitante del índice *I* es que se deben conocer los sustratos a los que la enzima es afin; sin embargo se puede sospechar que una enzima ha ganado promiscuidad aun sin conocer sus potenciales sustratos. Otro punto a señalar es que las variables *K_{cat}*, *K_m* son mediciones realizadas *in vitro* y no se consideran todos los sustratos presentes *in vivo*. Para solventar esta dificultad e investigar variaciones de sustratos nativos se pueden buscar productos similares a los ya conocidos por medio de análisis metabólicos [57] como los empleados en la detección de rutas no conservadas en la biosíntesis de productos naturales [50]. En particular para este fin se ha utilizado espectrometría de masas MS/MS, [57] combinada con molecular networking para identificar productos similares [59]

0.1.5 El papel de la dinamica molecular en la promiscuidad

La estructura tridimensional de una proteina es obtenida mediante previa purificacion y cristalizacion. Aunque mucho se ha hablado de la relacion estructura funcion, al cristalizar se obtienen estados conformacionales homogeneos, que bien pueden no ser la unica conformacion que adopta la proteina en solucion. [61]. En particular en el problema de promiscuidad, se ha observado que la variacion funcional no queda obviamente reflejada en la variacion estructural, lo que sugiere un rol significativo para la dinamica molecular [62]. Se postula que un aspecto de la dinamica molecular relevante para la diversificacion de especificidad por sustrato es el numero de conformeros [63]. Por ejemplo, en la actinobacteria *Corynebacterium diphtheriae* parece que el contexto genomico correlaciona con perdida de promiscuidad de PriA ya que al poseer el genoma una copia de *trpF*, la enzima perdió esta funcion quimica conservando solo la funcion EC 5.3.1.16 correspondiente a la ruta de histidina. Esta sub-funcionalizacion se refleja en la perdida de estados conformacionales cambiando desde 1 estado en *C. diphtheriae* hasta 4 presentes en la dinamica de PriA de *M. tuberculosis* [51].

Las regiones rígidas de una enzima proporcionan orientacion adecuada con respecto a los grupos cataliticos, mientras que las regiones flexibles permiten al sitio activo adaptarse a los sustratos con diferentes formas y tamaños [5]. Esta consideracion sugiere que la flexibilidad del sitio activo es otra caracteristica de la dinamica molecular a considerar para obtener informacion de la capacidad de ligacion de una enzima a distintos sustratos [64]. Recientemente el indice de flexibilidad dinamica (dfi) se utilizo como una medida cuantitativa basado en la respuesta a perturbaciones de aminoacidos (PRS). Este indice se incremento en regiones cercanas al sitio activo de beta lactamasas promiscuas respecto al correspondiente dfi de β -lactamasas especialistas existentes [16].

0.1.6 Modelo biologico diversidad de Actinobacteria

Al escoger un conjunto acotado para investigar familias de enzimas promiscuas se debe recordar que la funcionalidad es jerarquica por lo que para mejorar la anotacion, es deseable reflejar el proceso evolutivo y restringirse a un grupo de organismos taxonomicamente relacionados [65]. Actinobacteria es un phylum que posee promiscuidad tanto en el metabolismo periferico como en el core metabolico. Entre datos publicos (NCBI) y privados estan disponibles alrededor de 1200 genomas no redundantes de especies de Actinobacteria. Como punto de partida, se han estudiado las relaciones filogeneticas y grupos de ortologia [66], en particular en Actinobacteria para identificar relaciones entre las familias del phylum, se obtuvieron arboles multilocus de entre 100 y 157 genomas [68]. Estos estudios sugieren como separar los genomas disponibles para hacer el calculo de grupos de ortologia. Finalmente, se han realizado estudios de plasticidad genomica en *Streptomyces* considerando 5 y 17 organismos de los 300

genomas disponibles en la actualidad [70] donde reportan 2,018 familias en el core genome y 32,574 en el pangenoma.

0.1.7 Modelo metabolico biosintesis de aminoacidos.

Al hacer el calculo vemos que Streptomyces, un genero del phylum Actinobacteria cuenta en su genoma con un promedio de 8316 secuencias codificantes segun la especie. Gran parte de estas secuencias pueden ser agrupadas en subsistemas metabolicos como metabolismo de carbohidratos o de lipidos; de estos subsistemas uno de los mas amplios es el metabolismo de aminoacidos con entre 429 y 910 secuencias segun el organismo. La sintesis de aminoacidos es un subsistema presente en todas las especies pero con suficientes variaciones que permiten hacer observaciones evolutivas. En un gran numero de Actinobacterias las rutas de histidina y triptofano de 7 y 11 pasos respectivamente convergen en una enzima bifuncional llamada PriA, que realiza tanto la funcion de HisA como la de TrpF [8]. La cantidad de familias en el subsistema de metabolismo de aminoacidos, su variabilidad, su conservacion entre distintos grupos taxonomicos y la existencia de estos ejemplos en Actinobacteria lo posicionan como un buen punto de partida para la busqueda de promiscuidad tanto de familias promiscuas como de miembros promiscuos de las mismas.

0.2 Antecedentes

En las cuatro decadas de estudio de la promiscuidad enzimatica, hemos aprendido que es un fenomeno distribuido en distintos subsistemas metabolicos [72] y que su existencia puede deberse tanto al desarrollo de nuevas funciones para fines adaptativos [20], como al rescate de una funcion perdida [30]. Por ello la dinamica de perdida y ganancia de genes asociada al contexto genomico en bacterias se relaciona con cambio en la funcion enzimatica [44]. Precisando, respecto a la ganancia de genes, se postula que la bifuncionalidad precede la duplicacion [40]. Lo que implica que dada una duplicacion muy posiblemente previamente la promiscuidad estuvo presente [74].

Se han desarrollado tecnicas bioquimicas y metabolicas de medicion [15], asi como algoritmos computacionales de predicción de promiscuidad [52]. Un aspecto a mejorar dentro del modelado es la restriccion del conjunto de estudio a un grupo taxonomico tan reducido que exista congruencia en las familias de ortologia y a la vez tan amplio que permita observar efectos evolutivos; el phylum Actinobacteria ha probado tener ejemplos de promiscuidad. Si bien la secuencia no ha sido suficiente para la correcta predicción de promiscuidad [45], es posible que dentro de las tecnicas computacionales la flexibilidad durante la dinamica molecular este correlacionada con la promiscuidad de los miembros de una familia [61].

0.2.1 Modelo biológico

De los mas de mil genomas actualmente disponibles de Actinobacterias, se seleccionaron 888 (correspondientes a 49 familias), que no estan excesivamente fragmentados; es decir con un estimado de al menos 5 genes por contig (Tabla 2). Estos genomas fueron divididos en tres grupos (http://pubseed.theseed.org/wc.cgi?request=show_otus&base=/homes/nselem/Data/CS), uno de ellos correspondiente a Streptomycetaceae, la familia con la mayor cantidad de genomas disponibles; los otros dos grupos siguieron la taxonomia propuesta por Gao & Gupta en 2012. En el grupo de 290 genomas de Streptomycetaceae 2,126,832 ORFS fueron clasificados en 288,390 familias; de las 919,292 ORF del grupo I de Actinobacteria resultaron 269,406 familias. Las relaciones taxonomicas fueron corroboradas con algoritmos propios basados en best bidirectional hits (BBH).

0.2.2 Subsistemas metabólicos

Los operones his y trp de histidina [76] y triptofano [77] respectivamente, participantes del metabolismo de aminoacidos estan ampliamente distribuidos en los organismos bacterianos. En Actinobacteria la familia promiscua PriA participa en ambas rutas biosinteticas, para su estudio se han generado datos bioquimicos, genomicos y estructurales (Tabla 3). En bacterias gram negativas estan presentes los operones his y trp y en lugar de PriA su familia homologa HisA. PriA comprende un conjunto de subfamilias en Actinobacteria. En Streptomyces, el gen trpF se desplaza de la vecindad genomica de trp, con lo que el homologo de hisA gana promiscuidad aunque con baja actividad de TrpF, a esta subfamilia se le llama PriB [78]. En otras Actinobacterias trpF se pierde totalmente y la familia homologa de HisA, se vuelve promiscua [8] realizando tanto la funcion quimica correspondiente a HisA como la de TrpF. Finalmente en la familia subHisA se pierde la funcion TrpF debido posiblemente a la ganancia del operon trp completo [51] y en la familia subtrpF se conserva solo a la funcion TrpF debido a la perdida del operon his [Juarez vazquez et al 2015 in prep]. Existen al menos 43 familias de Actinobacteria sin explorar respecto a la funcionalidad de PriA.

0.2.3 Contexto y vecindades genomicas

En 2012 fueron analizados 102 genomas de 29 familias de Actinobacteria [79]. sugiriendo que al menos en Corynebacteria el contexto y la vecindad genomica incidian en la sub-funcionalizacion de PriA en subHisA [51]. Respecto a IlvC, otra familia involucrada en la sintesis de aminoacidos fue estudiada y caracterizada bioquimicamente en 1 Corynebacterium y 8 Streptomyces [45]. Para ampliar estos resultados, utilizando la anotacion de RAST y una generalizacion de la definicion de vecindad de STRING, se diseño un algoritmo para identificar vecindades similares asi como

uno de visualizacion de contexto, ambos disponibles como software libre en [github nselem/perlas](#) .

El algoritmo de clasificacion de vecindades permite agruparlas en clusters y calificar estos clusters segun su conservacion dado un grupo de bacterias. La definicion de vecindad y similitud de vecindad esta descrita posteriormente en los metodos. El algoritmo fue aplicado a la familia IlvC en 290 Streptomyces resultando 9 clusters Datos entre los mas poblados el primero cuenta con 279 elementos, otro con 9 elemento y dos mas con 7 miembros (Fig 3), resultados experimentals son congruentes con que existe divergencia funcional entre miembros de clusters distintos [45]

0.2.4 Metodos bioinformaticos

Al evaluar PROMISE [52] en un set de datos de la familia HisA/PriA [55] obtuve que su mejor desempeño es con huella molecular de tamaño 6, donde clasifica correctamente casi todas las no promiscuas, (HisA) pero no sucede lo mismo con la familia PriA donde tiene exito en 16 de 45 casos. Al aplicar el mismo tamaño de huella a 9 miembros promiscuos de la familia IlvC no consigue predecir correctamente ninguno de ellos. Por lo menos para estas familias el conjunto de entrenamiento o los descriptores no son suficientes para la anotacion de promiscuidad.

0.2.5 Evomining

Evomining es una plataforma bioinformatica pensada para la identificacion de productos naturales que tiene entre sus exitos la identificacion de la biosintesis de arsenolipidos [65]. La busqueda de productos naturales cuenta entre sus premisas que estos se producen en vecindades genomicas llamadas clusters y que ademas clusters cercanos (ya sea en contenido genico o en la secuencia de sus componentes), exploran variaciones metabolicas, es decir sus enzimas catalizan reacciones sobre sustratos parecidos aunque no identicos [65]. La base de evomining es que las enzimas de metabolismo secundario son expansiones distantes de enzimas de rutas centrales, lo que da idea de la quimica que realizan dichas expansiones dejando por identificar el sustrato sobre el que trabajan. La primera version de evomining cuenta con 200 genomas de Actinobacteria, una base de datos de secuencias de enzimas de productos naturales y otra base de datos de secuencias de enzimas de rutas centrales curada a mano. Evomining esta ligada con el problema de la promiscuidad porque en estas familias expandidas ya sea por duplicacion o por transferencia horizontal, las expansiones pueden retener la funcion quimica de las rutas centrales y viceversa, la funcion quimica expandida suele estar presente antes de la duplicacion.

Si se combinara evomining con la premisa de que vecindades distintas son marcadoras de funciones quimicas distintas, al encontrar una familia expandida con vecindades genomicas diferentes se podria solventar la deficiencia de otros metodos bioinformaticos consistente en que para identificar familias promiscuas se debe conocer previamente

un miembro promiscuo de la misma. (Fig 4) Asi pues al combinar evomining con herramientas de vecindad genomica tanto de comparacion como de visualizacion estaremos mejorando su funcionalidad en la identificacion de familias promiscuas.

0.2.6 Caracterizacion in vivo

Algunas enzimas PriA no han mostrado promiscuidad in vitro pero si in vivo ya que sobreviven en un medio sin triptofano, es decir in vivo complementan la funcion trpF. Para la construccion de cepas de Streptomyces con variantes no nativas de priA minimizando la modificacion genomica y el efecto de sobreexpresion, se planea utilizar E. coli como intermediario para realizar seleccion por auxotrofia. Se cuenta con un conjunto de plasmidos para transformar a E. coli asi como con las mutantes sencillas de E. coli para trpF y hisA que permiten realizar seleccion por auxotrofias. Ademas tenemos una colección de cepas nativas de Streptomyces asi como un mutante de PriA de S. coelicolor. Se optimizo una reaccion de PCR para la amplificacion de un segmento de DNA de S. coelicolor que contiene a priA.

0.2.7 Caracterizacion bioquimica in vitro.

De la familia PriA y sus subfamilias se han caracterizado bioquimicamente miembros selectos de Actinomycetaceae, Bifidobacteriaceae, Micrococcaceae, Acidimicrobiaceae, Corynebacterium, Mycobacteriaceae, Streptomycetaceae, Camera (provenientes de metagenoma), reconstrucciones ancestrales, 80 mutantes de Corynebacterium, y 2 mutantes de Camera mediante cineticas enzimaticas para calcular las constantes Kcat,Km. El genero Streptomyces, el que cuenta con mayor cantidad de genomas disponibles representa una oportunidad muy poco explotada de explorar la influencia del contexto y la vecindad genomicas en secuencias de PriA (Tabla 3, Figura 5).

0.2.8 Modelado de dinamica molecular

La dinamica es un metodo que permite hacer simulaciones de particulas que sirve para obtener informacion de propiedades macroscopicas de un conjunto de atomos [80]. Es util en el marco de mi proyecto porque permite la exploracion del espacio conformacional, y se ha visto que este esta relacionado con la actividad de la enzima [82], ademas dado un conformero permite verificar su estabilidad. Resuelve la ecuacion de movimiento de Newton con base a una configuracion inicial, las fuerzas interatomicas como los enlaces covalentes, las fuerzas de Van der Waals y la carga de las particulas[58]. Entonces para generar una simulacion de dinamica molecular, debe contarse con una estructura como punto de partida, ya sea esta cristalografica o modelada de novo o por homologia. El laboratorio de bioinformatica y biofisica computacional ha desarrollado un protocolo de generacion de modelos homologos estructurales y dinamicas moleculares (Carrillo-Tripp et al 2015 in prep); con este pipeline se han

generado dos estructuras de Camera [55], 30 estructuras y dinamicas de miembros de Actinobacteriaceae y Bifidobacteriaceae (Vazquez-Juarez et al in prep.) y finalmente una estructura de subHisA de *Corynebacterium diphtheriae*. En la familia Streptomyces, interesante debido a su variacion en contexto genomico y en mediciones in vitro aun no se modelan dinamicas moleculares aunque 40 estructuras por homologia estan en proceso.

En un estudio de subHisA [79] se utilizo el metodo de dinamica molecular y se comparo el numero de conformeros entre miembros de subHisA y PriA, resultando mayor el de PriA como corresponde a una enzima promiscua. El estudio sobre la relacion dinamica-flexibilidad de β -lactamasas utiliza replica exchange, una variacion de dinamica molecular que corre replicas en paralelo a distintas temperaturas [83]. Una desventaja de este metodo es que por el costo computacional de las replicas agregar explicitamente otras moleculas a la simulacion como el solvente no es posible en tiempo razonable. Una vez generadas las dinamicas moleculares se procedera a calcular tanto el numero de conformeros como el indice de flexibilidad dsi [16]. Se esta desarrollando PEDB, promiscuous enzyme database, una base datos genomicos, evolutivos, bioquimicos y estructurales y de metabolismo de PriA en Actinobacteria donde se procedera al analisis de los mismos (<http://148.247.230.43/nselem/PHP/queries.html>).

En conclusion la promiscuidad enzimatica es un fenomeno complejo debido a multiples causas. Existe una gran variedad de estudios con enfoques puntuales sobre aspectos estructurales, dinamicos y evolutivos de familias de enzimas promiscuas, sin embargo hasta ahora no se han reportado trabajos multidisciplinarios que involucren a todas las partes involucradas (Fig 6)

0.3 Objetivo General

Estudiar el fenomeno de promiscuidad enzimatica tanto desarrollando estrategias para identificar familias promiscuas dentro de un grupo taxonomico, como comparando variaciones de promiscuidad in vitro e in vivo con variaciones en contexto genomico y flexibilidad en miembros de una familia. (Figura 7)

0.4 Objetivos particulares

Mejorar evomining como metodo de identificacion de familias enzimaticas promiscuas aprovechando los cambios en vecindades genomicas como caracteristicas informativas provenientes de datos filogenomicos. Estudiar la relacion entre historias filogenomicas y procesos biofisicos con la promiscuidad in vitro, a traves de mediciones de ciertas caracteristicas de la familia PriA. Caracterizar cambios de promiscuidad enzimatica in vivo mediante perfiles metabolomicos de actividades de PriA y enzimas asociadas.

0.5 Estrategias

0.5.1 La promiscuidad en familias enzimaticas.

Mejorar Evomining mediante la identificacion de cambios de vecindad genomica en familias selectas de metabolismo central convirtiendola en una plataforma de codigo libre disponible para otros investigadores.

Obtener informacion genomica del phylum Actinobacteria.

Colectar genomas de Actinobacteria de NCBI y de colecciones privadas.

Anotar consistentemente las secuencias codificantes de estos genomas.

Utilizar un anotador automatizado y desarrollar los scripts necesarios para anotar los genomas.

Establecer las relaciones filogeneticas de los genomas colectados.

Mediante el uso del core genome construir un arbol filogenomico que permita establecer un marco sobre el cual hablar de cambio y que facilite reclasificar los genomas mal nombrados.

Identificar cambios en la vecindad genomica en familias selectas de enzimas de metabolismo central. Clasificar sistematicamente las secuencias de familias codificantes segun su similitud en familias enzimaticas.

Desarrollar las herramientas bioinformaticas necesarias para separar clusters de vecindades genomicas.

Sistematizar Evomining para convertirla una plataforma descargable y utilizable en cualquier set de datos bacterianos relacionados taxonomicamente proporcionados por el usuario.

Ampliar el contenido de Evomining al integrar los genomas colectados de Actinobacteria. Sistematizar la base de datos de metabolismo central.

Desarrollar la visualizacion e integrar la clasificacion de vecindades genomicas como una herramienta adicional en la busqueda de promiscuidad.

Promiscuidad in vitro dentro de miembros de una familia promiscua de enzimas.

Dados los sustratos conocidos de PriA investigar las posibles correlaciones entre mediciones de constantes cataliticas, contexto genomico, vecindad genomica, numero de conformeros e indice de flexibilidad.

Seleccionar miembros homologos de la familia de enzimas.

Se escogieron 41 Streptomyces repartidos en un arbol de rpoB de 400 Streptomyces con genoma disponible. Esta seleccion incluye los seis Streptomyces de los que se

cuenta con cinetica enzimatica de PriA, tres de ellos con estructura cristalografica.
####Medir cineticas enzimaticas, contexto genomico, vecindad genomica, flexibilidad y numero de conformeros.

Determinar la pertenencia a uno de cuatro posibles contextos genomicos respecto al gen trpF. Estudiar la existencia de distintas vecindades genomicas. Determinar la cinetica enzimatica de 9 enzimas mas buscando variabilidad en contexto genomico (sugeridas en la tabla 4). Obtener mediante una colaboracion 37 modelos estructurales por homologia y modelar dinamica molecular.

La siguiente tabla contiene la diversidad de contextos y vecindades genomicas de 41 Streptomyces respecto al gen trpF.

Determinar posibles correlaciones entre los datos producidos.

Numero de conformeros e indice de promiscuidad.

indice de flexibilidad y numero de conformeros.

Numero de conformeros y contexto genomico.

indice de flexibilidad y contexto genomico.

Contexto genomico e indice de promiscuidad I.

Analizar las vecindades genomicas e indice de promiscuidad I.

0.5.2 Desarrollar una metodologia para la deteccion in vivo de promiscuidad enzimatica.

Debido a cambios en flexibilidad o cambios de contexto genomico, se puede sospechar de diferencias en la funcion quimica de dos miembros de una familia de enzimas, sin conocer las diferencias a nivel de sustratos. Para investigar estos cambio in vivo se propone estudiar diferencias en perfiles metabolomicos de una colección de cepas en condiciones diversas.

Crear cepas geneticamente modificadas con variantes funcionales no nativas de PriA y enzimas asociadas.

Dado un organismo modelo sustituir su homologo nativo de priA por una variante no nativa ya sea de priA o trpF de Actinobacterias selectas de las que se sospecha cambio en promiscuidad.

####Separar posibles productos y minimizar los falsos positivos debidos a perturbaciones metabolicas no relacionadas a PriA.

Separar los metabolitos mediante cromatografia dirigida por tamaño. Obtener un espectro de masas antes y despues de la sustitucion de la variante y sobre las diferencias en el espectro realizar espectrometria de masas en tandem (MS/MS) es decir refragmentar y analizar que los fragmentos contengan partes parecidas a los sustratos conocidos.

0.6 Metodologia

A continuacion describire la metodologia para cada una de las estrategias expuestas previamente. Todos los scripts desarrollados fueron escritos en perl y estan disponibles en github <https://github.com/nselem/perlas>.

0.6.1 La promiscuidad en familias enzimaticas.

Actinobacteria genomic

Para obtener informacion genomica del phylum Actinobacteria mediante la colección de genomas de NCBI se revisaron todas las familias de Actinobacteria de la base genoma de NCBI y se seleccionaron los genomas con minimo 5 genes por contig. Se crearon scripts para utilizar la interfaz e-utils de NCBI y descargar estos genomas desde la terminal a partir de una lista de identificadores.

Annotation

Para anotar consistentemente las secuencias codificantes de estos genomas se utilizo el anotador automatizado RAST y se desarrollaron los scripts necesarios para anotar los genomas desde la terminal, conectado asi NCBI y RAST.

Genomic DB phylogeny

Establecer las relaciones filogeneticas de los genomas colectados. Mediante el uso del core genome para construir un arbol filogenomico, para reclasificar los genomas mal nombrados.

Para obtener el core genome y en base a el reclasificar los genomas se diseño el algoritmo estrellas basado en Best Bidirectional Hits (blast all vs all).

Estrellas. Se realiza un blast all vs all de genomas deseados. Para cada secuencia, centrado en cada genoma se realiza una lista (estrella) de sus mejores hits bidireccionales. Si las listas de todos los genomas coinciden es un BBH multiple y se agrega la lista al core genome. (Fig 9) Una vez con el core genome completo se puede reconstruir la filogenia. Este metodo fue exitoso en la detección de una familia marcadora de *Clavibacter michiganensis* (2014 Rodriguez-Orduña in prep).

0.6.2 Identificar cambios en la vecindad genomica en familias selectas de enzimas de metabolismo central.

Clasificar sistematicamente las secuencias de familias codificantes segun su similitud en familias enzimaticas.

Como se menciono en los antecedentes, se han separado 888 genomas de Actinobacteria en 3 grupos taxonomicos utilizando para la anotacion la tecnologia de subsistemas de RAST. Para la separacion en familias iso funcionales (ortologos, paralogos y expansiones) no se utilizo RAST, especificamente el script What Changed (WC) que asigna un numero a cada familia, esta herramienta esta basada en k-mers, su codigo esta disponible en github: (https://github.com/kbase/kbseed/blob/master/service-scripts/svr_CS.pl). Ademas de en los tres grupos ya mencionados, tambien se realizara una clasificacion para trescientos genomas de Actinobacteria distribuidos en todas sus familias taxonomicas.

Para desarrollar las herramientas bioinformaticas necesarias para separar clusters de vecindades genomicas a continuacion se describe detalladamente como se definio vecindad genomica y la relacion implementada de similitud.

1. Un conjunto expandido es un conjunto que contiene secuencias homologas asi como sus expansiones: paralogos y transferencias horizontales. Dado un conjunto de genomas, se pueden calcular y enumerar todos sus contextos extendidos utilizando WC.
2. Un PEG es un elemento de un conjunto expandido. Dado un PEG p, se define $CE(p)$ el numero del conjunto expandido de p, como el numero asignado por WC al conjunto expandido a que p pertenece.
3. La vecindad de un PEG es el conjunto de PEGs cercanos a el. Dado un umbral en terminos de distancia de pares de bases entre puntos medios para precisar la definicion de cercano, se pueden calcular todos los contextos de un genoma.
4. Una vecindad A es n-similar a otra vecindad B si $C = \{aA \mid bB, CE(b) = CE(a)\}$ tiene al menos cardinalidad n. Es decir si existen al menos n elementos de A que pertenecen al mismo conjunto expandido que algun elemento de B.
5. Un conjunto de vecindades es un conjunto de PEGs clusterizado segun la relacion n-similaridad. Si A es n-similar a B y B es n-similar a C entonces, aun si A no fuese n-similar a C, los PEGs generadores de A,B,C son agrupados dentro del mismoconjunto de vecindades.
6. Un cluster es un conjunto de conjunto de vecindades.
7. Los clusters son evaluados segun el numero y la cardinalidad de sus conjuntos de vecindades.

Sea Cl un cluster, donde CC_i es un conjunto de contextos y n_i es la cardinalidad de CC_i $Cl = \{CC_1, CC_2, \dots, CC_k\}$

Sean M la cardinalidad maxima de un conjunto de contextos y m la cardinalidad maxima sin considerar M.

$\#\$ \$ \quad M \neq \max\{ni\} \quad i \neq \{1, 2, \dots, k\}$

$m \neq \max ni \quad i \neq \{1, 2, \dots, k\} \quad ni \neq M$

$$\sum_{j=1}^n (\delta\theta_j)^2 \leq \frac{\beta_i^2}{\delta_i^2 + \rho_i^2} \left[2\rho_i^2 + \frac{\delta_i^2 \beta_i^2}{\delta_i^2 + \rho_i^2} \right] \equiv \omega_i^2$$

M representa el contexto mas difundido de la enzima, dentro del grupo taxonomico considerado; mes relevante porque si m es grande significa que hay un segundo contexto genomico conservado en dicho grupo taxonomico, y entonces posiblemente una ganancia de funcion.

La evaluacion de Cl esta dada por una combinacion lineal de k,m y M
 $S(Cl) = f(k, m, M) = c_1k + c_2m + c_3M$

Este algoritmo se puede mejorar considerando la orientacion de los genes del cluster asi como clusters de los vecinos.

Organizar y presentar los datos en una plataforma.

Para contribuir al desarrollo de la plataforma Evomining se desarrollaran scripts de visualizacion de arboles filogeneticos y contextos genomicos.

Para facilitar el analisis visual de una vecindad genomica ya la vez generar imagenes de alta calidad facilmente exportables para su uso en publicaciones, se desarrollaran scripts de visualizacion que utilizaran el formato Scalable Vector Graphics (SVG), dicho formato es basicamente un archivo de texto XML que contiene instrucciones para que el navegador realice un dibujo (W3school/SVG 2015). Al ser vectores, las imagenes generadas en SVG no pierden resolucion al ser escaladas y justamente por ser escalables permiten explorar con detalle grandes cantidades de datos organizados por ejemplo en arboles filogeneticos. Los scripts a desarrollar extraeran para cada gen informacion necesaria como coordenadas, direccion, funcion quimica, etc, proveniente de la anotacion de RAST y de los scripts de comparacion de vecindades genomicas. La primera version de evomining fue desarrollada en el lenguaje perl; este lenguaje cuenta con un modulo para facilitar la elaboracion de SVG (perlmaven/SVG 2015) por lo que al utilizar SVG no se agregan nuevos requerimientos a su desarrollo y se facilita su portabilidad.

Se amplificara Evomining de los 200 genomas con que contaba su version inicial a los 880 colectados mudando la curacion manual de su base de datos de rutas centrales a la anotacion por subsistemas de RAST. Finalmente se presentara la variacion en vecindades genomicos como una herramienta adicional que ayude en la busqueda de promiscuidad en familias de enzimas pertenecientes al metabolismo central.

0.6.3 Promiscuidad in vitro

Datos cineticos:

En todos los ensayos enzimaticos se busca medir una señal que permita una distincion clara entre sustrato y producto [84]. La cinetica enzimatica de PriA proveniente del genero Streptomyces sera determinada como ya se ha reportado previamente, mediante el monitoreo de cambios en fluorescencia (isomerizacion del sustrato PRA) o en absorbancia (isomerizacion del sustrato PROFAR). En el caso de la isomerizacion de PRA, debido a que contiene un anillo de antranilato, la fluorescencia del sustrato PRA es 50 veces mayor que la del producto 1-(2-carboxyphenylamino)-1-deoxy-D-ribulose 5-phosphate (CdRP) por lo que se utiliza la disminucion en fluorescencia como medida de la conversion del sustrato en producto [85]. Se mandaran sintetizar estas variantes para posteriormente sobre expresarlas en E. coli. Se creceran cepas modificadas de E. coli (W-, H-) en medio minimo M9 enriquecido con una mezcla de aminoacidos excepto L-histidina y L-triptofano y se seleccionaran por rescate de auxotrofia. Para obtener la enzima necesaria para los ensayos enzimaticos se utilizaran plasmidos disponibles para construcciones de sobreexpresion de proteina, despues de la produccion la enzima se purificara utilizando cromatografia por afinidad a niquel [78].

Finalmente se recopilaran datos cineticos de PriA tanto privados como los publicos reportados a la fecha en la BRAunschweig ENzyme Database BRENDA [86]. Una vez colectados los datos se anotaran en PEDB, nuestra base de datos ad hoc, y se tomara como medida de promiscuidad el I-index [15] que se define como: $I = \frac{1}{N} \sum_{i=1}^N \frac{1}{K_i} \text{cat Kim}_i / \text{cat Kim}_i$

Dinamica molecular

Para generar dinamicas moleculares primer lugar se recolectaran las estructuras tridimensionales de miembros de PriA de Actinobacteria. Despues se procedera a modelar por homologia las estructuras tridimensionales faltantes utilizando el pipeline del laboratorio de bioinformatica y biofisica computacional. Este pipeline utiliza el software Rosetta para el modelado para las estructuras y GROMACS Groningen Machine for Chemical Simulation, [87] para el modelado de la dinamica molecular. Esta parte del trabajo se realizara en colaboracion con el laboratorio de bioinformatica y biofisica computacional.

0.6.4 Promiscuidad in vivo

Se realizaran construcciones con variantes no nativas de priA y/o trpF en Streptomyces coelicolor. Para las construcciones se amplificara mediante PCR un fragmento alrededor de PriA que se insertara en un vector. Este vector recombinara en E. coli con un casete provisto de un gen marcador de resistencia a antibiotico y este gen recombinado

se pasara por conjugacion a *S. coelicolor* donde se espera que realice una doble recombinacion. El paso por *E. coli* es llevado a cabo porque *Streptomyces* no se puede transformar por electroporacion. Se seleccionaran las cepas de *Streptomyces* resistentes al antibiotico como prueba de que ya no poseen su priA nativa. Posteriormente, mediante un procedimiento analogo se sustituirá el gen marcador, por variantes no nativas de priA/trpF.

La cromatografia se refiere a un conjunto de metodos que separan y analizan mezclas de moléculas. Basicamente estos metodos se basan en diferencias en el tamaño, intercambio de iones y afinidad. [58] Posteriormente se combinan con espectrometria de masas que es una tecnica que mide el radio masa-carga de las partículas fragmentadas en iones. [58]. Los datos obtenidos de espectrometria de masas se procesaran utilizando redes moleculares, que consiste en agrupar los productos segun la similitud de sus partes. Plan: 3 replicas tecnicas, 2 replicas biologicas de 5 cepas.

0.6.5 Consideraciones

Falsos negativos respecto a promiscuidad estan muy extendidos en la literatura y en las bases de datos, en parte porque la mayoria de las funciones son asignadas por similitud de secuencia y dado un falso negativo el error se propaga en secuencias similares. Por otro lado es muy dificil demostrar un verdadero negativo a menos que se prueben todas las posibilidades de sustrato para la enzima. Sin embargo el espacio de sustratos puede acotarse gracias a tecnicas como el docking que esta intimamente relacionado con la dinamica molecular [58]. Limitar el espacio de sustratos puede retroalimentarse con el estudio de la promiscuidad in vivo y viceversa.

Con los metodos propuestos en este trabajo solo se podra detectar perdida o ganancia de promiscuidad entre enzimas de organismos respecto a otros miembros dentro un grupo taxonomico, no asi el estado de promiscuidad intrinseco a la enzima. Si dada una enzima no se detectan variaciones en contexto, vecindad genomica o flexibilidad dentro de un grupo taxonomico cercano, entonces no podemos decir en principio nada acerca de la promiscuidad de la variante, posiblemente es promiscua pero al mantenerse constante en todos los parametros descritos, con estos metodos no se puede sugerir promiscuidad. Es posible que al mirar en un grupo taxonomico mas amplio se detecte una neofuncionalizacion de la familia aunque tambien es posible que exista una variable z como la flexibilidad de sustrato [23] que no se este considerando y que explique o sea el mejor indicador para esta familia de promiscuidad enzimática.

Se debe considerar que si existe una correlacion vecindad genomica-promiscuidad, esta no indica causa efecto, mas bien, es plausible que la vecindad sea un amplificacion de diferencias en secuencia, a un numero igual de variaciones en secuencia la existencia de un cambio de vecindad indica un proceso mas largo y mas cambios, es una amplificacion de las marcas dejadas por transformaciones funcionales.

Si bien no se resuelve el problema de anotar promiscuidad automaticamente, este trabajo pretende aprovechar que los contextos genomicos ayudan a la identificacion de

familias promiscuas para mejorar una plataforma de productos naturales, pretende tambien una confirmacion de que los cambios en la dinamica molecular ayudan a identificar los miembros mas promiscuos hacia actividades recien adquiridas, asi como tambien ser pionero en la investigacion de promiscuidad in vivo.

- Gene cluster plants[89]
- Archaeal core [90]
- Natural products genomic era[91]
- Methanosarcina reconstruction [92]
- Archaea phylum[93]
- Prediction for possible products of promiscuous enzymes[???]
- Saxitoxin [94]
- Plants clusters [95]
- MiBIG [96]
- Metagenomics on Streptomyces [97]
- Sulfolobus reconstruction [98]
- Archaeal Natural products[99]
- Computational Pangenomics [100]
- Cuántos genes “obtenidos por EvoMining” son core/ cloud/stand alone
- Qué porcentaje de genes únicos recupera EvoMining
- Eucarya paralogs reshape gene clusters [101]
- Microbial dark mater [102]
- Archaea anaerobica carbon [103] Archaea Eucarya gap loki[104]
- Archaea and eucarya[105]
- BPGA [106] genes esenciales bacteria minima[107]
- Radical [108]
- RaxML large phylogenies [109]
- R phylogenies [110]
- Streptomyces exploradores [111]
- LUCA [112] Luchando por el reconocimiento de Archaea[113],[114] The primary kingdoms [115]
- Prediccion aRchaeas [116]
- RASt archaea [117] Book Archaea [118]
- Computational methods for bacterial and archaeal genomes [119]
- Archaeas boook [120]
- Bacterial /archaeal genome [121]
- Bacteria Archaea genome [122]
- Tree of life and HGC [123]
- Genomas retrospectiva 20 años [124]
- GC content plasmido genoma [125] Genoma minimo[126]
- Phylogeny R [127]
- Cyanobacteria fluctuacion genomica y adaptacion [128]
- Ecology of cyanobacterua [129]
- Histidine biosynthesis[130]
- PriA reconstruction [131]

Escala temporal bacterias [132]

Pangenome size [133]

variabilidad del 16s [134]

Chapter 1

EvoMining

1.1 Introduction

Enzyme promiscuity on metabolic families, can be looked on enzymes that are over a divergent process.

1.2 Gen families expansions on genomes

1.2.1 Pangenomes

Expansions are located on pangenome, Tools to analyse pangenome BPgA

1.3 EvoMining

EvoMining looks expansions on prokaryotic pangenome.
Biological idea.

EvoMining was available as a consult website with 230 members of the Actinobacteria phylum as genomic data base, 226 unclassified nBCCs, and not interchangeable central database 339 queries for nine pathways, including amino acid biosynthesis, glycolysis, pentose phosphate pathway, and tricarboxylic acids cycle. [65] EvoMining was proved on Actinobacteria Arseno-lipids

1.4 Pangenome

The sequenced genome of an individual in some species is just a partial print of the species genetic repertoire. Individuals can gain and loss genes.

[123] Pangenome is the total sequenced gene pool in a taxonomically related group. Supergenome all the possible extant genes. About 10 times genomes. There are open, closed pangenomes. Most genomes has a core a shell and a unique genes.

Gene history its a tree history

HGT doubles mutation rate on prokaryotes.

Maybe HGT is an selected feature, if is the case, so could be np production.

Some archaeas has open pangenome. [37]

HGT doubles mutation rate on prokaryotes. [123] Maybe HGT is an selected feature, if is the case, so could be np production.

Some archaeas has open pangenome. [37] Shell trees converge to core trees [108]

1.5 EvoMining Implementation

EvoMining was expanded from a website (<http://evodivmet.langebio.cinvestav.mx/EvoMining/index.html>) with limited datasets to an easy to install distribution that allows flexibility on genomic, central and natural product databases. Evomining user distribution was developed on perl on Ubuntu-14.04 but wrapped on Docker. Docker is a software containerization platform that allows repeatability regardless of the environment. Docker engine is available for Linux, Cloud, macOS 10.10.3 Yosemite or newer and even 64bit Windows 10.

Dependencies that were packaged at EvoMining docker app are Apache2, muscle3.8.31, newick-utils-1.6, quicktree, blast-2.2.30, Gblocks_Linux64_0.91b perl and from cpan CGI, SVG and Statistics::Basic modules.

Github defines itself as an online project hosting using Git. Its free for open source-code hosting and facilitates team work. Includes source-code browser, in-line editing, and wikis.

Dockerhub is an apps project hosting.

Dockerhub nselem

EvoMining code is open source and it is available at a github repository [github/EvoMining](https://github.com/EvoMining)

Github and Dockerhub can be connected by the use of repositories automatically built. Among the advantages of automated builds are that the DockerHub repository is automatically kept up-to-date with code changes on GitHub and that its Dockerfile is available to anyone with access to the Docker Hub repository. EvoMining is stored on

a DockerHub automated build repository linked to github EvoMining repository so that code is always actualized.

To download EvoMining image from docker Hub once Docker engine is installed its necessary to run the following command at a terminal:

```
docker pull nselem/newevomining
```

To run EvoMining container

```
docker run -i -t -v /home/nelly/docker-evomining:/var/www/html -p 80:80 evomining /bin/bash
```

To start evoMining app `perl startEvomining`

“ Detailed tutorial, EvoMining description, pipeline and user guide are available at a wiki on github at EvoMining wiki.

Other genomic apps were containerized to docker images during this work.

- *myRAST* docker- <https://github.com/nselem/myrast>

RAST is a bacterial and Archaeal genome annotator [48] This app allows myRAST functionality to upload

It allows EvoMining genome database annotation.

- *Orthocores* docker-<https://github.com/nselem/orthocore>

Helps to obtain genomic core paralog free and construct genomic trees

- *CORASON* docker-<https://github.com/nselem/EvoDivMet/wiki>

- *PseudoCore* github- <>

Genomic Core with a reference genome has the advantage of more genomes, but it is not paralog free

- *RadiCal* docker image

To detect core differences on a set of genomes

- *BPGA* to analize pangenome

EvoMining Dockerization was chosen to avoid future compatibility problems, for example dependencies unavailability, or incompatibility between future versions of its software components. As much as reproducible research was a concerned while developing EvoMining app, reproducibility is also important on data analysis, for that reason this document was written using R-markdown and latex template from Reed College [136]. While R-markdown allows to write and run R code and interpolate text paragraph to explain scripts and analysis.

1.6 EvoMining Databases

Evomining containerized app is a user-interactive genomic tool dedicated to the study of protein function.

1. Genomes DB
2. Natural Products DB

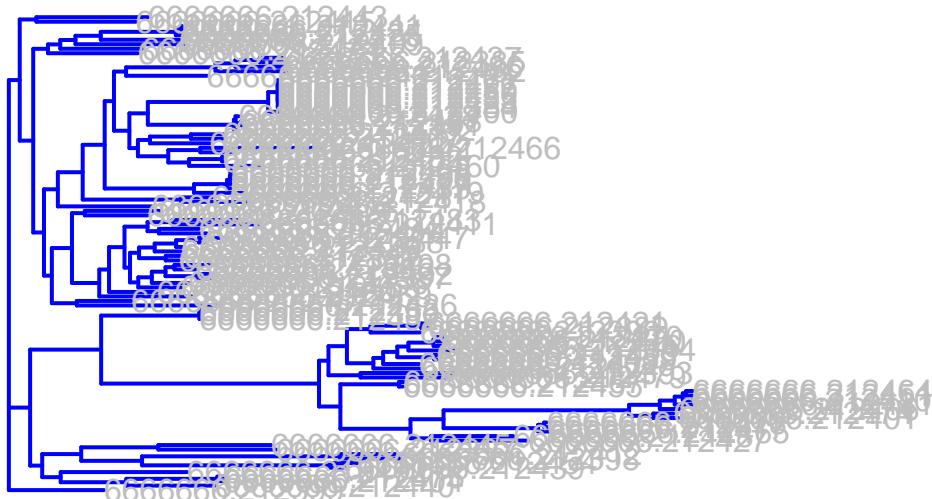
3. Central Pathways DB

Archaea, Actinobacteria, Cyanobacteria were used as genome DB, MIBiG was used as Natural Product DB and different Central Pathways were used.

Genome DB

RAST annotation of genomes was done.

Phylogeny



To capture differences on genomes we sort them phylogenetically. Phylogenies can be constructed using different paradigms as Parsimony, Maximum Likelihood, and Bayesian inference. Short descriptions of the main phylogeny methods are included below.

Why is a tree useful {Book reference} why trees are useful for?

* Distance methods

* Parsimony * Maximum Likelihood * Mr bayes

General Trees

Actinobacteria Tree, ArchaeaTree, CyanobacteriaTree.

It's easy to create a list. It can be unordered like

To create a sublist, just indent the values a bit (at least four spaces or a tab). (Here's one case where indentation is key!)

1. Item 1
2. Item 2
3. Item 3
 - Item 3a
 - Item 3b

Central DB

We chose central pathways from [137]

* BBH Best Bidirectional Hits with studied enzymes from Central Actinobacterial pathways were selected.

- By abundance
- By expansions on genomes

[largefiles,<https://help.github.com/articles/installing-git-large-file-storage/>]

1.7 Data Bases

1.7.1 Central pathways

Central database were chosen by BBH from -Actino

Corynebacterium glutamicum

242137 6666666.112876 Streptomyces coelicolor A3(2) NC_003888.3 1 8667507
2015-03-27

288055 6666666.146923 Mycobacterium tuberculosis H37Rv NC_000962.3 1
4411532

-Archaea closed

390224 6666666.211599 Methanosaerina acetivorans C2A C2A AE010299.1 1 5751492
SELECTED Euryarchaeota Methanomicrobia

390346 6666666.211718 Nanoarchaeum equitans Kin4-M - AE017199.1 1 490885 SE-
LECTED DPANN group Nanoarchaeota

390660 6666666.211909 Natronomonas pharaonis DSM 2160 Gabara CR936257.1 1
2595221 SELECTED Euryarchaeota Halobacteria

390189 6666666.211567 Sulfolobus solfataricus P2 P2 AE006641.1 1 2992245 SE-
LECTED TACK group Crenarchaeota

-Cyanos

391213 6666666.212444 Cyanothecace sp. ATCC 51142 CP000806.1 1 4934271 Cyanobac-
teria; Oscillatoriophycideae; Oscillatoriales

391246 6666666.212477 Synechococcus sp. PCC 7002 CP000951.1 1 3008047 Cyanobac-
teria; Synechococcales; Synechococcaceae

351204 6666666.189647 Arthrosira platensis C1 1 6089210

1.7.2 Genome Dynamics

Among BBH central databases, genomic dynamics was included.

Whats change site:WC Data

groups were formed with 100Cyanos, 100Archaea , 118 Actinos Closed, 43StreptosClosed

Selected organisms were

```
table <- read.csv("chapter1/WC_Central/WC_Organisms.txt", row.names = 1, sep="\t")
kable(table, caption = "WC_Organisms \\label{tab:WC_Organisms}", caption.short = "WC_
```

Those families present on at least as much as genomes on the group

Cyanos 100 647

Abundant.Families.100Cyanos

Actinos 118 132

Abundant.Families.43Strepto

Archaea 100 35

Abundant.Families.Actinos

Streptomyces 43 1263

Abundant.Families.Archaeas

Those families expanded on at least two groups

```
cat *Abun* | cut -f3| sort | uniq -c | sort >Abundance.all
```

Those Families expanded on Archaea and not expanded on Actino

```
comm -23 f3Archaeas f3Actinos >ArchaeasNoActinos
```

Those Families expanded on Actino and not on Archaea

```
comm -13 f3Archaeas f3Actinos >ActinosNoArchaea
```

Those families expanded on Streptomyces but not in ActinoBacteria

```
comm -13 f343Strepto f3Actinos >ActinosNoStrepto
```

Those Families expanded on Actinobacteria and not in Streptomyces

```
comm -23 f343Strepto f3Actinos >StreptoNoActinos
```

Those Families expanded on Cyano and not in Actino

```
comm -23 f3Cyanos f3Actinos >CyanosNoActinos
```

Natural Products DB

Natural products was improved from previous version

1.7.3 AntisMASH optional DB

AntiSMASH is [138]

Archaeas Results Archaea is a kingdom of recent discovery were not many natural products has been known. On Actinobacteria, evoMining has proved its value to find new kinds of natural products. The clue to this discovery was that Actinobacteria has genomic expansions. Now Archaea has genomic expansions, even more has central pathways genomic expansions. Are these expansions derived from a genomic duplication?

Has Archaea natural products detected by antismash, and if not, where are these NP's or may Archaea doesn't have NP's.

applying EvoMining to Archaea

1.7.4 Otras estrategias para los clusters Argon context Idea

1.8 Argonne

```
ssh nselem@login.mcs.anl.gov
phrase
ssh nselem@maple
password

cs close strain
wc whats chain

we source (edit bashrc)
link ln (create a link to ross directory)
run out of power:
screen

in Seqs (not mine)
cat
6666666.103569 6666666.112815 6666666.112823 6666666.112833 6666666.112841
6666666.112849 6666666.112857 > /home/nse/Concat_Full
to find paralogous sets
svrRepresentativeSequences -b -f Id_Clust -s 0.5 < Concat_Full > TempFull&
perl -p -i -e 's///' readable.tree to clean the tree
To find contexts o pegs of paralogous sets

Context middle point 5000 bp (using text tables)
scp 6666666.112839.txt nselem@maple:/homes/nselem/Strepto_01/.

fig|6666666.112839.peg.26
```

copy families.all file
on the file we have column1 family name column 5 peg id

cluster_objects < elements_to_cluster > ClusteFile

write a file with pegs
1 peg1 adjacent1, adjacent2
1 peg2
2
2

write a file similiar but with the family number

1 peg1 fn1, fn2
1 peg2
2
2

compare each peg on this file from the same family

Write the conections file

peg1 peg2
peg1 peg3
peg2 peg3

cluster this file and score the cluster

Define

1. a "function set" is generated by the what's changed directory as a "family"
2. a "paralog set" is a set of function sets in which paralogous members span the sets
3. a PEG is in a paralog set if it is in one ofthe function sets that make up the
4. a "context" of a PEG is the set of close pegs
 - 4.1 First cluster operation would give us: context sets (CS)
5. a "context set" is a set of PEGs with "similar contexts"
 - 5.1 second clustering operation would give us:cluster (Cl)
6. a "cluster" is a set of context sets (each context set is a different compute:
Compute the context sets that are made from PEGs that occur in PS.
Compute the contexts of PEGs in PS.

cluster these contexts using the “similar contexts” relation

This gives a set of clusters, and the members of the clusters are context sets
That is, a cluster is a set of context sets

a. the number of contexts sets i

score the clusters

Take a paralog set PS.

Be the context sets: CS_1, CS_2, ..., CS_k members of the paralogous set

k the number of contexts sets on the paralogous set

n_i the cardinality of CS_i

PS={CS1,CS2,...,CS3}

C1={[CS_1,n_1],[CS_2,n_2],..., [CS_k,n_k]}

```
let be M=max(n_i)  i=1,2,...k (Maximum cardinality of Context sets)
m=max(n_i)  i=1,2,...k, i!=M (second greatest cardinality of context sets)
(We are interested that a second copy is distributed)
```

We are interested on k,M,n to form a scoring function for the cluster set
S=f(k,m,M)=c_1*k+c_2*m+c_3*M

history

Para hacer un nuevo set de datos

```
591 cd Data/CS
592 mkdir Directorio
593 vi Directorio/rep.genomes
594 cd Directorio/
600 nohup svr_CS -d Directorio&
```

Contenido de rep.genomes

```
rast|390693 nselem35 q8Vf6ib
rast|390675 nselem35 q8Vf6ib
rast|388811 nselem35 q8Vf6ib
```

When you click the **Knit** button above a document will be generated that includes both content as well as the output of any embedded **R** code chunks within the document.
You can embed an **R** code chunk like this (**cars** is a built-in **R** dataset):

```
summary(cars)
```

speed	dist
Min. : 4.0	Min. : 2.00
1st Qu.:12.0	1st Qu.: 26.00
Median :15.0	Median : 36.00
Mean :15.4	Mean : 42.98

```
3rd Qu.: 19.0   3rd Qu.: 56.00
Max.      : 25.0   Max.      : 120.00
```

1.8.1 Inline code

If you'd like to put the results of your analysis directly into your discussion, add inline code like this:

The `cos` of 2π is 1.

Another example would be the direct calculation of the standard deviation:

The standard deviation of `speed` in `cars` is 5.2876444.

One last neat feature is the use of the `ifelse` conditional statement which can be used to output text depending on the result of an **R** calculation:

The standard deviation is less than 6.

Note the use of `>` here, which signifies a quotation environment that will be indented.

As you see with `2π` above, mathematics can be added by surrounding the mathematical text with dollar signs. More examples of this are in [Mathematics and Science] if you uncomment the code in [Math].

1.9 Recomendaciones de Luis

Para evoMining

Probar distintos métodos de filogenia y después hacer la coloración.

maximum likelihood, Protest phymol

Atracción de ramas largas.

raxml

trim all vs Gblocks (Tony Galvadon)

Comparar dos árboles

Para ver si la evolución de los genes concatenados ha sido simultánea

Robinson and Foulds

Joe Felsenstein

Phylogenetic tree

2. dist tree

quarter decomposition

peter gogarten fendou Mao

Sets de experimentos.

Para el experimento de los streptomyces con ruta centrales el core, analizar el problema

de dominios múltiples.

Dominios

Nan Song, Dannie durand

Después del blast

Para obtener

Pablo Vinuesa: Get Homologues

Burkhordelias y su toxina (Preguntar a Beto)

Cianobacterias y la ruta de fijación de nitrógeno.

Servidor Viernes a las 12:00

1.10 CORASON: Other genome Mining tools context-based

1.11 CORe Analysis of Syntenic Orthologs to prioritize Natural Product-Biosynthetic Gene Cluster

Genome fluidity on Bacteria is source of biosynthetic gene clusters (BGCs) abundance, in fact almost all bacterial genome sequenced contributes with new genes and gene clusters to the Bacterial Pan-genome. As a consequence of gene diversity helped by sequence technology advances, researchers often have a large set of genomes that wish to analyze in search of a particular gene cluster variation. Answering BGCs analysis needs CORASON allows users to find and visualize variations of a given gene cluster sorting them according to the conserved core phylogeny.

To find cluster variations, given a query protein sequence that belongs to a reference cluster, CORASON will search on a Bacterial genome database all gene clusters that contains orthologues of the query-protein and at least another sequence from the reference cluster. Orthologues on variation clusters are coloured within a gradient according to its identity percentage with the reference cluster sequences.

The cluster core attempts to identify a set of functions conserved on this particular biosynthetic BGC. The core genome on a taxonomical group is the set of coding sequences that are shared between all group members, this definition may be adapted to the cluster core by using a set of gene clusters instead of a set of genomes. A report about gene function will be provided whenever a cluster core exists also core sequences will be concatenated to construct a phylogenetic tree and sort variation clusters accordingly.

Functional annotations are provided by RAST annotation service due to that CORASON genomic databases must be RAST files. Any archaeal or bacterial genome can be

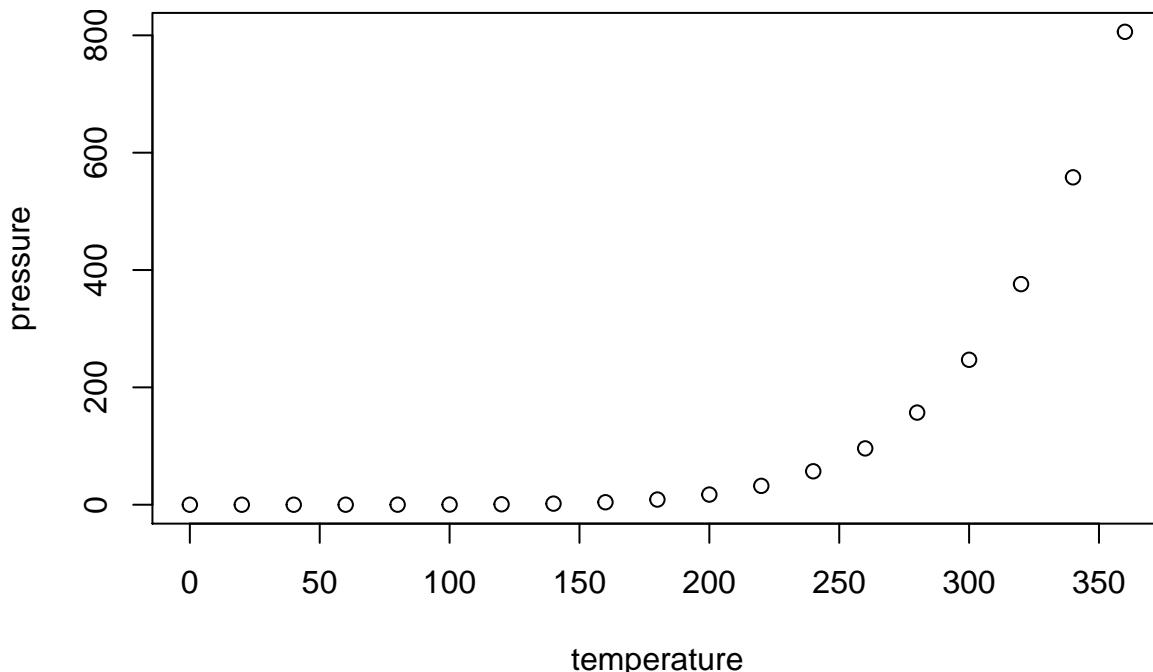
RAST annotated either on the website or by command line using myrast server.

Finally, in order to provide an easy to install distribution CORASON was packaged on docker containerization platform. Software dependencies such as BLAST 2.2.30, muscle3.8.3, GBlocksLinux64_0.91b, quicktree, newick-utils-1.6, and CORASON code were wrapped together on CORASON docker container. Tutorial and software are available at [nselem/github](https://nselem.github.io/).

CORASON inputs are a genomic database, a reference cluster and an enzyme inside this cluster, outputs are newick trees, core functional report and a cluster variation SVG file. SVG format among being high quality scalable graphics, also allow to display metadata such as gene function and genome coordinates just by mouse over figures on a browser facilitating genomic analysis.

In conclusion CORASON is an easy to install comparative genomic visual tool on a customizable genome database that allows users to visualize variations of a reference gene cluster identifying its core functions and finally sorting variations according to their evolutionary history helping to prioritize clusters that may be involved on chemical novelty.

You can also embed plots. For example, here is a way to use the base **R** graphics package to produce a plot using the built-in **pressure** dataset:



Note that the `echo = FALSE` parameter was added to the code chunk to prevent printing of the **R** code that generated the plot. There are plenty of other ways to add chunk options. More information is available at <http://yihui.name/knitr/options/>.

Another useful chunk option is the setting of `cache = TRUE` as you see here. If

document rendering becomes time consuming due to long computations or plots that are expensive to generate you can use knitr caching to improve performance. Later in this file, you'll see a way to reference plots created in **R** or external figures.

1.12 Loading and exploring data

Included in this template is a file called `flights.csv`. This file includes a subset of the larger dataset of information about all flights that departed from Seattle and Portland in 2014. More information about this dataset and its **R** package is available at <http://github.com/ismayc/pnwflights14>. This subset includes only Portland flights and only rows that were complete with no missing values. Merges were also done with the `airports` and `airlines` data sets in the `pnwflights14` package to get more descriptive airport and airline names.

We can load in this data set using the following command:

```
flights <- read.csv("data/flights.csv")
```

The data is now stored in the data frame called `flights` in **R**. To get a better feel for the variables included in this dataset we can use a variety of functions. Here we can see the dimensions (rows by columns) and also the names of the columns.

```
dim(flights)
```

```
[1] 52808     16
```

```
names(flights)
```

```
[1] "month"        "day"          "dep_time"      "dep_delay"  
[5] "arr_time"     "arr_delay"     "carrier"       "tailnum"  
[9] "flight"        "dest"         "air_time"      "distance"  
[13] "hour"          "minute"        "carrier_name" "dest_name"
```

Another good idea is to take a look at the dataset in table form. With this dataset having more than 50,000 rows, we won't explicitly show the results of the command here. I recommend you enter the command into the Console **after** you have run the **R** chunks above to load the data into **R**.

```
View(flights)
```

While not required, it is highly recommended you use the `dplyr` package to manipulate and summarize your data set as needed. It uses a syntax that is easy to understand using chaining operations. Below I've created a few examples of using `dplyr` to get information about the Portland flights in 2014. You will also see the use of the `ggplot2` package, which produces beautiful, high-quality academic visuals.

We begin by checking to ensure that needed packages are installed and then we load them into our current working environment:

```

# List of packages required for this analysis
pkg <- c("dplyr", "ggplot2", "knitr", "devtools")
# Check if packages are not installed and assign the
# names of the packages not installed to the variable new.pkg
new.pkg <- pkg[!(pkg %in% installed.packages())]
# If there are any packages in the list that aren't installed,
# install them
if (length(new.pkg))
  install.packages(new.pkg, repos = "http://cran.rstudio.com")
# Load packages
library(dplyr)
library(ggplot2)
library(knitr)

```

The example we show here does the following:

- Selects only the `carrier_name` and `arr_delay` from the `flights` dataset and then assigns this subset to a new variable called `flights2`.
- Using `flights2`, we determine the largest arrival delay for each of the carriers.

```

flights2 <- flights %>% dplyr::select(carrier_name, arr_delay)
max_delays <- flights2 %>% group_by(carrier_name) %>%
  summarize(max_arr_delay = max(arr_delay, na.rm = TRUE))

```

We next introduce a useful function in the `knitr` package for making nice tables in *R Markdown* called `kable`. It produces the *L^AT_EX* code required to make the table and is much easier to use than manually entering values into a table by copying and pasting values into Excel or *L^AT_EX*. This again goes to show how nice reproducible documents can be! There is no need to copy-and-paste values to create a table. (Note the use of `results = "asis"` here which will produce the table instead of the code to create the table. You'll learn more about the `\label` later.) The `caption.short` argument is used to include a shorter version of the title to appear in the List of Tables at the beginning of the document.

```

kable(max_delays, col.names = c("Airline", "Max Arrival Delay"),
      caption = "Maximum Delays by Airline \label{tab:max_delay}",
      caption.short = "Max Delays by Airline")

```

Table 1.1: Maximum Delays by Airline

Airline	Max Arrival Delay
Alaska Airlines Inc.	338
American Airlines Inc.	1539
Delta Air Lines Inc.	651
Frontier Airlines Inc.	575
Hawaiian Airlines Inc.	407

Airline	Max Arrival Delay
JetBlue Airways	273
SkyWest Airlines Inc.	421
Southwest Airlines Co.	694
United Air Lines Inc.	472
US Airways Inc.	347
Virgin America	366

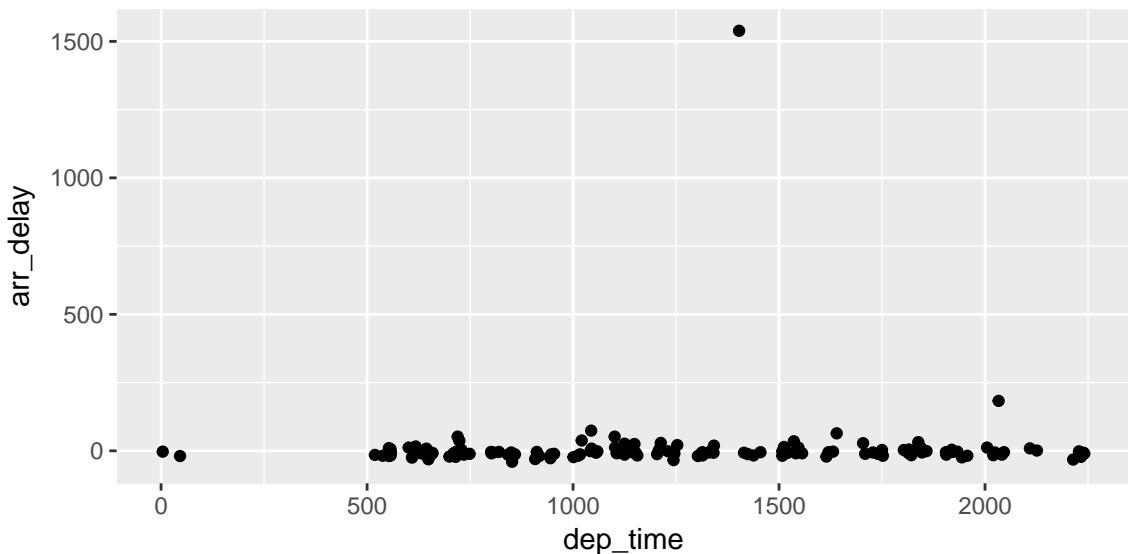
We can further look into the properties of the largest value here for American Airlines Inc. To do so, we can isolate the row corresponding to the arrival delay of 1539 minutes for American in our original `flights` dataset.

```
flights %>% dplyr::filter(arr_delay == 1539,
                           carrier_name == "American Airlines Inc.") %>%
  dplyr::select(-c(month, day, carrier, dest_name, hour,
                  minute, carrier_name, arr_delay))
```

	dep_time	dep_delay	arr_time	tailnum	flight	dest	air_time	distance
1	1403	1553	1934	N595AA	1568	DFW	182	1616

We see that the flight occurred on March 3rd and departed a little after 2 PM on its way to Dallas/Fort Worth. Lastly, we show how we can visualize the arrival delay of all departing flights from Portland on March 3rd against time of departure.

```
flights %>% dplyr::filter(month == 3, day == 3) %>%
  ggplot(aes(x = dep_time, y = arr_delay)) +
  geom_point()
```



Chapter 2

PriA Family

PriA isomerase is a promiscuous enzyme involved in histidine and Triptophan pathways. This enzyme family catalyze conversions HisA and TrpF converting ProFAR on and PRA into products. PriA can be found at Actinobacteria phylum.

```
# List of packages required for this analysis
pkg <- c("dplyr", "ggplot2", "knitr", "devtools", "RColorBrewer")
# Check if packages are not installed and assign the
# names of the packages not installed to the variable new.pkg
new.pkg <- pkg[!(pkg %in% installed.packages())]
# If there are any packages in the list that aren't installed,
# install them
if (length(new.pkg))
  install.packages(new.pkg, repos = "http://cran.rstudio.com")
# Load packages
library(dplyr)
library(plyr)
library(reshape)
library(ggplot2)
library(knitr)
library(RColorBrewer)
hm.palette <- colorRampPalette(rev(brewer.pal(11, 'Spectral'))), space='Lab'
library(genstats) ## Next libraries are for coursera
library(devtools)
library(BioBase)
library(scales) #
library(xlsx) # For save data on excel
```

2.1 Methods

52 Streptomyces genera has differences on PriA function. PriA ## Math Docking simulation were calculated for Streptomyces enzymes. TrpF enzymes from Strptomyces Mg1, Jonesia denitrificans, were added as controls

Procedures can be found at Docking Protocols

1.Phylogenetic Tree 39 Streptomyces sequences, as outgroup E coli, Arthrobacter Aurescens, Salmonella enterica and Acidimicrobium ferrooxidans PriA's were included.

CORASON PriA All streptomyces have a partially conserved PriA cluster. CT34 has a secondary copy whose Best hit on NCBI is Lentzea's PriA with 50% identity 98% coverage

TrpF1 TrpF1 queries gave hits with TrpC enzyme present on every Streptomyces, additionally S rimosus, S coelicolor, S venezuelae and S. NRRL S-1813 had an extra copy. S rimosus TrpC vicinity has PKS and siderophore genes.

TrpF2 Conserved cluster with NRPS sequences flanking TrpF2

TrpF3 Non conserved cluster

TrpF4 purpeofuscus and S bikiniensis 2. Heatmap

Additionally to the sequences selected by phylogeny, Jonesia denitrificans and Streptomyces sp Mg1 TrpF sequences were added as control .

Substrate table

```
table <- read.csv("chapter2/Substrate.data", row.names = 1,sep="\t")
kable(table,  caption = "Substrates \\label{tab:substrates}",caption.short = "Substrates")
```

Table 2.1: Substra

	id	Number	Kind	Reference	Names
S13	dte6_open	LUZ			
S15	dte13_open	LUZ			
S14	dte6_closed	LUZ			
S16	dte13_closed	LUZ			
S10	C04376		James		5'-Phosphoribosyl-N-formylglycine
S12	C03838		James		5'-Phosphoribosylglycinamide
S9	C04640		James		2-(Formamido)-N1-(5'-phosphorib
S18	CompoundV		Adams	CompundV	This compound is an intermedia
S5	C05923		James		2,5-Diaminopyrimidine nucleoside
S4	C05922		James		Formamidopyrimidine nucleoside
S8	C01268		James		5-Amino-6-(5'-phosphoribosylamino)
S17	PraP		Verduzco	PraP	

	id	Number	Kind	Reference	Names
S7	C04302		James		PRA
S6	C00144		James		GMP
S11	C00044		James		GTP
S1	C01253		James		ADP-D-ribosyl-[dinitroge
S2	C01201		James		N(omega)-(ADP-D-ribosy
S3	C04896				ProFAR
S19	S_17146		Due et al	17146	2,5-dimethyl-N-(4-oxocycl
S20	S_16827		Due et al	16827	(E)-N-(3-chloro-5-methyl-
mrBaye	s PriA Julian.nx	s on mazo	rca goes to	PriA Julian.c	on.tre
PriAju	lian.con.tre wa	s open wi	th figtree a	nd saved as	SVG
To get	coordinates: ‘	coordtree	.pl PriAJul	an.SVG‘	
Heatpl	ot color are fr	om ggplot	R		
mydata	.xls lo guardoe	n mydata.	cvs		
perl r	ead_mydata.pl m	ydata.csv	>Heat.color	s	
mnuall	y edit Heat.col	ors by ad	ding headers	enzymas y s	ubstrates
perl h	eatFromRGB.pl H	eatColor	YPriA Julian		
Hice e	l heatplot en S	VG con el	script		

Observaciones Mauricio

- falta el pie de figura Substrate docking over enzymes from extended PriA families.
Substrates 1-20

- falta el dendograma arriba de los sustratos (indicar cuál es pra y cuál profar)
- falta la escala de colores (con valores y unidades). Cuando agregues el dendograma de los sustratos va a quedar un cuadrante vacío en la parte superior izquierda, en ese espacio pon la escala de forma horizontal
- intenta aumentar el contraste de color entre el valor mínimo y máximo de la escala

Intente varias Figuras

- repite las etiquetas de los sustratos abajo del heatmap
Pendiente
- hay inconsistencias en los nombres de la enzimas (eg, Ssvi y Svi, SMgl y Smgl, etc)
Árbol nuevo sin datos faltantes
- para el caso de las enzimas sin datos, usa negro en lugar de amarillo
LISTO
- “Controles TrpF/subTrpF” (debe estar en inglés), puede ser confuso poner dos etiquetas para la misma función

```
docking <- read.csv("chapter2/SmallHeat.data", header=TRUE, sep="\t")
EnzymeOrder=factor(docking$Enzima,levels=unique(docking$Enzima))
docking.m <- melt(docking,id = "Enzima")
docking.m <- ddply(docking.m, .(variable), transform,rescale = rescale(value))
docking.m$Enzima <- factor(docking.m$Enzima, levels = rev(docking.m$Enzima[order(EnzymeOrder)]))

##### on white and blue
blueHeatPlot<-ggplot(docking.m, aes(x=variable, y=Enzima)) + labs(x = "Substrates", y =
ggsave("chapter2/blueHeatPlot.pdf", plot = blueHeatPlot,height = 36, width = 24)

## black and white
blackHeatPlot<-ggplot(docking.m, aes(x=variable, y=Enzima)) + labs(x = "Substrates", y =
ggsave("chapter2/blackHeatPlot.pdf", plot = blackHeatPlot,height = 36, width = 24)

g <- ggplot_build(blackHeatPlot)
g$data[[1]]["fill"]

      fill
1 #636363
2 #636363
3 #676767
4 #7C7C7C
5   black
6 #595959
7 #A6A6A6
8 #484848
9 #5C5C5C
10 #B6B6B6
11 #484848
12   black
13   black
14 #313131
15 #3E3E3E
16 #636363
17 #525252
18 #848484
19 #606060
20 #9A9A9A
21 #373737
22 #9E9E9E
23 #484848
24 #717171
25 #636363
```

```
26 #6A6A6A
27 #676767
28 #3E3E3E
29 #606060
30 #797979
31 #676767
32 #797979
33 #717171
34 #636363
35 #676767
36 #414141
37 #444444
38     black
39 #3A3A3A
40 #414141
41 #6A6A6A
42 #4E4E4E
43 #525252
44 #C6C6C6
45 #939393
46 #808080
47 #C6C6C6
48 #636363
49 #A6A6A6
50 #676767
51     black
52 #808080
53 #DEDEDE
54 #C2C2C2
55 #2B2B2B
56 #A2A2A2
57 #BABABA
58 #848484
59 #808080
60 #5C5C5C
61 #8B8B8B
62 #606060
63 #5C5C5C
64 #676767
65 #636363
66     black
67 #6A6A6A
68 #939393
69 #606060
70 #4B4B4B
```

```
71  #EAEAEA
72  #484848
73  black
74  black
75  #808080
76  #595959
77  #4B4B4B
78  #676767
79  #6A6A6A
80  #979797
81  #484848
82  #4E4E4E
83  #525252
84  #808080
85  #5C5C5C
86  #4E4E4E
87  #595959
88  #4B4B4B
89  #4E4E4E
90  #555555
91  #606060
92  #555555
93  #595959
94  #5C5C5C
95  #525252
96  #525252
97  #555555
98  #525252
99  black
100 #4E4E4E
101 #6E6E6E
102 #4B4B4B
103 #606060
104 #4E4E4E
105 #717171
106 #8F8F8F
107 #757575
108 #DADADA
109 #797979
110 #717171
111 #525252
112 black
113 #8B8B8B
114 #AAAAAA
115 #A2A2A2
```

```
116 #2E2E2E
117 #222222
118 #BABABA
119 #979797
120 #797979
121 #979797
122 #8F8F8F
123 #676767
124 #555555
125 #757575
126 #6A6A6A
127 black
128 #5C5C5C
129 #4B4B4B
130 #555555
131 #4E4E4E
132 #9A9A9A
133 #606060
134 black
135 black
136 #595959
137 #636363
138 #636363
139 #757575
140 #676767
141 #676767
142 #4B4B4B
143 #525252
144 #595959
145 #595959
146 #6A6A6A
147 #595959
148 #676767
149 #4E4E4E
150 #555555
151 #4E4E4E
152 #525252
153 #525252
154 #4B4B4B
155 #6A6A6A
156 #606060
157 #4E4E4E
158 #595959
159 #5C5C5C
160 black
```

```
161 #636363
162 #636363
163 #595959
164 #525252
165 #676767
166 #9A9A9A
167 #B6B6B6
168 #A6A6A6
169 #FFFFFF
170 #6A6A6A
171 #EAEAEA
172 #5C5C5C
173 black
174 #7C7C7C
175 #AAAAAA
176 #BEBEBE
177 #343434
178 #414141
179 #A6A6A6
180 #808080
181 #636363
182 #808080
183 #979797
184 #595959
185 #444444
186 #555555
187 #525252
188 black
189 #606060
190 #4B4B4B
191 #595959
192 #444444
193 #595959
194 #525252
195 black
196 black
197 #484848
198 #4E4E4E
199 #606060
200 #717171
201 #4E4E4E
202 #4B4B4B
203 #4E4E4E
204 #444444
205 #4E4E4E
```

```
206 #414141
207 #606060
208 #5C5C5C
209 #636363
210 #484848
211 #3E3E3E
212 #484848
213 #484848
214 #484848
215 #525252
216 #5C5C5C
217 #4E4E4E
218 #4E4E4E
219 #4B4B4B
220 #595959
221 black
222 #444444
223 #5C5C5C
224 #5C5C5C
225 #4B4B4B
226 #595959
227 #222222
228 #AEAEAE
229 #636363
230 #414141
231 #414141
232 #5C5C5C
233 #444444
234 black
235 #757575
236 #5C5C5C
237 #7C7C7C
238 #2B2B2B
239 #1C1C1C
240 #373737
241 #4E4E4E
242 #5C5C5C
243 #606060
244 #606060
245 #444444
246 #606060
247 #555555
248 #4B4B4B
249 black
250 #5C5C5C
```

```
251 #636363
252 #595959
253 #3A3A3A
254 #343434
255 #444444
256 black
257 black
258 #4E4E4E
259 #6E6E6E
260 #6E6E6E
261 #676767
262 #414141
263 #555555
264 #5C5C5C
265 #4B4B4B
266 #3E3E3E
267 #595959
268 #3A3A3A
269 #5C5C5C
270 #3A3A3A
271 #4E4E4E
272 #525252
273 #444444
274 #5C5C5C
275 #484848
276 #484848
277 #636363
278 #606060
279 #444444
280 #6E6E6E
281 #444444
282 black
283 #717171
284 #6A6A6A
285 #595959
286 #797979
287 #717171
288 #8F8F8F
289 #414141
290 #6A6A6A
291 #808080
292 #1C1C1C
293 #676767
294 #888888
295 black
```

```
296 #2B2B2B
297 #5C5C5C
298 #636363
299 #4B4B4B
300 #797979
301 #5C5C5C
302 #3A3A3A
303 #373737
304 #3A3A3A
305 #595959
306 #3A3A3A
307 #414141
308 #3A3A3A
309 #4E4E4E
310 black
311 #4E4E4E
312 #6E6E6E
313 #595959
314 #484848
315 #3A3A3A
316 #3E3E3E
317 black
318 black
319 #555555
320 #525252
321 #444444
322 #606060
323 #555555
324 #444444
325 #5C5C5C
326 #3E3E3E
327 #5C5C5C
328 #636363
329 #444444
330 #636363
331 #444444
332 #555555
333 #525252
334 #606060
335 #4B4B4B
336 #4B4B4B
337 #4E4E4E
338 #525252
339 #484848
340 #484848
```

```
341 #3E3E3E
342 #525252
343 black
344 #4E4E4E
345 #676767
346 #444444
347 #757575
348 #606060
349 #606060
350 #313131
351 #676767
352 #5C5C5C
353 #222222
354 #6A6A6A
355 #797979
356 black
357 #252525
358 #4E4E4E
359 #595959
360 #3A3A3A
361 #606060
362 #484848
363 #373737
364 #252525
365 #2B2B2B
366 #595959
367 #444444
368 #555555
369 #444444
370 #595959
371 black
372 #525252
373 #5C5C5C
374 #4E4E4E
375 #313131
376 #4B4B4B
377 #444444
378 black
379 black
380 #6A6A6A
381 #484848
382 #4E4E4E
383 #6E6E6E
384 #3A3A3A
385 #444444
```

```
386 #3A3A3A
387 #4B4B4B
388 #484848
389 #595959
390 #525252
391 #717171
392 #525252
393 #4B4B4B
394 #484848
395 #484848
396 #373737
397 #525252
398 #4B4B4B
399 #636363
400 #676767
401 #444444
402 #3A3A3A
403 #414141
404 black
405 #4B4B4B
406 #5C5C5C
407 #484848
408 #6E6E6E
409 #5C5C5C
410 #717171
411 #282828
412 #6A6A6A
413 #555555
414 #1C1C1C
415 #6E6E6E
416 #8B8B8B
417 black
418 #313131
419 #606060
420 #636363
421 #2E2E2E
422 #636363
423 #4E4E4E
424 #343434
425 #222222
426 #2B2B2B
427 #595959
428 #6E6E6E
429 #676767
430 #717171
```

```
431 #757575
432 black
433 #7C7C7C
434 #676767
435 #797979
436 #717171
437 #7C7C7C
438 #7C7C7C
439 black
440 black
441 #757575
442 #797979
443 #8B8B8B
444 #7C7C7C
445 #808080
446 #939393
447 #6E6E6E
448 #676767
449 #7C7C7C
450 #636363
451 #797979
452 #8F8F8F
453 #797979
454 #757575
455 #717171
456 #8F8F8F
457 #6A6A6A
458 #6E6E6E
459 #808080
460 #8B8B8B
461 #797979
462 #848484
463 #7C7C7C
464 #606060
465 black
466 #B2B2B2
467 #8B8B8B
468 #717171
469 #8B8B8B
470 #848484
471 #B2B2B2
472 #595959
473 #888888
474 #B6B6B6
475 #373737
```

```
476 #9A9A9A
477 #939393
478 black
479 #555555
480 #676767
481 #717171
482 #6A6A6A
483 #979797
484 #8F8F8F
485 #4E4E4E
486 #444444
487 #525252
488 #676767
489 #AEAEAE
490 #B6B6B6
491 #979797
492 #A2A2A2
493 black
494 #808080
495 #BEBEBE
496 #A6A6A6
497 #8B8B8B
498 #A2A2A2
499 #8F8F8F
500 black
501 black
502 #888888
503 #B6B6B6
504 #C2C2C2
505 #C6C6C6
506 #B6B6B6
507 #C6C6C6
508 #B6B6B6
509 #B6B6B6
510 #BEBEBE
511 #AEAEAE
512 #979797
513 #BABABA
514 #9A9A9A
515 #C2C2C2
516 #AAAAAA
517 #A2A2A2
518 #A6A6A6
519 #888888
520 #B2B2B2
```

```
521 #AEAEAE
522 #BEBEBE
523 #797979
524 #8B8B8B
525 #717171
526 black
527 #B6B6B6
528 #CACACA
529 #8F8F8F
530 #B2B2B2
531 #A6A6A6
532 #EAEAEA
533 #555555
534 #BABABA
535 #CECECE
536 #4E4E4E
537 #9E9E9E
538 #B2B2B2
539 black
540 #676767
541 #B2B2B2
542 #A6A6A6
543 #A6A6A6
544 #E2E2E2
545 #B2B2B2
546 #636363
547 #595959
548 #484848
549 #BABABA
550 #AAAAAA
551 #8B8B8B
552 #A6A6A6
553 #9E9E9E
554 black
555 #5C5C5C
556 #9A9A9A
557 #939393
558 #717171
559 #979797
560 #A2A2A2
561 black
562 black
563 #848484
564 #9A9A9A
565 #BEBEBE
```

```
566 #BABABA
567 #9E9E9E
568 #BABABA
569 #B2B2B2
570 #B6B6B6
571 #AAAAAA
572 #8B8B8B
573 #8F8F8F
574 #AAAAAA
575 #939393
576 #BABABA
577 #636363
578 #939393
579 #A2A2A2
580 #808080
581 #A2A2A2
582 #AEAEAE
583 #AAAAAA
584 #7C7C7C
585 #A6A6A6
586 #6E6E6E
587 black
588 #AEAEAE
589 #C6C6C6
590 #C6C6C6
591 #BEBEBE
592 #848484
593 #D2D2D2
594 #676767
595 #B2B2B2
596 #CECECE
597 #414141
598 #BEBEBE
599 #B6B6B6
600 black
601 #5C5C5C
602 #BEBEBE
603 #BEBEBE
604 #979797
605 #CECECE
606 #A2A2A2
607 #6A6A6A
608 #595959
609 #4B4B4B
610 #AEAEAE
```

```
611 #757575
612 #757575
613 #717171
614 #848484
615 black
616 #808080
617 #808080
618 #717171
619 #717171
620 #848484
621 #797979
622 black
623 black
624 #808080
625 #8F8F8F
626 #848484
627 #939393
628 #757575
629 #979797
630 #888888
631 #8F8F8F
632 #6E6E6E
633 #8F8F8F
634 #6E6E6E
635 #979797
636 #6E6E6E
637 #848484
638 #8B8B8B
639 #9A9A9A
640 #717171
641 #808080
642 #8F8F8F
643 #8F8F8F
644 #939393
645 #6A6A6A
646 #848484
647 #848484
648 black
649 #939393
650 #939393
651 #8F8F8F
652 #7C7C7C
653 #9A9A9A
654 #B2B2B2
655 #606060
```

```
656 #AAAAAA
657 #C2C2C2
658 #2B2B2B
659 #9E9E9E
660 #AEAEAE
661 black
662 #595959
663 #797979
664 #848484
665 #717171
666 #939393
667 #8F8F8F
668 #676767
669 #555555
670 #606060
671 #717171
672 #5C5C5C
673 #6A6A6A
674 #757575
675 #8F8F8F
676 black
677 #5C5C5C
678 #717171
679 #6A6A6A
680 #5C5C5C
681 #757575
682 #757575
683 black
684 black
685 #7C7C7C
686 #757575
687 #717171
688 #717171
689 #636363
690 #6E6E6E
691 #636363
692 #717171
693 #797979
694 #676767
695 #595959
696 #6E6E6E
697 #636363
698 #6E6E6E
699 #606060
700 #6E6E6E
```

701 #636363
702 #676767
703 #797979
704 #6A6A6A
705 #6A6A6A
706 #636363
707 #6A6A6A
708 #676767
709 black
710 #808080
711 #757575
712 #676767
713 #717171
714 #888888
715 #9E9E9E
716 #4E4E4E
717 #717171
718 #8B8B8B
719 #414141
720 #848484
721 #979797
722 black
723 #4B4B4B
724 #717171
725 #717171
726 #636363
727 #939393
728 #808080
729 #525252
730 #3A3A3A
731 #4B4B4B
732 #6A6A6A
733 #848484
734 #888888
735 #797979
736 #8B8B8B
737 black
738 #888888
739 #979797
740 #848484
741 #808080
742 #9A9A9A
743 #797979
744 black
745 black

```
746 #888888
747 #8F8F8F
748 #808080
749 #979797
750 #848484
751 #808080
752 #8B8B8B
753 #939393
754 #939393
755 #979797
756 #6E6E6E
757 #9A9A9A
758 #6E6E6E
759 #8B8B8B
760 #797979
761 #9A9A9A
762 #808080
763 #7C7C7C
764 #888888
765 #888888
766 #8B8B8B
767 #939393
768 #9E9E9E
769 #757575
770 black
771 #8F8F8F
772 #979797
773 #848484
774 #939393
775 #9A9A9A
776 #BEBEBE
777 #636363
778 #8F8F8F
779 #AAAAAA
780 #3E3E3E
781 #979797
782 #9E9E9E
783 black
784 #595959
785 #AAAAAA
786 #AAAAAA
787 #848484
788 #B6B6B6
789 #9E9E9E
790 #6A6A6A
```

```
791 #4E4E4E
792 #6A6A6A
793 #B6B6B6
794 #8F8F8F
795 #939393
796 #9A9A9A
797 #9E9E9E
798 black
799 #848484
800 #939393
801 #888888
802 #797979
803 #AAAAAA
804 #888888
805 black
806 black
807 #939393
808 #888888
809 #888888
810 #979797
811 #8F8F8F
812 #8F8F8F
813 #808080
814 #939393
815 #979797
816 #888888
817 #757575
818 #939393
819 #717171
820 #8F8F8F
821 #939393
822 #9E9E9E
823 #8B8B8B
824 #6E6E6E
825 #939393
826 #8F8F8F
827 #888888
828 #7C7C7C
829 #8B8B8B
830 #888888
831 black
832 #A2A2A2
833 #A2A2A2
834 #8B8B8B
835 #BABABA
```

```
836 #AAAAAA
837 #BEBEBE
838 #888888
839 #8F8F8F
840 #B6B6B6
841 #3E3E3E
842 #A6A6A6
843 #B2B2B2
844 black
845 #636363
846 #9A9A9A
847 #9E9E9E
848 #888888
849 #C2C2C2
850 #8F8F8F
851 #676767
852 #4E4E4E
853 #525252
854 #979797
855 #9A9A9A
856 #BEBEBE
857 #D2D2D2
858 #DEDEDE
859 black
860 #8B8B8B
861 #CACACA
862 #A2A2A2
863 #B6B6B6
864 #AEAEAE
865 #8B8B8B
866 black
867 black
868 #6E6E6E
869 #A2A2A2
870 #DADADA
871 #DEDEDE
872 #C6C6C6
873 #DADADA
874 #BABABA
875 #C2C2C2
876 #DADADA
877 #B6B6B6
878 #5C5C5C
879 #CECECE
880 #444444
```

```
881 #C6C6C6
882 #8B8B8B
883 #939393
884 #B6B6B6
885 #808080
886 #A2A2A2
887 #A2A2A2
888 #DEDEDE
889 #7C7C7C
890 #BABABA
891 #B2B2B2
892 black
893 #C2C2C2
894 #CECECE
895 #979797
896 #C6C6C6
897 #AEAEAE
898 #FBFBFB
899 #676767
900 #CECECE
901 #EAEAEA
902 #595959
903 #CACACA
904 #AAAAAA
905 black
906 #888888
907 #D2D2D2
908 #C2C2C2
909 #AAAAAA
910 #EAEAEA
911 #CECECE
912 #6E6E6E
913 #525252
914 #676767
915 #CACACA
916 #9E9E9E
917 #848484
918 #A6A6A6
919 #C6C6C6
920 black
921 #757575
922 #A2A2A2
923 #2E2E2E
924 #808080
925 #BEBEBE
```

```
926 #5C5C5C
927 black
928 black
929 #808080
930 #636363
931 #595959
932 #717171
933 #808080
934 #7C7C7C
935 #8B8B8B
936 #3A3A3A
937 #6A6A6A
938 #979797
939 #595959
940 #4E4E4E
941 #555555
942 #6A6A6A
943 #636363
944 #343434
945 #A6A6A6
946 #4B4B4B
947 #B2B2B2
948 #C6C6C6
949 #A2A2A2
950 #8B8B8B
951 #B2B2B2
952 #6A6A6A
953 black
954 #222222
955 #525252
956 #1F1F1F
957 #1F1F1F
958 #1F1F1F
959 #CACACA
960 #7C7C7C
961 #BEBEBE
962 #C6C6C6
963 #636363
964 #B2B2B2
965 #7C7C7C
966 black
967 #5C5C5C
968 #B6B6B6
969 #9E9E9E
970 #4B4B4B
```

```
971 #717171
972 #C2C2C2
973 #676767
974 #5C5C5C
975 #595959
976 #888888
977 #595959
978 #757575
979 #AAAAAA
980 #D2D2D2
981 black
982 #717171
983 #9E9E9E
984 #1F1F1F
985 #797979
986 #C6C6C6
987 #888888
988 black
989 black
990 #808080
991 #5C5C5C
992 #3E3E3E
993 #939393
994 #808080
995 #A6A6A6
996 #888888
997 #191919
998 #A2A2A2
999 #979797
1000 #4B4B4B
1001 #808080
1002 #3E3E3E
1003 #676767
1004 #3E3E3E
1005 #3E3E3E
1006 #A6A6A6
1007 #595959
1008 #AAAAAA
1009 #CACACA
1010 #9A9A9A
1011 #797979
1012 #C2C2C2
1013 #1C1C1C
1014 black
1015 #252525
```

```
1016 #7C7C7C
1017 #1C1C1C
1018 #3A3A3A
1019 #1C1C1C
1020 #CECECE
1021 #8F8F8F
1022 #C2C2C2
1023 #E2E2E2
1024 #595959
1025 #C2C2C2
1026 #AAAAAA
1027 black
1028 #606060
1029 #AEAEAE
1030 #8F8F8F
1031 #000000
1032 #A2A2A2
1033 #CECECE
1034 #6A6A6A
1035 #636363
1036 #595959
1037 #9A9A9A
1038 #9A9A9A
1039 #8F8F8F
1040 #888888
1041 #CECECE
1042 black
1043 #343434
1044 #B2B2B2
1045 #8B8B8B
1046 #AEAEAE
1047 #9A9A9A
1048 #808080
1049 black
1050 black
1051 #4B4B4B
1052 #979797
1053 #848484
1054 #A6A6A6
1055 #7C7C7C
1056 #9A9A9A
1057 #AAAAAA
1058 #A6A6A6
1059 #DADADA
1060 #939393
```

1061 #595959
1062 #9E9E9E
1063 #6E6E6E
1064 #8F8F8F
1065 #343434
1066 #757575
1067 #8F8F8F
1068 #6E6E6E
1069 #7C7C7C
1070 #9E9E9E
1071 #8B8B8B
1072 #6A6A6A
1073 #A6A6A6
1074 #676767
1075 black
1076 #A6A6A6
1077 #8B8B8B
1078 #2E2E2E
1079 #808080
1080 #595959
1081 #FBFBFB
1082 #676767
1083 #CACACA
1084 #C2C2C2
1085 #414141
1086 #A6A6A6
1087 #8B8B8B
1088 black
1089 #636363
1090 #AEAEAE
1091 #A6A6A6
1092 #A2A2A2
1093 #D2D2D2
1094 #C2C2C2
1095 #5C5C5C
1096 #444444
1097 #525252
1098 #AEAEAE
1099 #717171
1100 #6E6E6E
1101 #7C7C7C
1102 #7C7C7C
1103 black
1104 #676767
1105 #797979

```
1106 #606060
1107 #6E6E6E
1108 #808080
1109 #757575
1110 black
1111 black
1112 #797979
1113 #7C7C7C
1114 #7C7C7C
1115 #757575
1116 #6A6A6A
1117 #6A6A6A
1118 #636363
1119 #717171
1120 #595959
1121 #6E6E6E
1122 #6E6E6E
1123 #676767
1124 #6E6E6E
1125 #606060
1126 #757575
1127 #808080
1128 #6E6E6E
1129 #6A6A6A
1130 #7C7C7C
1131 #717171
1132 #7C7C7C
1133 #6E6E6E
1134 #636363
1135 #6A6A6A
1136 black
1137 #797979
1138 #6E6E6E
1139 #6E6E6E
1140 #6A6A6A
1141 #8B8B8B
1142 #B2B2B2
1143 #6E6E6E
1144 #606060
1145 #979797
1146 #595959
1147 #797979
1148 #757575
1149 black
1150 #555555
```

1151 #7C7C7C
1152 #8B8B8B
1153 #848484
1154 #9E9E9E
1155 #808080
1156 #606060
1157 #4B4B4B
1158 #4B4B4B
1159 #797979
1160 #6E6E6E
1161 #6A6A6A
1162 #808080
1163 #757575
1164 black
1165 #606060
1166 #676767
1167 #636363
1168 #676767
1169 #797979
1170 #6A6A6A
1171 black
1172 black
1173 #676767
1174 #717171
1175 #757575
1176 #717171
1177 #636363
1178 #6A6A6A
1179 #6E6E6E
1180 #6E6E6E
1181 #636363
1182 #676767
1183 #6E6E6E
1184 #717171
1185 #6E6E6E
1186 #676767
1187 #676767
1188 #717171
1189 #676767
1190 #636363
1191 #6A6A6A
1192 #808080
1193 #797979
1194 #636363
1195 #676767

```

1196 #6E6E6E
1197 black
1198 #676767
1199 #6E6E6E
1200 #636363
1201 #636363
1202 #8F8F8F
1203 #979797
1204 #606060
1205 #636363
1206 #9A9A9A
1207 #484848
1208 #757575
1209 #6E6E6E
1210 black
1211 #4B4B4B
1212 #797979
1213 #808080
1214 #7C7C7C
1215 #888888
1216 #757575
1217 #5C5C5C
1218 #484848
1219 #444444
1220 #7C7C7C

g$data[[1]]

```

	fill	x	y	PANEL	group	xmin	xmax	ymin	ymax	alpha
1	#636363	1	61		1	61	0.5	1.5	60.5	61.5
2	#636363	1	60		1	60	0.5	1.5	59.5	60.5
3	#676767	1	59		1	59	0.5	1.5	58.5	59.5
4	#7C7C7C	1	58		1	58	0.5	1.5	57.5	58.5
5	black	1	57		1	57	0.5	1.5	56.5	57.5
6	#595959	1	56		1	56	0.5	1.5	55.5	56.5
7	#A6A6A6	1	55		1	55	0.5	1.5	54.5	55.5
8	#484848	1	54		1	54	0.5	1.5	53.5	54.5
9	#5C5C5C	1	53		1	53	0.5	1.5	52.5	53.5
10	#B6B6B6	1	52		1	52	0.5	1.5	51.5	52.5
11	#484848	1	51		1	51	0.5	1.5	50.5	51.5
12	black	1	50		1	50	0.5	1.5	49.5	50.5
13	black	1	49		1	49	0.5	1.5	48.5	49.5
14	#313131	1	48		1	48	0.5	1.5	47.5	48.5
15	#3E3E3E	1	47		1	47	0.5	1.5	46.5	47.5
16	#636363	1	46		1	46	0.5	1.5	45.5	46.5

17	#525252	1	45	1	45	0.5	1.5	44.5	45.5	NA
18	#848484	1	44	1	44	0.5	1.5	43.5	44.5	NA
19	#606060	1	43	1	43	0.5	1.5	42.5	43.5	NA
20	#9A9A9A	1	42	1	42	0.5	1.5	41.5	42.5	NA
21	#373737	1	41	1	41	0.5	1.5	40.5	41.5	NA
22	#9E9E9E	1	40	1	40	0.5	1.5	39.5	40.5	NA
23	#484848	1	39	1	39	0.5	1.5	38.5	39.5	NA
24	#717171	1	38	1	38	0.5	1.5	37.5	38.5	NA
25	#636363	1	37	1	37	0.5	1.5	36.5	37.5	NA
26	#6A6A6A	1	36	1	36	0.5	1.5	35.5	36.5	NA
27	#676767	1	35	1	35	0.5	1.5	34.5	35.5	NA
28	#3E3E3E	1	34	1	34	0.5	1.5	33.5	34.5	NA
29	#606060	1	33	1	33	0.5	1.5	32.5	33.5	NA
30	#797979	1	32	1	32	0.5	1.5	31.5	32.5	NA
31	#676767	1	31	1	31	0.5	1.5	30.5	31.5	NA
32	#797979	1	30	1	30	0.5	1.5	29.5	30.5	NA
33	#717171	1	29	1	29	0.5	1.5	28.5	29.5	NA
34	#636363	1	28	1	28	0.5	1.5	27.5	28.5	NA
35	#676767	1	27	1	27	0.5	1.5	26.5	27.5	NA
36	#414141	1	26	1	26	0.5	1.5	25.5	26.5	NA
37	#444444	1	25	1	25	0.5	1.5	24.5	25.5	NA
38	black	1	24	1	24	0.5	1.5	23.5	24.5	NA
39	#3A3A3A	1	23	1	23	0.5	1.5	22.5	23.5	NA
40	#414141	1	22	1	22	0.5	1.5	21.5	22.5	NA
41	#6A6A6A	1	21	1	21	0.5	1.5	20.5	21.5	NA
42	#4E4E4E	1	20	1	20	0.5	1.5	19.5	20.5	NA
43	#525252	1	19	1	19	0.5	1.5	18.5	19.5	NA
44	#C6C6C6	1	18	1	18	0.5	1.5	17.5	18.5	NA
45	#939393	1	17	1	17	0.5	1.5	16.5	17.5	NA
46	#808080	1	16	1	16	0.5	1.5	15.5	16.5	NA
47	#C6C6C6	1	15	1	15	0.5	1.5	14.5	15.5	NA
48	#636363	1	14	1	14	0.5	1.5	13.5	14.5	NA
49	#A6A6A6	1	13	1	13	0.5	1.5	12.5	13.5	NA
50	#676767	1	12	1	12	0.5	1.5	11.5	12.5	NA
51	black	1	11	1	11	0.5	1.5	10.5	11.5	NA
52	#808080	1	10	1	10	0.5	1.5	9.5	10.5	NA
53	#DEDEDE	1	9	1	9	0.5	1.5	8.5	9.5	NA
54	#C2C2C2	1	8	1	8	0.5	1.5	7.5	8.5	NA
55	#2B2B2B	1	7	1	7	0.5	1.5	6.5	7.5	NA
56	#A2A2A2	1	6	1	6	0.5	1.5	5.5	6.5	NA
57	#BABABA	1	5	1	5	0.5	1.5	4.5	5.5	NA
58	#848484	1	4	1	4	0.5	1.5	3.5	4.5	NA
59	#808080	1	3	1	3	0.5	1.5	2.5	3.5	NA
60	#5C5C5C	1	2	1	2	0.5	1.5	1.5	2.5	NA
61	#8B8B8B	1	1	1	1	0.5	1.5	0.5	1.5	NA

62	#606060	2	61	1	122	1.5	2.5	60.5	61.5	NA
63	#5C5C5C	2	60	1	121	1.5	2.5	59.5	60.5	NA
64	#676767	2	59	1	120	1.5	2.5	58.5	59.5	NA
65	#636363	2	58	1	119	1.5	2.5	57.5	58.5	NA
66	black	2	57	1	118	1.5	2.5	56.5	57.5	NA
67	#6A6A6A	2	56	1	117	1.5	2.5	55.5	56.5	NA
68	#939393	2	55	1	116	1.5	2.5	54.5	55.5	NA
69	#606060	2	54	1	115	1.5	2.5	53.5	54.5	NA
70	#4B4B4B	2	53	1	114	1.5	2.5	52.5	53.5	NA
71	#EAEAEA	2	52	1	113	1.5	2.5	51.5	52.5	NA
72	#484848	2	51	1	112	1.5	2.5	50.5	51.5	NA
73	black	2	50	1	111	1.5	2.5	49.5	50.5	NA
74	black	2	49	1	110	1.5	2.5	48.5	49.5	NA
75	#808080	2	48	1	109	1.5	2.5	47.5	48.5	NA
76	#595959	2	47	1	108	1.5	2.5	46.5	47.5	NA
77	#4B4B4B	2	46	1	107	1.5	2.5	45.5	46.5	NA
78	#676767	2	45	1	106	1.5	2.5	44.5	45.5	NA
79	#6A6A6A	2	44	1	105	1.5	2.5	43.5	44.5	NA
80	#979797	2	43	1	104	1.5	2.5	42.5	43.5	NA
81	#484848	2	42	1	103	1.5	2.5	41.5	42.5	NA
82	#4E4E4E	2	41	1	102	1.5	2.5	40.5	41.5	NA
83	#525252	2	40	1	101	1.5	2.5	39.5	40.5	NA
84	#808080	2	39	1	100	1.5	2.5	38.5	39.5	NA
85	#5C5C5C	2	38	1	99	1.5	2.5	37.5	38.5	NA
86	#4E4E4E	2	37	1	98	1.5	2.5	36.5	37.5	NA
87	#595959	2	36	1	97	1.5	2.5	35.5	36.5	NA
88	#4B4B4B	2	35	1	96	1.5	2.5	34.5	35.5	NA
89	#4E4E4E	2	34	1	95	1.5	2.5	33.5	34.5	NA
90	#555555	2	33	1	94	1.5	2.5	32.5	33.5	NA
91	#606060	2	32	1	93	1.5	2.5	31.5	32.5	NA
92	#555555	2	31	1	92	1.5	2.5	30.5	31.5	NA
93	#595959	2	30	1	91	1.5	2.5	29.5	30.5	NA
94	#5C5C5C	2	29	1	90	1.5	2.5	28.5	29.5	NA
95	#525252	2	28	1	89	1.5	2.5	27.5	28.5	NA
96	#525252	2	27	1	88	1.5	2.5	26.5	27.5	NA
97	#555555	2	26	1	87	1.5	2.5	25.5	26.5	NA
98	#525252	2	25	1	86	1.5	2.5	24.5	25.5	NA
99	black	2	24	1	85	1.5	2.5	23.5	24.5	NA
100	#4E4E4E	2	23	1	84	1.5	2.5	22.5	23.5	NA
101	#6E6E6E	2	22	1	83	1.5	2.5	21.5	22.5	NA
102	#4B4B4B	2	21	1	82	1.5	2.5	20.5	21.5	NA
103	#606060	2	20	1	81	1.5	2.5	19.5	20.5	NA
104	#4E4E4E	2	19	1	80	1.5	2.5	18.5	19.5	NA
105	#717171	2	18	1	79	1.5	2.5	17.5	18.5	NA
106	#8F8F8F	2	17	1	78	1.5	2.5	16.5	17.5	NA

107	#757575	2	16	1	77	1.5	2.5	15.5	16.5	NA
108	#DADADA	2	15	1	76	1.5	2.5	14.5	15.5	NA
109	#797979	2	14	1	75	1.5	2.5	13.5	14.5	NA
110	#717171	2	13	1	74	1.5	2.5	12.5	13.5	NA
111	#525252	2	12	1	73	1.5	2.5	11.5	12.5	NA
112	black	2	11	1	72	1.5	2.5	10.5	11.5	NA
113	#8B8B8B	2	10	1	71	1.5	2.5	9.5	10.5	NA
114	#AAAAAA	2	9	1	70	1.5	2.5	8.5	9.5	NA
115	#A2A2A2	2	8	1	69	1.5	2.5	7.5	8.5	NA
116	#2E2E2E	2	7	1	68	1.5	2.5	6.5	7.5	NA
117	#222222	2	6	1	67	1.5	2.5	5.5	6.5	NA
118	#BABABA	2	5	1	66	1.5	2.5	4.5	5.5	NA
119	#979797	2	4	1	65	1.5	2.5	3.5	4.5	NA
120	#797979	2	3	1	64	1.5	2.5	2.5	3.5	NA
121	#979797	2	2	1	63	1.5	2.5	1.5	2.5	NA
122	#8F8F8F	2	1	1	62	1.5	2.5	0.5	1.5	NA
123	#676767	3	61	1	183	2.5	3.5	60.5	61.5	NA
124	#555555	3	60	1	182	2.5	3.5	59.5	60.5	NA
125	#757575	3	59	1	181	2.5	3.5	58.5	59.5	NA
126	#6A6A6A	3	58	1	180	2.5	3.5	57.5	58.5	NA
127	black	3	57	1	179	2.5	3.5	56.5	57.5	NA
128	#5C5C5C	3	56	1	178	2.5	3.5	55.5	56.5	NA
129	#4B4B4B	3	55	1	177	2.5	3.5	54.5	55.5	NA
130	#555555	3	54	1	176	2.5	3.5	53.5	54.5	NA
131	#4E4E4E	3	53	1	175	2.5	3.5	52.5	53.5	NA
132	#9A9A9A	3	52	1	174	2.5	3.5	51.5	52.5	NA
133	#606060	3	51	1	173	2.5	3.5	50.5	51.5	NA
134	black	3	50	1	172	2.5	3.5	49.5	50.5	NA
135	black	3	49	1	171	2.5	3.5	48.5	49.5	NA
136	#595959	3	48	1	170	2.5	3.5	47.5	48.5	NA
137	#636363	3	47	1	169	2.5	3.5	46.5	47.5	NA
138	#636363	3	46	1	168	2.5	3.5	45.5	46.5	NA
139	#757575	3	45	1	167	2.5	3.5	44.5	45.5	NA
140	#676767	3	44	1	166	2.5	3.5	43.5	44.5	NA
141	#676767	3	43	1	165	2.5	3.5	42.5	43.5	NA
142	#4B4B4B	3	42	1	164	2.5	3.5	41.5	42.5	NA
143	#525252	3	41	1	163	2.5	3.5	40.5	41.5	NA
144	#595959	3	40	1	162	2.5	3.5	39.5	40.5	NA
145	#595959	3	39	1	161	2.5	3.5	38.5	39.5	NA
146	#6A6A6A	3	38	1	160	2.5	3.5	37.5	38.5	NA
147	#595959	3	37	1	159	2.5	3.5	36.5	37.5	NA
148	#676767	3	36	1	158	2.5	3.5	35.5	36.5	NA
149	#4E4E4E	3	35	1	157	2.5	3.5	34.5	35.5	NA
150	#555555	3	34	1	156	2.5	3.5	33.5	34.5	NA
151	#4E4E4E	3	33	1	155	2.5	3.5	32.5	33.5	NA

152	#525252	3	32	1	154	2.5	3.5	31.5	32.5	NA
153	#525252	3	31	1	153	2.5	3.5	30.5	31.5	NA
154	#4B4B4B	3	30	1	152	2.5	3.5	29.5	30.5	NA
155	#6A6A6A	3	29	1	151	2.5	3.5	28.5	29.5	NA
156	#606060	3	28	1	150	2.5	3.5	27.5	28.5	NA
157	#4E4E4E	3	27	1	149	2.5	3.5	26.5	27.5	NA
158	#595959	3	26	1	148	2.5	3.5	25.5	26.5	NA
159	#5C5C5C	3	25	1	147	2.5	3.5	24.5	25.5	NA
160	black	3	24	1	146	2.5	3.5	23.5	24.5	NA
161	#636363	3	23	1	145	2.5	3.5	22.5	23.5	NA
162	#636363	3	22	1	144	2.5	3.5	21.5	22.5	NA
163	#595959	3	21	1	143	2.5	3.5	20.5	21.5	NA
164	#525252	3	20	1	142	2.5	3.5	19.5	20.5	NA
165	#676767	3	19	1	141	2.5	3.5	18.5	19.5	NA
166	#9A9A9A	3	18	1	140	2.5	3.5	17.5	18.5	NA
167	#B6B6B6	3	17	1	139	2.5	3.5	16.5	17.5	NA
168	#A6A6A6	3	16	1	138	2.5	3.5	15.5	16.5	NA
169	#FFFFFF	3	15	1	137	2.5	3.5	14.5	15.5	NA
170	#6A6A6A	3	14	1	136	2.5	3.5	13.5	14.5	NA
171	#EAEAEA	3	13	1	135	2.5	3.5	12.5	13.5	NA
172	#5C5C5C	3	12	1	134	2.5	3.5	11.5	12.5	NA
173	black	3	11	1	133	2.5	3.5	10.5	11.5	NA
174	#7C7C7C	3	10	1	132	2.5	3.5	9.5	10.5	NA
175	#AAAAAA	3	9	1	131	2.5	3.5	8.5	9.5	NA
176	#BEBEBE	3	8	1	130	2.5	3.5	7.5	8.5	NA
177	#343434	3	7	1	129	2.5	3.5	6.5	7.5	NA
178	#414141	3	6	1	128	2.5	3.5	5.5	6.5	NA
179	#A6A6A6	3	5	1	127	2.5	3.5	4.5	5.5	NA
180	#808080	3	4	1	126	2.5	3.5	3.5	4.5	NA
181	#636363	3	3	1	125	2.5	3.5	2.5	3.5	NA
182	#808080	3	2	1	124	2.5	3.5	1.5	2.5	NA
183	#979797	3	1	1	123	2.5	3.5	0.5	1.5	NA
184	#595959	4	61	1	244	3.5	4.5	60.5	61.5	NA
185	#444444	4	60	1	243	3.5	4.5	59.5	60.5	NA
186	#555555	4	59	1	242	3.5	4.5	58.5	59.5	NA
187	#525252	4	58	1	241	3.5	4.5	57.5	58.5	NA
188	black	4	57	1	240	3.5	4.5	56.5	57.5	NA
189	#606060	4	56	1	239	3.5	4.5	55.5	56.5	NA
190	#4B4B4B	4	55	1	238	3.5	4.5	54.5	55.5	NA
191	#595959	4	54	1	237	3.5	4.5	53.5	54.5	NA
192	#444444	4	53	1	236	3.5	4.5	52.5	53.5	NA
193	#595959	4	52	1	235	3.5	4.5	51.5	52.5	NA
194	#525252	4	51	1	234	3.5	4.5	50.5	51.5	NA
195	black	4	50	1	233	3.5	4.5	49.5	50.5	NA
196	black	4	49	1	232	3.5	4.5	48.5	49.5	NA

197	#484848	4 48	1	231	3.5	4.5	47.5	48.5	NA
198	#4E4E4E	4 47	1	230	3.5	4.5	46.5	47.5	NA
199	#606060	4 46	1	229	3.5	4.5	45.5	46.5	NA
200	#717171	4 45	1	228	3.5	4.5	44.5	45.5	NA
201	#4E4E4E	4 44	1	227	3.5	4.5	43.5	44.5	NA
202	#4B4B4B	4 43	1	226	3.5	4.5	42.5	43.5	NA
203	#4E4E4E	4 42	1	225	3.5	4.5	41.5	42.5	NA
204	#444444	4 41	1	224	3.5	4.5	40.5	41.5	NA
205	#4E4E4E	4 40	1	223	3.5	4.5	39.5	40.5	NA
206	#414141	4 39	1	222	3.5	4.5	38.5	39.5	NA
207	#606060	4 38	1	221	3.5	4.5	37.5	38.5	NA
208	#5C5C5C	4 37	1	220	3.5	4.5	36.5	37.5	NA
209	#636363	4 36	1	219	3.5	4.5	35.5	36.5	NA
210	#484848	4 35	1	218	3.5	4.5	34.5	35.5	NA
211	#3E3E3E	4 34	1	217	3.5	4.5	33.5	34.5	NA
212	#484848	4 33	1	216	3.5	4.5	32.5	33.5	NA
213	#484848	4 32	1	215	3.5	4.5	31.5	32.5	NA
214	#484848	4 31	1	214	3.5	4.5	30.5	31.5	NA
215	#525252	4 30	1	213	3.5	4.5	29.5	30.5	NA
216	#5C5C5C	4 29	1	212	3.5	4.5	28.5	29.5	NA
217	#4E4E4E	4 28	1	211	3.5	4.5	27.5	28.5	NA
218	#4E4E4E	4 27	1	210	3.5	4.5	26.5	27.5	NA
219	#4B4B4B	4 26	1	209	3.5	4.5	25.5	26.5	NA
220	#595959	4 25	1	208	3.5	4.5	24.5	25.5	NA
221	black	4 24	1	207	3.5	4.5	23.5	24.5	NA
222	#444444	4 23	1	206	3.5	4.5	22.5	23.5	NA
223	#5C5C5C	4 22	1	205	3.5	4.5	21.5	22.5	NA
224	#5C5C5C	4 21	1	204	3.5	4.5	20.5	21.5	NA
225	#4B4B4B	4 20	1	203	3.5	4.5	19.5	20.5	NA
226	#595959	4 19	1	202	3.5	4.5	18.5	19.5	NA
227	#222222	4 18	1	201	3.5	4.5	17.5	18.5	NA
228	#AEAEAE	4 17	1	200	3.5	4.5	16.5	17.5	NA
229	#636363	4 16	1	199	3.5	4.5	15.5	16.5	NA
230	#414141	4 15	1	198	3.5	4.5	14.5	15.5	NA
231	#414141	4 14	1	197	3.5	4.5	13.5	14.5	NA
232	#5C5C5C	4 13	1	196	3.5	4.5	12.5	13.5	NA
233	#444444	4 12	1	195	3.5	4.5	11.5	12.5	NA
234	black	4 11	1	194	3.5	4.5	10.5	11.5	NA
235	#757575	4 10	1	193	3.5	4.5	9.5	10.5	NA
236	#5C5C5C	4 9	1	192	3.5	4.5	8.5	9.5	NA
237	#7C7C7C	4 8	1	191	3.5	4.5	7.5	8.5	NA
238	#2B2B2B	4 7	1	190	3.5	4.5	6.5	7.5	NA
239	#1C1C1C	4 6	1	189	3.5	4.5	5.5	6.5	NA
240	#373737	4 5	1	188	3.5	4.5	4.5	5.5	NA
241	#4E4E4E	4 4	1	187	3.5	4.5	3.5	4.5	NA

242	#5C5C5C	4	3	1	186	3.5	4.5	2.5	3.5	NA
243	#606060	4	2	1	185	3.5	4.5	1.5	2.5	NA
244	#606060	4	1	1	184	3.5	4.5	0.5	1.5	NA
245	#444444	5	61	1	305	4.5	5.5	60.5	61.5	NA
246	#606060	5	60	1	304	4.5	5.5	59.5	60.5	NA
247	#555555	5	59	1	303	4.5	5.5	58.5	59.5	NA
248	#4B4B4B	5	58	1	302	4.5	5.5	57.5	58.5	NA
249	black	5	57	1	301	4.5	5.5	56.5	57.5	NA
250	#5C5C5C	5	56	1	300	4.5	5.5	55.5	56.5	NA
251	#636363	5	55	1	299	4.5	5.5	54.5	55.5	NA
252	#595959	5	54	1	298	4.5	5.5	53.5	54.5	NA
253	#3A3A3A	5	53	1	297	4.5	5.5	52.5	53.5	NA
254	#343434	5	52	1	296	4.5	5.5	51.5	52.5	NA
255	#444444	5	51	1	295	4.5	5.5	50.5	51.5	NA
256	black	5	50	1	294	4.5	5.5	49.5	50.5	NA
257	black	5	49	1	293	4.5	5.5	48.5	49.5	NA
258	#4E4E4E	5	48	1	292	4.5	5.5	47.5	48.5	NA
259	#6E6E6E	5	47	1	291	4.5	5.5	46.5	47.5	NA
260	#6E6E6E	5	46	1	290	4.5	5.5	45.5	46.5	NA
261	#676767	5	45	1	289	4.5	5.5	44.5	45.5	NA
262	#414141	5	44	1	288	4.5	5.5	43.5	44.5	NA
263	#555555	5	43	1	287	4.5	5.5	42.5	43.5	NA
264	#5C5C5C	5	42	1	286	4.5	5.5	41.5	42.5	NA
265	#4B4B4B	5	41	1	285	4.5	5.5	40.5	41.5	NA
266	#3E3E3E	5	40	1	284	4.5	5.5	39.5	40.5	NA
267	#595959	5	39	1	283	4.5	5.5	38.5	39.5	NA
268	#3A3A3A	5	38	1	282	4.5	5.5	37.5	38.5	NA
269	#5C5C5C	5	37	1	281	4.5	5.5	36.5	37.5	NA
270	#3A3A3A	5	36	1	280	4.5	5.5	35.5	36.5	NA
271	#4E4E4E	5	35	1	279	4.5	5.5	34.5	35.5	NA
272	#525252	5	34	1	278	4.5	5.5	33.5	34.5	NA
273	#444444	5	33	1	277	4.5	5.5	32.5	33.5	NA
274	#5C5C5C	5	32	1	276	4.5	5.5	31.5	32.5	NA
275	#484848	5	31	1	275	4.5	5.5	30.5	31.5	NA
276	#484848	5	30	1	274	4.5	5.5	29.5	30.5	NA
277	#636363	5	29	1	273	4.5	5.5	28.5	29.5	NA
278	#606060	5	28	1	272	4.5	5.5	27.5	28.5	NA
279	#444444	5	27	1	271	4.5	5.5	26.5	27.5	NA
280	#6E6E6E	5	26	1	270	4.5	5.5	25.5	26.5	NA
281	#444444	5	25	1	269	4.5	5.5	24.5	25.5	NA
282	black	5	24	1	268	4.5	5.5	23.5	24.5	NA
283	#717171	5	23	1	267	4.5	5.5	22.5	23.5	NA
284	#6A6A6A	5	22	1	266	4.5	5.5	21.5	22.5	NA
285	#595959	5	21	1	265	4.5	5.5	20.5	21.5	NA
286	#797979	5	20	1	264	4.5	5.5	19.5	20.5	NA

287	#717171	5 19	1	263	4.5	5.5	18.5	19.5	NA
288	#8F8F8F	5 18	1	262	4.5	5.5	17.5	18.5	NA
289	#414141	5 17	1	261	4.5	5.5	16.5	17.5	NA
290	#6A6A6A	5 16	1	260	4.5	5.5	15.5	16.5	NA
291	#808080	5 15	1	259	4.5	5.5	14.5	15.5	NA
292	#1C1C1C	5 14	1	258	4.5	5.5	13.5	14.5	NA
293	#676767	5 13	1	257	4.5	5.5	12.5	13.5	NA
294	#888888	5 12	1	256	4.5	5.5	11.5	12.5	NA
295	black	5 11	1	255	4.5	5.5	10.5	11.5	NA
296	#2B2B2B	5 10	1	254	4.5	5.5	9.5	10.5	NA
297	#5C5C5C	5 9	1	253	4.5	5.5	8.5	9.5	NA
298	#636363	5 8	1	252	4.5	5.5	7.5	8.5	NA
299	#4B4B4B	5 7	1	251	4.5	5.5	6.5	7.5	NA
300	#797979	5 6	1	250	4.5	5.5	5.5	6.5	NA
301	#5C5C5C	5 5	1	249	4.5	5.5	4.5	5.5	NA
302	#3A3A3A	5 4	1	248	4.5	5.5	3.5	4.5	NA
303	#373737	5 3	1	247	4.5	5.5	2.5	3.5	NA
304	#3A3A3A	5 2	1	246	4.5	5.5	1.5	2.5	NA
305	#595959	5 1	1	245	4.5	5.5	0.5	1.5	NA
306	#3A3A3A	6 61	1	366	5.5	6.5	60.5	61.5	NA
307	#414141	6 60	1	365	5.5	6.5	59.5	60.5	NA
308	#3A3A3A	6 59	1	364	5.5	6.5	58.5	59.5	NA
309	#4E4E4E	6 58	1	363	5.5	6.5	57.5	58.5	NA
310	black	6 57	1	362	5.5	6.5	56.5	57.5	NA
311	#4E4E4E	6 56	1	361	5.5	6.5	55.5	56.5	NA
312	#6E6E6E	6 55	1	360	5.5	6.5	54.5	55.5	NA
313	#595959	6 54	1	359	5.5	6.5	53.5	54.5	NA
314	#484848	6 53	1	358	5.5	6.5	52.5	53.5	NA
315	#3A3A3A	6 52	1	357	5.5	6.5	51.5	52.5	NA
316	#3E3E3E	6 51	1	356	5.5	6.5	50.5	51.5	NA
317	black	6 50	1	355	5.5	6.5	49.5	50.5	NA
318	black	6 49	1	354	5.5	6.5	48.5	49.5	NA
319	#555555	6 48	1	353	5.5	6.5	47.5	48.5	NA
320	#525252	6 47	1	352	5.5	6.5	46.5	47.5	NA
321	#444444	6 46	1	351	5.5	6.5	45.5	46.5	NA
322	#606060	6 45	1	350	5.5	6.5	44.5	45.5	NA
323	#555555	6 44	1	349	5.5	6.5	43.5	44.5	NA
324	#444444	6 43	1	348	5.5	6.5	42.5	43.5	NA
325	#5C5C5C	6 42	1	347	5.5	6.5	41.5	42.5	NA
326	#3E3E3E	6 41	1	346	5.5	6.5	40.5	41.5	NA
327	#5C5C5C	6 40	1	345	5.5	6.5	39.5	40.5	NA
328	#636363	6 39	1	344	5.5	6.5	38.5	39.5	NA
329	#444444	6 38	1	343	5.5	6.5	37.5	38.5	NA
330	#636363	6 37	1	342	5.5	6.5	36.5	37.5	NA
331	#444444	6 36	1	341	5.5	6.5	35.5	36.5	NA

332	#555555	6	35	1	340	5.5	6.5	34.5	35.5	NA
333	#525252	6	34	1	339	5.5	6.5	33.5	34.5	NA
334	#606060	6	33	1	338	5.5	6.5	32.5	33.5	NA
335	#4B4B4B	6	32	1	337	5.5	6.5	31.5	32.5	NA
336	#4B4B4B	6	31	1	336	5.5	6.5	30.5	31.5	NA
337	#4E4E4E	6	30	1	335	5.5	6.5	29.5	30.5	NA
338	#525252	6	29	1	334	5.5	6.5	28.5	29.5	NA
339	#484848	6	28	1	333	5.5	6.5	27.5	28.5	NA
340	#484848	6	27	1	332	5.5	6.5	26.5	27.5	NA
341	#3E3E3E	6	26	1	331	5.5	6.5	25.5	26.5	NA
342	#525252	6	25	1	330	5.5	6.5	24.5	25.5	NA
343	black	6	24	1	329	5.5	6.5	23.5	24.5	NA
344	#4E4E4E	6	23	1	328	5.5	6.5	22.5	23.5	NA
345	#676767	6	22	1	327	5.5	6.5	21.5	22.5	NA
346	#444444	6	21	1	326	5.5	6.5	20.5	21.5	NA
347	#757575	6	20	1	325	5.5	6.5	19.5	20.5	NA
348	#606060	6	19	1	324	5.5	6.5	18.5	19.5	NA
349	#606060	6	18	1	323	5.5	6.5	17.5	18.5	NA
350	#313131	6	17	1	322	5.5	6.5	16.5	17.5	NA
351	#676767	6	16	1	321	5.5	6.5	15.5	16.5	NA
352	#5C5C5C	6	15	1	320	5.5	6.5	14.5	15.5	NA
353	#222222	6	14	1	319	5.5	6.5	13.5	14.5	NA
354	#6A6A6A	6	13	1	318	5.5	6.5	12.5	13.5	NA
355	#797979	6	12	1	317	5.5	6.5	11.5	12.5	NA
356	black	6	11	1	316	5.5	6.5	10.5	11.5	NA
357	#252525	6	10	1	315	5.5	6.5	9.5	10.5	NA
358	#4E4E4E	6	9	1	314	5.5	6.5	8.5	9.5	NA
359	#595959	6	8	1	313	5.5	6.5	7.5	8.5	NA
360	#3A3A3A	6	7	1	312	5.5	6.5	6.5	7.5	NA
361	#606060	6	6	1	311	5.5	6.5	5.5	6.5	NA
362	#484848	6	5	1	310	5.5	6.5	4.5	5.5	NA
363	#373737	6	4	1	309	5.5	6.5	3.5	4.5	NA
364	#252525	6	3	1	308	5.5	6.5	2.5	3.5	NA
365	#2B2B2B	6	2	1	307	5.5	6.5	1.5	2.5	NA
366	#595959	6	1	1	306	5.5	6.5	0.5	1.5	NA
367	#444444	7	61	1	427	6.5	7.5	60.5	61.5	NA
368	#555555	7	60	1	426	6.5	7.5	59.5	60.5	NA
369	#444444	7	59	1	425	6.5	7.5	58.5	59.5	NA
370	#595959	7	58	1	424	6.5	7.5	57.5	58.5	NA
371	black	7	57	1	423	6.5	7.5	56.5	57.5	NA
372	#525252	7	56	1	422	6.5	7.5	55.5	56.5	NA
373	#5C5C5C	7	55	1	421	6.5	7.5	54.5	55.5	NA
374	#4E4E4E	7	54	1	420	6.5	7.5	53.5	54.5	NA
375	#313131	7	53	1	419	6.5	7.5	52.5	53.5	NA
376	#4B4B4B	7	52	1	418	6.5	7.5	51.5	52.5	NA

377	#444444	7	51	1	417	6.5	7.5	50.5	51.5	NA
378	black	7	50	1	416	6.5	7.5	49.5	50.5	NA
379	black	7	49	1	415	6.5	7.5	48.5	49.5	NA
380	#6A6A6A	7	48	1	414	6.5	7.5	47.5	48.5	NA
381	#484848	7	47	1	413	6.5	7.5	46.5	47.5	NA
382	#4E4E4E	7	46	1	412	6.5	7.5	45.5	46.5	NA
383	#6E6E6E	7	45	1	411	6.5	7.5	44.5	45.5	NA
384	#3A3A3A	7	44	1	410	6.5	7.5	43.5	44.5	NA
385	#444444	7	43	1	409	6.5	7.5	42.5	43.5	NA
386	#3A3A3A	7	42	1	408	6.5	7.5	41.5	42.5	NA
387	#4B4B4B	7	41	1	407	6.5	7.5	40.5	41.5	NA
388	#484848	7	40	1	406	6.5	7.5	39.5	40.5	NA
389	#595959	7	39	1	405	6.5	7.5	38.5	39.5	NA
390	#525252	7	38	1	404	6.5	7.5	37.5	38.5	NA
391	#717171	7	37	1	403	6.5	7.5	36.5	37.5	NA
392	#525252	7	36	1	402	6.5	7.5	35.5	36.5	NA
393	#4B4B4B	7	35	1	401	6.5	7.5	34.5	35.5	NA
394	#484848	7	34	1	400	6.5	7.5	33.5	34.5	NA
395	#484848	7	33	1	399	6.5	7.5	32.5	33.5	NA
396	#373737	7	32	1	398	6.5	7.5	31.5	32.5	NA
397	#525252	7	31	1	397	6.5	7.5	30.5	31.5	NA
398	#4B4B4B	7	30	1	396	6.5	7.5	29.5	30.5	NA
399	#636363	7	29	1	395	6.5	7.5	28.5	29.5	NA
400	#676767	7	28	1	394	6.5	7.5	27.5	28.5	NA
401	#444444	7	27	1	393	6.5	7.5	26.5	27.5	NA
402	#3A3A3A	7	26	1	392	6.5	7.5	25.5	26.5	NA
403	#414141	7	25	1	391	6.5	7.5	24.5	25.5	NA
404	black	7	24	1	390	6.5	7.5	23.5	24.5	NA
405	#4B4B4B	7	23	1	389	6.5	7.5	22.5	23.5	NA
406	#5C5C5C	7	22	1	388	6.5	7.5	21.5	22.5	NA
407	#484848	7	21	1	387	6.5	7.5	20.5	21.5	NA
408	#6E6E6E	7	20	1	386	6.5	7.5	19.5	20.5	NA
409	#5C5C5C	7	19	1	385	6.5	7.5	18.5	19.5	NA
410	#717171	7	18	1	384	6.5	7.5	17.5	18.5	NA
411	#282828	7	17	1	383	6.5	7.5	16.5	17.5	NA
412	#6A6A6A	7	16	1	382	6.5	7.5	15.5	16.5	NA
413	#555555	7	15	1	381	6.5	7.5	14.5	15.5	NA
414	#1C1C1C	7	14	1	380	6.5	7.5	13.5	14.5	NA
415	#6E6E6E	7	13	1	379	6.5	7.5	12.5	13.5	NA
416	#8B8B8B	7	12	1	378	6.5	7.5	11.5	12.5	NA
417	black	7	11	1	377	6.5	7.5	10.5	11.5	NA
418	#313131	7	10	1	376	6.5	7.5	9.5	10.5	NA
419	#606060	7	9	1	375	6.5	7.5	8.5	9.5	NA
420	#636363	7	8	1	374	6.5	7.5	7.5	8.5	NA
421	#2E2E2E	7	7	1	373	6.5	7.5	6.5	7.5	NA

422	#636363	7	6	1	372	6.5	7.5	5.5	6.5	NA
423	#4E4E4E	7	5	1	371	6.5	7.5	4.5	5.5	NA
424	#343434	7	4	1	370	6.5	7.5	3.5	4.5	NA
425	#222222	7	3	1	369	6.5	7.5	2.5	3.5	NA
426	#2B2B2B	7	2	1	368	6.5	7.5	1.5	2.5	NA
427	#595959	7	1	1	367	6.5	7.5	0.5	1.5	NA
428	#6E6E6E	8	61	1	488	7.5	8.5	60.5	61.5	NA
429	#676767	8	60	1	487	7.5	8.5	59.5	60.5	NA
430	#717171	8	59	1	486	7.5	8.5	58.5	59.5	NA
431	#757575	8	58	1	485	7.5	8.5	57.5	58.5	NA
432	black	8	57	1	484	7.5	8.5	56.5	57.5	NA
433	#7C7C7C	8	56	1	483	7.5	8.5	55.5	56.5	NA
434	#676767	8	55	1	482	7.5	8.5	54.5	55.5	NA
435	#797979	8	54	1	481	7.5	8.5	53.5	54.5	NA
436	#717171	8	53	1	480	7.5	8.5	52.5	53.5	NA
437	#7C7C7C	8	52	1	479	7.5	8.5	51.5	52.5	NA
438	#7C7C7C	8	51	1	478	7.5	8.5	50.5	51.5	NA
439	black	8	50	1	477	7.5	8.5	49.5	50.5	NA
440	black	8	49	1	476	7.5	8.5	48.5	49.5	NA
441	#757575	8	48	1	475	7.5	8.5	47.5	48.5	NA
442	#797979	8	47	1	474	7.5	8.5	46.5	47.5	NA
443	#8B8B8B	8	46	1	473	7.5	8.5	45.5	46.5	NA
444	#7C7C7C	8	45	1	472	7.5	8.5	44.5	45.5	NA
445	#808080	8	44	1	471	7.5	8.5	43.5	44.5	NA
446	#939393	8	43	1	470	7.5	8.5	42.5	43.5	NA
447	#6E6E6E	8	42	1	469	7.5	8.5	41.5	42.5	NA
448	#676767	8	41	1	468	7.5	8.5	40.5	41.5	NA
449	#7C7C7C	8	40	1	467	7.5	8.5	39.5	40.5	NA
450	#636363	8	39	1	466	7.5	8.5	38.5	39.5	NA
451	#797979	8	38	1	465	7.5	8.5	37.5	38.5	NA
452	#8F8F8F	8	37	1	464	7.5	8.5	36.5	37.5	NA
453	#797979	8	36	1	463	7.5	8.5	35.5	36.5	NA
454	#757575	8	35	1	462	7.5	8.5	34.5	35.5	NA
455	#717171	8	34	1	461	7.5	8.5	33.5	34.5	NA
456	#8F8F8F	8	33	1	460	7.5	8.5	32.5	33.5	NA
457	#6A6A6A	8	32	1	459	7.5	8.5	31.5	32.5	NA
458	#6E6E6E	8	31	1	458	7.5	8.5	30.5	31.5	NA
459	#808080	8	30	1	457	7.5	8.5	29.5	30.5	NA
460	#8B8B8B	8	29	1	456	7.5	8.5	28.5	29.5	NA
461	#797979	8	28	1	455	7.5	8.5	27.5	28.5	NA
462	#848484	8	27	1	454	7.5	8.5	26.5	27.5	NA
463	#7C7C7C	8	26	1	453	7.5	8.5	25.5	26.5	NA
464	#606060	8	25	1	452	7.5	8.5	24.5	25.5	NA
465	black	8	24	1	451	7.5	8.5	23.5	24.5	NA
466	#B2B2B2	8	23	1	450	7.5	8.5	22.5	23.5	NA

467	#8B8B8B	8 22	1	449	7.5	8.5	21.5	22.5	NA
468	#717171	8 21	1	448	7.5	8.5	20.5	21.5	NA
469	#8B8B8B	8 20	1	447	7.5	8.5	19.5	20.5	NA
470	#848484	8 19	1	446	7.5	8.5	18.5	19.5	NA
471	#B2B2B2	8 18	1	445	7.5	8.5	17.5	18.5	NA
472	#595959	8 17	1	444	7.5	8.5	16.5	17.5	NA
473	#888888	8 16	1	443	7.5	8.5	15.5	16.5	NA
474	#B6B6B6	8 15	1	442	7.5	8.5	14.5	15.5	NA
475	#373737	8 14	1	441	7.5	8.5	13.5	14.5	NA
476	#9A9A9A	8 13	1	440	7.5	8.5	12.5	13.5	NA
477	#939393	8 12	1	439	7.5	8.5	11.5	12.5	NA
478	black	8 11	1	438	7.5	8.5	10.5	11.5	NA
479	#555555	8 10	1	437	7.5	8.5	9.5	10.5	NA
480	#676767	8 9	1	436	7.5	8.5	8.5	9.5	NA
481	#717171	8 8	1	435	7.5	8.5	7.5	8.5	NA
482	#A6A6A6	8 7	1	434	7.5	8.5	6.5	7.5	NA
483	#979797	8 6	1	433	7.5	8.5	5.5	6.5	NA
484	#8F8F8F	8 5	1	432	7.5	8.5	4.5	5.5	NA
485	#4E4E4E	8 4	1	431	7.5	8.5	3.5	4.5	NA
486	#444444	8 3	1	430	7.5	8.5	2.5	3.5	NA
487	#525252	8 2	1	429	7.5	8.5	1.5	2.5	NA
488	#676767	8 1	1	428	7.5	8.5	0.5	1.5	NA
489	#AEAEAE	9 61	1	549	8.5	9.5	60.5	61.5	NA
490	#B6B6B6	9 60	1	548	8.5	9.5	59.5	60.5	NA
491	#979797	9 59	1	547	8.5	9.5	58.5	59.5	NA
492	#A2A2A2	9 58	1	546	8.5	9.5	57.5	58.5	NA
493	black	9 57	1	545	8.5	9.5	56.5	57.5	NA
494	#808080	9 56	1	544	8.5	9.5	55.5	56.5	NA
495	#BEBEBE	9 55	1	543	8.5	9.5	54.5	55.5	NA
496	#A6A6A6	9 54	1	542	8.5	9.5	53.5	54.5	NA
497	#8B8B8B	9 53	1	541	8.5	9.5	52.5	53.5	NA
498	#A2A2A2	9 52	1	540	8.5	9.5	51.5	52.5	NA
499	#8F8F8F	9 51	1	539	8.5	9.5	50.5	51.5	NA
500	black	9 50	1	538	8.5	9.5	49.5	50.5	NA
501	black	9 49	1	537	8.5	9.5	48.5	49.5	NA
502	#888888	9 48	1	536	8.5	9.5	47.5	48.5	NA
503	#B6B6B6	9 47	1	535	8.5	9.5	46.5	47.5	NA
504	#C2C2C2	9 46	1	534	8.5	9.5	45.5	46.5	NA
505	#C6C6C6	9 45	1	533	8.5	9.5	44.5	45.5	NA
506	#B6B6B6	9 44	1	532	8.5	9.5	43.5	44.5	NA
507	#C6C6C6	9 43	1	531	8.5	9.5	42.5	43.5	NA
508	#B6B6B6	9 42	1	530	8.5	9.5	41.5	42.5	NA
509	#B6B6B6	9 41	1	529	8.5	9.5	40.5	41.5	NA
510	#BEBEBE	9 40	1	528	8.5	9.5	39.5	40.5	NA
511	#AEAEAE	9 39	1	527	8.5	9.5	38.5	39.5	NA

512	#979797	9	38	1	526	8.5	9.5	37.5	38.5	NA
513	#BABABA	9	37	1	525	8.5	9.5	36.5	37.5	NA
514	#9A9A9A	9	36	1	524	8.5	9.5	35.5	36.5	NA
515	#C2C2C2	9	35	1	523	8.5	9.5	34.5	35.5	NA
516	#AAAAAA	9	34	1	522	8.5	9.5	33.5	34.5	NA
517	#A2A2A2	9	33	1	521	8.5	9.5	32.5	33.5	NA
518	#A6A6A6	9	32	1	520	8.5	9.5	31.5	32.5	NA
519	#888888	9	31	1	519	8.5	9.5	30.5	31.5	NA
520	#B2B2B2	9	30	1	518	8.5	9.5	29.5	30.5	NA
521	#AEAEAE	9	29	1	517	8.5	9.5	28.5	29.5	NA
522	#BEBEBE	9	28	1	516	8.5	9.5	27.5	28.5	NA
523	#797979	9	27	1	515	8.5	9.5	26.5	27.5	NA
524	#8B8B8B	9	26	1	514	8.5	9.5	25.5	26.5	NA
525	#717171	9	25	1	513	8.5	9.5	24.5	25.5	NA
526	black	9	24	1	512	8.5	9.5	23.5	24.5	NA
527	#B6B6B6	9	23	1	511	8.5	9.5	22.5	23.5	NA
528	#CACACA	9	22	1	510	8.5	9.5	21.5	22.5	NA
529	#8F8F8F	9	21	1	509	8.5	9.5	20.5	21.5	NA
530	#B2B2B2	9	20	1	508	8.5	9.5	19.5	20.5	NA
531	#A6A6A6	9	19	1	507	8.5	9.5	18.5	19.5	NA
532	#EAEAEA	9	18	1	506	8.5	9.5	17.5	18.5	NA
533	#555555	9	17	1	505	8.5	9.5	16.5	17.5	NA
534	#BABABA	9	16	1	504	8.5	9.5	15.5	16.5	NA
535	#CECECE	9	15	1	503	8.5	9.5	14.5	15.5	NA
536	#4E4E4E	9	14	1	502	8.5	9.5	13.5	14.5	NA
537	#9E9E9E	9	13	1	501	8.5	9.5	12.5	13.5	NA
538	#B2B2B2	9	12	1	500	8.5	9.5	11.5	12.5	NA
539	black	9	11	1	499	8.5	9.5	10.5	11.5	NA
540	#676767	9	10	1	498	8.5	9.5	9.5	10.5	NA
541	#B2B2B2	9	9	1	497	8.5	9.5	8.5	9.5	NA
542	#A6A6A6	9	8	1	496	8.5	9.5	7.5	8.5	NA
543	#A6A6A6	9	7	1	495	8.5	9.5	6.5	7.5	NA
544	#E2E2E2	9	6	1	494	8.5	9.5	5.5	6.5	NA
545	#B2B2B2	9	5	1	493	8.5	9.5	4.5	5.5	NA
546	#636363	9	4	1	492	8.5	9.5	3.5	4.5	NA
547	#595959	9	3	1	491	8.5	9.5	2.5	3.5	NA
548	#484848	9	2	1	490	8.5	9.5	1.5	2.5	NA
549	#BABABA	9	1	1	489	8.5	9.5	0.5	1.5	NA
550	#AAAAAA	10	61	1	610	9.5	10.5	60.5	61.5	NA
551	#8B8B8B	10	60	1	609	9.5	10.5	59.5	60.5	NA
552	#A6A6A6	10	59	1	608	9.5	10.5	58.5	59.5	NA
553	#9E9E9E	10	58	1	607	9.5	10.5	57.5	58.5	NA
554	black	10	57	1	606	9.5	10.5	56.5	57.5	NA
555	#5C5C5C	10	56	1	605	9.5	10.5	55.5	56.5	NA
556	#9A9A9A	10	55	1	604	9.5	10.5	54.5	55.5	NA

557	#939393	10	54	1	603	9.5	10.5	53.5	54.5	NA
558	#717171	10	53	1	602	9.5	10.5	52.5	53.5	NA
559	#979797	10	52	1	601	9.5	10.5	51.5	52.5	NA
560	#A2A2A2	10	51	1	600	9.5	10.5	50.5	51.5	NA
561	black	10	50	1	599	9.5	10.5	49.5	50.5	NA
562	black	10	49	1	598	9.5	10.5	48.5	49.5	NA
563	#848484	10	48	1	597	9.5	10.5	47.5	48.5	NA
564	#9A9A9A	10	47	1	596	9.5	10.5	46.5	47.5	NA
565	#BEBEBE	10	46	1	595	9.5	10.5	45.5	46.5	NA
566	#BABABA	10	45	1	594	9.5	10.5	44.5	45.5	NA
567	#9E9E9E	10	44	1	593	9.5	10.5	43.5	44.5	NA
568	#BABABA	10	43	1	592	9.5	10.5	42.5	43.5	NA
569	#B2B2B2	10	42	1	591	9.5	10.5	41.5	42.5	NA
570	#B6B6B6	10	41	1	590	9.5	10.5	40.5	41.5	NA
571	#AAAAAA	10	40	1	589	9.5	10.5	39.5	40.5	NA
572	#8B8B8B	10	39	1	588	9.5	10.5	38.5	39.5	NA
573	#8F8F8F	10	38	1	587	9.5	10.5	37.5	38.5	NA
574	#AAAAAA	10	37	1	586	9.5	10.5	36.5	37.5	NA
575	#939393	10	36	1	585	9.5	10.5	35.5	36.5	NA
576	#BABABA	10	35	1	584	9.5	10.5	34.5	35.5	NA
577	#636363	10	34	1	583	9.5	10.5	33.5	34.5	NA
578	#939393	10	33	1	582	9.5	10.5	32.5	33.5	NA
579	#A2A2A2	10	32	1	581	9.5	10.5	31.5	32.5	NA
580	#808080	10	31	1	580	9.5	10.5	30.5	31.5	NA
581	#A2A2A2	10	30	1	579	9.5	10.5	29.5	30.5	NA
582	#AEAEAE	10	29	1	578	9.5	10.5	28.5	29.5	NA
583	#AAAAAA	10	28	1	577	9.5	10.5	27.5	28.5	NA
584	#7C7C7C	10	27	1	576	9.5	10.5	26.5	27.5	NA
585	#A6A6A6	10	26	1	575	9.5	10.5	25.5	26.5	NA
586	#E6E6E6	10	25	1	574	9.5	10.5	24.5	25.5	NA
587	black	10	24	1	573	9.5	10.5	23.5	24.5	NA
588	#AEAEAE	10	23	1	572	9.5	10.5	22.5	23.5	NA
589	#C6C6C6	10	22	1	571	9.5	10.5	21.5	22.5	NA
590	#C6C6C6	10	21	1	570	9.5	10.5	20.5	21.5	NA
591	#BEBEBE	10	20	1	569	9.5	10.5	19.5	20.5	NA
592	#848484	10	19	1	568	9.5	10.5	18.5	19.5	NA
593	#D2D2D2	10	18	1	567	9.5	10.5	17.5	18.5	NA
594	#676767	10	17	1	566	9.5	10.5	16.5	17.5	NA
595	#B2B2B2	10	16	1	565	9.5	10.5	15.5	16.5	NA
596	#CECECE	10	15	1	564	9.5	10.5	14.5	15.5	NA
597	#414141	10	14	1	563	9.5	10.5	13.5	14.5	NA
598	#BEBEBE	10	13	1	562	9.5	10.5	12.5	13.5	NA
599	#B6B6B6	10	12	1	561	9.5	10.5	11.5	12.5	NA
600	black	10	11	1	560	9.5	10.5	10.5	11.5	NA
601	#5C5C5C	10	10	1	559	9.5	10.5	9.5	10.5	NA

602	#BEBEBE	10	9	1	558	9.5	10.5	8.5	9.5	NA
603	#BEBEBE	10	8	1	557	9.5	10.5	7.5	8.5	NA
604	#979797	10	7	1	556	9.5	10.5	6.5	7.5	NA
605	#CECECE	10	6	1	555	9.5	10.5	5.5	6.5	NA
606	#A2A2A2	10	5	1	554	9.5	10.5	4.5	5.5	NA
607	#6A6A6A	10	4	1	553	9.5	10.5	3.5	4.5	NA
608	#595959	10	3	1	552	9.5	10.5	2.5	3.5	NA
609	#4B4B4B	10	2	1	551	9.5	10.5	1.5	2.5	NA
610	#AEAEAE	10	1	1	550	9.5	10.5	0.5	1.5	NA
611	#757575	11	61	1	671	10.5	11.5	60.5	61.5	NA
612	#757575	11	60	1	670	10.5	11.5	59.5	60.5	NA
613	#717171	11	59	1	669	10.5	11.5	58.5	59.5	NA
614	#848484	11	58	1	668	10.5	11.5	57.5	58.5	NA
615	black	11	57	1	667	10.5	11.5	56.5	57.5	NA
616	#808080	11	56	1	666	10.5	11.5	55.5	56.5	NA
617	#808080	11	55	1	665	10.5	11.5	54.5	55.5	NA
618	#717171	11	54	1	664	10.5	11.5	53.5	54.5	NA
619	#717171	11	53	1	663	10.5	11.5	52.5	53.5	NA
620	#848484	11	52	1	662	10.5	11.5	51.5	52.5	NA
621	#797979	11	51	1	661	10.5	11.5	50.5	51.5	NA
622	black	11	50	1	660	10.5	11.5	49.5	50.5	NA
623	black	11	49	1	659	10.5	11.5	48.5	49.5	NA
624	#808080	11	48	1	658	10.5	11.5	47.5	48.5	NA
625	#8F8F8F	11	47	1	657	10.5	11.5	46.5	47.5	NA
626	#848484	11	46	1	656	10.5	11.5	45.5	46.5	NA
627	#939393	11	45	1	655	10.5	11.5	44.5	45.5	NA
628	#757575	11	44	1	654	10.5	11.5	43.5	44.5	NA
629	#979797	11	43	1	653	10.5	11.5	42.5	43.5	NA
630	#888888	11	42	1	652	10.5	11.5	41.5	42.5	NA
631	#8F8F8F	11	41	1	651	10.5	11.5	40.5	41.5	NA
632	#6E6E6E	11	40	1	650	10.5	11.5	39.5	40.5	NA
633	#8F8F8F	11	39	1	649	10.5	11.5	38.5	39.5	NA
634	#6E6E6E	11	38	1	648	10.5	11.5	37.5	38.5	NA
635	#979797	11	37	1	647	10.5	11.5	36.5	37.5	NA
636	#6E6E6E	11	36	1	646	10.5	11.5	35.5	36.5	NA
637	#848484	11	35	1	645	10.5	11.5	34.5	35.5	NA
638	#8B8B8B	11	34	1	644	10.5	11.5	33.5	34.5	NA
639	#9A9A9A	11	33	1	643	10.5	11.5	32.5	33.5	NA
640	#717171	11	32	1	642	10.5	11.5	31.5	32.5	NA
641	#808080	11	31	1	641	10.5	11.5	30.5	31.5	NA
642	#8F8F8F	11	30	1	640	10.5	11.5	29.5	30.5	NA
643	#8F8F8F	11	29	1	639	10.5	11.5	28.5	29.5	NA
644	#939393	11	28	1	638	10.5	11.5	27.5	28.5	NA
645	#6A6A6A	11	27	1	637	10.5	11.5	26.5	27.5	NA
646	#848484	11	26	1	636	10.5	11.5	25.5	26.5	NA

647	#848484	11	25	1	635	10.5	11.5	24.5	25.5	NA
648	black	11	24	1	634	10.5	11.5	23.5	24.5	NA
649	#939393	11	23	1	633	10.5	11.5	22.5	23.5	NA
650	#939393	11	22	1	632	10.5	11.5	21.5	22.5	NA
651	#8F8F8F	11	21	1	631	10.5	11.5	20.5	21.5	NA
652	#7C7C7C	11	20	1	630	10.5	11.5	19.5	20.5	NA
653	#9A9A9A	11	19	1	629	10.5	11.5	18.5	19.5	NA
654	#B2B2B2	11	18	1	628	10.5	11.5	17.5	18.5	NA
655	#606060	11	17	1	627	10.5	11.5	16.5	17.5	NA
656	#AAAAAA	11	16	1	626	10.5	11.5	15.5	16.5	NA
657	#C2C2C2	11	15	1	625	10.5	11.5	14.5	15.5	NA
658	#2B2B2B	11	14	1	624	10.5	11.5	13.5	14.5	NA
659	#9E9E9E	11	13	1	623	10.5	11.5	12.5	13.5	NA
660	#AEAEAE	11	12	1	622	10.5	11.5	11.5	12.5	NA
661	black	11	11	1	621	10.5	11.5	10.5	11.5	NA
662	#595959	11	10	1	620	10.5	11.5	9.5	10.5	NA
663	#797979	11	9	1	619	10.5	11.5	8.5	9.5	NA
664	#848484	11	8	1	618	10.5	11.5	7.5	8.5	NA
665	#717171	11	7	1	617	10.5	11.5	6.5	7.5	NA
666	#939393	11	6	1	616	10.5	11.5	5.5	6.5	NA
667	#8F8F8F	11	5	1	615	10.5	11.5	4.5	5.5	NA
668	#676767	11	4	1	614	10.5	11.5	3.5	4.5	NA
669	#555555	11	3	1	613	10.5	11.5	2.5	3.5	NA
670	#606060	11	2	1	612	10.5	11.5	1.5	2.5	NA
671	#717171	11	1	1	611	10.5	11.5	0.5	1.5	NA
672	#5C5C5C	12	61	1	732	11.5	12.5	60.5	61.5	NA
673	#6A6A6A	12	60	1	731	11.5	12.5	59.5	60.5	NA
674	#757575	12	59	1	730	11.5	12.5	58.5	59.5	NA
675	#8F8F8F	12	58	1	729	11.5	12.5	57.5	58.5	NA
676	black	12	57	1	728	11.5	12.5	56.5	57.5	NA
677	#5C5C5C	12	56	1	727	11.5	12.5	55.5	56.5	NA
678	#717171	12	55	1	726	11.5	12.5	54.5	55.5	NA
679	#6A6A6A	12	54	1	725	11.5	12.5	53.5	54.5	NA
680	#5C5C5C	12	53	1	724	11.5	12.5	52.5	53.5	NA
681	#757575	12	52	1	723	11.5	12.5	51.5	52.5	NA
682	#757575	12	51	1	722	11.5	12.5	50.5	51.5	NA
683	black	12	50	1	721	11.5	12.5	49.5	50.5	NA
684	black	12	49	1	720	11.5	12.5	48.5	49.5	NA
685	#7C7C7C	12	48	1	719	11.5	12.5	47.5	48.5	NA
686	#757575	12	47	1	718	11.5	12.5	46.5	47.5	NA
687	#717171	12	46	1	717	11.5	12.5	45.5	46.5	NA
688	#717171	12	45	1	716	11.5	12.5	44.5	45.5	NA
689	#636363	12	44	1	715	11.5	12.5	43.5	44.5	NA
690	#6E6E6E	12	43	1	714	11.5	12.5	42.5	43.5	NA
691	#636363	12	42	1	713	11.5	12.5	41.5	42.5	NA

692	#717171	12	41	1	712	11.5	12.5	40.5	41.5	NA
693	#797979	12	40	1	711	11.5	12.5	39.5	40.5	NA
694	#676767	12	39	1	710	11.5	12.5	38.5	39.5	NA
695	#595959	12	38	1	709	11.5	12.5	37.5	38.5	NA
696	#6E6E6E	12	37	1	708	11.5	12.5	36.5	37.5	NA
697	#636363	12	36	1	707	11.5	12.5	35.5	36.5	NA
698	#6E6E6E	12	35	1	706	11.5	12.5	34.5	35.5	NA
699	#606060	12	34	1	705	11.5	12.5	33.5	34.5	NA
700	#6E6E6E	12	33	1	704	11.5	12.5	32.5	33.5	NA
701	#636363	12	32	1	703	11.5	12.5	31.5	32.5	NA
702	#676767	12	31	1	702	11.5	12.5	30.5	31.5	NA
703	#797979	12	30	1	701	11.5	12.5	29.5	30.5	NA
704	#6A6A6A	12	29	1	700	11.5	12.5	28.5	29.5	NA
705	#6A6A6A	12	28	1	699	11.5	12.5	27.5	28.5	NA
706	#636363	12	27	1	698	11.5	12.5	26.5	27.5	NA
707	#6A6A6A	12	26	1	697	11.5	12.5	25.5	26.5	NA
708	#676767	12	25	1	696	11.5	12.5	24.5	25.5	NA
709	black	12	24	1	695	11.5	12.5	23.5	24.5	NA
710	#808080	12	23	1	694	11.5	12.5	22.5	23.5	NA
711	#757575	12	22	1	693	11.5	12.5	21.5	22.5	NA
712	#676767	12	21	1	692	11.5	12.5	20.5	21.5	NA
713	#717171	12	20	1	691	11.5	12.5	19.5	20.5	NA
714	#888888	12	19	1	690	11.5	12.5	18.5	19.5	NA
715	#9E9E9E	12	18	1	689	11.5	12.5	17.5	18.5	NA
716	#4E4E4E	12	17	1	688	11.5	12.5	16.5	17.5	NA
717	#717171	12	16	1	687	11.5	12.5	15.5	16.5	NA
718	#8B8B8B	12	15	1	686	11.5	12.5	14.5	15.5	NA
719	#414141	12	14	1	685	11.5	12.5	13.5	14.5	NA
720	#848484	12	13	1	684	11.5	12.5	12.5	13.5	NA
721	#979797	12	12	1	683	11.5	12.5	11.5	12.5	NA
722	black	12	11	1	682	11.5	12.5	10.5	11.5	NA
723	#4B4B4B	12	10	1	681	11.5	12.5	9.5	10.5	NA
724	#717171	12	9	1	680	11.5	12.5	8.5	9.5	NA
725	#717171	12	8	1	679	11.5	12.5	7.5	8.5	NA
726	#636363	12	7	1	678	11.5	12.5	6.5	7.5	NA
727	#939393	12	6	1	677	11.5	12.5	5.5	6.5	NA
728	#808080	12	5	1	676	11.5	12.5	4.5	5.5	NA
729	#525252	12	4	1	675	11.5	12.5	3.5	4.5	NA
730	#3A3A3A	12	3	1	674	11.5	12.5	2.5	3.5	NA
731	#4B4B4B	12	2	1	673	11.5	12.5	1.5	2.5	NA
732	#6A6A6A	12	1	1	672	11.5	12.5	0.5	1.5	NA
733	#848484	13	61	1	793	12.5	13.5	60.5	61.5	NA
734	#888888	13	60	1	792	12.5	13.5	59.5	60.5	NA
735	#797979	13	59	1	791	12.5	13.5	58.5	59.5	NA
736	#8B8B8B	13	58	1	790	12.5	13.5	57.5	58.5	NA

737	black	13	57	1	789	12.5	13.5	56.5	57.5	NA
738	#888888	13	56	1	788	12.5	13.5	55.5	56.5	NA
739	#979797	13	55	1	787	12.5	13.5	54.5	55.5	NA
740	#848484	13	54	1	786	12.5	13.5	53.5	54.5	NA
741	#808080	13	53	1	785	12.5	13.5	52.5	53.5	NA
742	#9A9A9A	13	52	1	784	12.5	13.5	51.5	52.5	NA
743	#797979	13	51	1	783	12.5	13.5	50.5	51.5	NA
744	black	13	50	1	782	12.5	13.5	49.5	50.5	NA
745	black	13	49	1	781	12.5	13.5	48.5	49.5	NA
746	#888888	13	48	1	780	12.5	13.5	47.5	48.5	NA
747	#8F8F8F	13	47	1	779	12.5	13.5	46.5	47.5	NA
748	#808080	13	46	1	778	12.5	13.5	45.5	46.5	NA
749	#979797	13	45	1	777	12.5	13.5	44.5	45.5	NA
750	#848484	13	44	1	776	12.5	13.5	43.5	44.5	NA
751	#808080	13	43	1	775	12.5	13.5	42.5	43.5	NA
752	#8B8B8B	13	42	1	774	12.5	13.5	41.5	42.5	NA
753	#939393	13	41	1	773	12.5	13.5	40.5	41.5	NA
754	#939393	13	40	1	772	12.5	13.5	39.5	40.5	NA
755	#979797	13	39	1	771	12.5	13.5	38.5	39.5	NA
756	#6E6E6E	13	38	1	770	12.5	13.5	37.5	38.5	NA
757	#9A9A9A	13	37	1	769	12.5	13.5	36.5	37.5	NA
758	#6E6E6E	13	36	1	768	12.5	13.5	35.5	36.5	NA
759	#8B8B8B	13	35	1	767	12.5	13.5	34.5	35.5	NA
760	#797979	13	34	1	766	12.5	13.5	33.5	34.5	NA
761	#9A9A9A	13	33	1	765	12.5	13.5	32.5	33.5	NA
762	#808080	13	32	1	764	12.5	13.5	31.5	32.5	NA
763	#7C7C7C	13	31	1	763	12.5	13.5	30.5	31.5	NA
764	#888888	13	30	1	762	12.5	13.5	29.5	30.5	NA
765	#888888	13	29	1	761	12.5	13.5	28.5	29.5	NA
766	#8B8B8B	13	28	1	760	12.5	13.5	27.5	28.5	NA
767	#939393	13	27	1	759	12.5	13.5	26.5	27.5	NA
768	#9E9E9E	13	26	1	758	12.5	13.5	25.5	26.5	NA
769	#757575	13	25	1	757	12.5	13.5	24.5	25.5	NA
770	black	13	24	1	756	12.5	13.5	23.5	24.5	NA
771	#8F8F8F	13	23	1	755	12.5	13.5	22.5	23.5	NA
772	#979797	13	22	1	754	12.5	13.5	21.5	22.5	NA
773	#848484	13	21	1	753	12.5	13.5	20.5	21.5	NA
774	#939393	13	20	1	752	12.5	13.5	19.5	20.5	NA
775	#9A9A9A	13	19	1	751	12.5	13.5	18.5	19.5	NA
776	#BEBEBE	13	18	1	750	12.5	13.5	17.5	18.5	NA
777	#636363	13	17	1	749	12.5	13.5	16.5	17.5	NA
778	#8F8F8F	13	16	1	748	12.5	13.5	15.5	16.5	NA
779	#AAAAAA	13	15	1	747	12.5	13.5	14.5	15.5	NA
780	#3E3E3E	13	14	1	746	12.5	13.5	13.5	14.5	NA
781	#979797	13	13	1	745	12.5	13.5	12.5	13.5	NA

782	#9E9E9E	13	12	1	744	12.5	13.5	11.5	12.5	NA
783	black	13	11	1	743	12.5	13.5	10.5	11.5	NA
784	#595959	13	10	1	742	12.5	13.5	9.5	10.5	NA
785	#AAAAAA	13	9	1	741	12.5	13.5	8.5	9.5	NA
786	#AAAAAA	13	8	1	740	12.5	13.5	7.5	8.5	NA
787	#848484	13	7	1	739	12.5	13.5	6.5	7.5	NA
788	#B6B6B6	13	6	1	738	12.5	13.5	5.5	6.5	NA
789	#9E9E9E	13	5	1	737	12.5	13.5	4.5	5.5	NA
790	#6A6A6A	13	4	1	736	12.5	13.5	3.5	4.5	NA
791	#4E4E4E	13	3	1	735	12.5	13.5	2.5	3.5	NA
792	#6A6A6A	13	2	1	734	12.5	13.5	1.5	2.5	NA
793	#B6B6B6	13	1	1	733	12.5	13.5	0.5	1.5	NA
794	#8F8F8F	14	61	1	854	13.5	14.5	60.5	61.5	NA
795	#939393	14	60	1	853	13.5	14.5	59.5	60.5	NA
796	#9A9A9A	14	59	1	852	13.5	14.5	58.5	59.5	NA
797	#9E9E9E	14	58	1	851	13.5	14.5	57.5	58.5	NA
798	black	14	57	1	850	13.5	14.5	56.5	57.5	NA
799	#848484	14	56	1	849	13.5	14.5	55.5	56.5	NA
800	#939393	14	55	1	848	13.5	14.5	54.5	55.5	NA
801	#888888	14	54	1	847	13.5	14.5	53.5	54.5	NA
802	#797979	14	53	1	846	13.5	14.5	52.5	53.5	NA
803	#AAAAAA	14	52	1	845	13.5	14.5	51.5	52.5	NA
804	#888888	14	51	1	844	13.5	14.5	50.5	51.5	NA
805	black	14	50	1	843	13.5	14.5	49.5	50.5	NA
806	black	14	49	1	842	13.5	14.5	48.5	49.5	NA
807	#939393	14	48	1	841	13.5	14.5	47.5	48.5	NA
808	#888888	14	47	1	840	13.5	14.5	46.5	47.5	NA
809	#888888	14	46	1	839	13.5	14.5	45.5	46.5	NA
810	#979797	14	45	1	838	13.5	14.5	44.5	45.5	NA
811	#8F8F8F	14	44	1	837	13.5	14.5	43.5	44.5	NA
812	#8F8F8F	14	43	1	836	13.5	14.5	42.5	43.5	NA
813	#808080	14	42	1	835	13.5	14.5	41.5	42.5	NA
814	#939393	14	41	1	834	13.5	14.5	40.5	41.5	NA
815	#979797	14	40	1	833	13.5	14.5	39.5	40.5	NA
816	#888888	14	39	1	832	13.5	14.5	38.5	39.5	NA
817	#757575	14	38	1	831	13.5	14.5	37.5	38.5	NA
818	#939393	14	37	1	830	13.5	14.5	36.5	37.5	NA
819	#717171	14	36	1	829	13.5	14.5	35.5	36.5	NA
820	#8F8F8F	14	35	1	828	13.5	14.5	34.5	35.5	NA
821	#939393	14	34	1	827	13.5	14.5	33.5	34.5	NA
822	#9E9E9E	14	33	1	826	13.5	14.5	32.5	33.5	NA
823	#8B8B8B	14	32	1	825	13.5	14.5	31.5	32.5	NA
824	#6E6E6E	14	31	1	824	13.5	14.5	30.5	31.5	NA
825	#939393	14	30	1	823	13.5	14.5	29.5	30.5	NA
826	#8F8F8F	14	29	1	822	13.5	14.5	28.5	29.5	NA

827	#888888	14	28	1	821	13.5	14.5	27.5	28.5	NA
828	#7C7C7C	14	27	1	820	13.5	14.5	26.5	27.5	NA
829	#8B8B8B	14	26	1	819	13.5	14.5	25.5	26.5	NA
830	#888888	14	25	1	818	13.5	14.5	24.5	25.5	NA
831	black	14	24	1	817	13.5	14.5	23.5	24.5	NA
832	#A2A2A2	14	23	1	816	13.5	14.5	22.5	23.5	NA
833	#A2A2A2	14	22	1	815	13.5	14.5	21.5	22.5	NA
834	#8B8B8B	14	21	1	814	13.5	14.5	20.5	21.5	NA
835	#BABABA	14	20	1	813	13.5	14.5	19.5	20.5	NA
836	#AAAAAA	14	19	1	812	13.5	14.5	18.5	19.5	NA
837	#BEBEBE	14	18	1	811	13.5	14.5	17.5	18.5	NA
838	#888888	14	17	1	810	13.5	14.5	16.5	17.5	NA
839	#8F8F8F	14	16	1	809	13.5	14.5	15.5	16.5	NA
840	#B6B6B6	14	15	1	808	13.5	14.5	14.5	15.5	NA
841	#3E3E3E	14	14	1	807	13.5	14.5	13.5	14.5	NA
842	#A6A6A6	14	13	1	806	13.5	14.5	12.5	13.5	NA
843	#B2B2B2	14	12	1	805	13.5	14.5	11.5	12.5	NA
844	black	14	11	1	804	13.5	14.5	10.5	11.5	NA
845	#636363	14	10	1	803	13.5	14.5	9.5	10.5	NA
846	#9A9A9A	14	9	1	802	13.5	14.5	8.5	9.5	NA
847	#9E9E9E	14	8	1	801	13.5	14.5	7.5	8.5	NA
848	#888888	14	7	1	800	13.5	14.5	6.5	7.5	NA
849	#C2C2C2	14	6	1	799	13.5	14.5	5.5	6.5	NA
850	#8F8F8F	14	5	1	798	13.5	14.5	4.5	5.5	NA
851	#676767	14	4	1	797	13.5	14.5	3.5	4.5	NA
852	#4E4E4E	14	3	1	796	13.5	14.5	2.5	3.5	NA
853	#525252	14	2	1	795	13.5	14.5	1.5	2.5	NA
854	#979797	14	1	1	794	13.5	14.5	0.5	1.5	NA
855	#9A9A9A	15	61	1	915	14.5	15.5	60.5	61.5	NA
856	#BEBEBE	15	60	1	914	14.5	15.5	59.5	60.5	NA
857	#D2D2D2	15	59	1	913	14.5	15.5	58.5	59.5	NA
858	#DEDEDE	15	58	1	912	14.5	15.5	57.5	58.5	NA
859	black	15	57	1	911	14.5	15.5	56.5	57.5	NA
860	#8B8B8B	15	56	1	910	14.5	15.5	55.5	56.5	NA
861	#CACACA	15	55	1	909	14.5	15.5	54.5	55.5	NA
862	#A2A2A2	15	54	1	908	14.5	15.5	53.5	54.5	NA
863	#B6B6B6	15	53	1	907	14.5	15.5	52.5	53.5	NA
864	#AEAEAE	15	52	1	906	14.5	15.5	51.5	52.5	NA
865	#8B8B8B	15	51	1	905	14.5	15.5	50.5	51.5	NA
866	black	15	50	1	904	14.5	15.5	49.5	50.5	NA
867	black	15	49	1	903	14.5	15.5	48.5	49.5	NA
868	#6E6E6E	15	48	1	902	14.5	15.5	47.5	48.5	NA
869	#A2A2A2	15	47	1	901	14.5	15.5	46.5	47.5	NA
870	#DADADA	15	46	1	900	14.5	15.5	45.5	46.5	NA
871	#DEDEDE	15	45	1	899	14.5	15.5	44.5	45.5	NA

872	#C6C6C6	15	44	1	898	14.5	15.5	43.5	44.5	NA
873	#DADADA	15	43	1	897	14.5	15.5	42.5	43.5	NA
874	#BABABA	15	42	1	896	14.5	15.5	41.5	42.5	NA
875	#C2C2C2	15	41	1	895	14.5	15.5	40.5	41.5	NA
876	#DADADA	15	40	1	894	14.5	15.5	39.5	40.5	NA
877	#B6B6B6	15	39	1	893	14.5	15.5	38.5	39.5	NA
878	#5C5C5C	15	38	1	892	14.5	15.5	37.5	38.5	NA
879	#CECECE	15	37	1	891	14.5	15.5	36.5	37.5	NA
880	#444444	15	36	1	890	14.5	15.5	35.5	36.5	NA
881	#C6C6C6	15	35	1	889	14.5	15.5	34.5	35.5	NA
882	#8B8B8B	15	34	1	888	14.5	15.5	33.5	34.5	NA
883	#939393	15	33	1	887	14.5	15.5	32.5	33.5	NA
884	#B6B6B6	15	32	1	886	14.5	15.5	31.5	32.5	NA
885	#808080	15	31	1	885	14.5	15.5	30.5	31.5	NA
886	#A2A2A2	15	30	1	884	14.5	15.5	29.5	30.5	NA
887	#A2A2A2	15	29	1	883	14.5	15.5	28.5	29.5	NA
888	#DEDEDE	15	28	1	882	14.5	15.5	27.5	28.5	NA
889	#7C7C7C	15	27	1	881	14.5	15.5	26.5	27.5	NA
890	#BABABA	15	26	1	880	14.5	15.5	25.5	26.5	NA
891	#B2B2B2	15	25	1	879	14.5	15.5	24.5	25.5	NA
892	black	15	24	1	878	14.5	15.5	23.5	24.5	NA
893	#C2C2C2	15	23	1	877	14.5	15.5	22.5	23.5	NA
894	#CECECE	15	22	1	876	14.5	15.5	21.5	22.5	NA
895	#979797	15	21	1	875	14.5	15.5	20.5	21.5	NA
896	#C6C6C6	15	20	1	874	14.5	15.5	19.5	20.5	NA
897	#AAEAEA	15	19	1	873	14.5	15.5	18.5	19.5	NA
898	#FBFBFB	15	18	1	872	14.5	15.5	17.5	18.5	NA
899	#676767	15	17	1	871	14.5	15.5	16.5	17.5	NA
900	#CECECE	15	16	1	870	14.5	15.5	15.5	16.5	NA
901	#EAEAEA	15	15	1	869	14.5	15.5	14.5	15.5	NA
902	#595959	15	14	1	868	14.5	15.5	13.5	14.5	NA
903	#CACACA	15	13	1	867	14.5	15.5	12.5	13.5	NA
904	#AAAAAA	15	12	1	866	14.5	15.5	11.5	12.5	NA
905	black	15	11	1	865	14.5	15.5	10.5	11.5	NA
906	#888888	15	10	1	864	14.5	15.5	9.5	10.5	NA
907	#D2D2D2	15	9	1	863	14.5	15.5	8.5	9.5	NA
908	#C2C2C2	15	8	1	862	14.5	15.5	7.5	8.5	NA
909	#AAAAAA	15	7	1	861	14.5	15.5	6.5	7.5	NA
910	#EAEAEA	15	6	1	860	14.5	15.5	5.5	6.5	NA
911	#CECECE	15	5	1	859	14.5	15.5	4.5	5.5	NA
912	#6E6E6E	15	4	1	858	14.5	15.5	3.5	4.5	NA
913	#525252	15	3	1	857	14.5	15.5	2.5	3.5	NA
914	#676767	15	2	1	856	14.5	15.5	1.5	2.5	NA
915	#CACACA	15	1	1	855	14.5	15.5	0.5	1.5	NA
916	#9E9E9E	16	61	1	976	15.5	16.5	60.5	61.5	NA

917	#848484	16	60	1	975	15.5	16.5	59.5	60.5	NA
918	#A6A6A6	16	59	1	974	15.5	16.5	58.5	59.5	NA
919	#C6C6C6	16	58	1	973	15.5	16.5	57.5	58.5	NA
920	black	16	57	1	972	15.5	16.5	56.5	57.5	NA
921	#757575	16	56	1	971	15.5	16.5	55.5	56.5	NA
922	#A2A2A2	16	55	1	970	15.5	16.5	54.5	55.5	NA
923	#2E2E2E	16	54	1	969	15.5	16.5	53.5	54.5	NA
924	#808080	16	53	1	968	15.5	16.5	52.5	53.5	NA
925	#BEBEBE	16	52	1	967	15.5	16.5	51.5	52.5	NA
926	#5C5C5C	16	51	1	966	15.5	16.5	50.5	51.5	NA
927	black	16	50	1	965	15.5	16.5	49.5	50.5	NA
928	black	16	49	1	964	15.5	16.5	48.5	49.5	NA
929	#808080	16	48	1	963	15.5	16.5	47.5	48.5	NA
930	#636363	16	47	1	962	15.5	16.5	46.5	47.5	NA
931	#595959	16	46	1	961	15.5	16.5	45.5	46.5	NA
932	#717171	16	45	1	960	15.5	16.5	44.5	45.5	NA
933	#808080	16	44	1	959	15.5	16.5	43.5	44.5	NA
934	#7C7C7C	16	43	1	958	15.5	16.5	42.5	43.5	NA
935	#8B8B8B	16	42	1	957	15.5	16.5	41.5	42.5	NA
936	#3A3A3A	16	41	1	956	15.5	16.5	40.5	41.5	NA
937	#6A6A6A	16	40	1	955	15.5	16.5	39.5	40.5	NA
938	#979797	16	39	1	954	15.5	16.5	38.5	39.5	NA
939	#595959	16	38	1	953	15.5	16.5	37.5	38.5	NA
940	#4E4E4E	16	37	1	952	15.5	16.5	36.5	37.5	NA
941	#555555	16	36	1	951	15.5	16.5	35.5	36.5	NA
942	#6A6A6A	16	35	1	950	15.5	16.5	34.5	35.5	NA
943	#636363	16	34	1	949	15.5	16.5	33.5	34.5	NA
944	#343434	16	33	1	948	15.5	16.5	32.5	33.5	NA
945	#A6A6A6	16	32	1	947	15.5	16.5	31.5	32.5	NA
946	#4B4B4B	16	31	1	946	15.5	16.5	30.5	31.5	NA
947	#B2B2B2	16	30	1	945	15.5	16.5	29.5	30.5	NA
948	#C6C6C6	16	29	1	944	15.5	16.5	28.5	29.5	NA
949	#A2A2A2	16	28	1	943	15.5	16.5	27.5	28.5	NA
950	#8B8B8B	16	27	1	942	15.5	16.5	26.5	27.5	NA
951	#B2B2B2	16	26	1	941	15.5	16.5	25.5	26.5	NA
952	#6A6A6A	16	25	1	940	15.5	16.5	24.5	25.5	NA
953	black	16	24	1	939	15.5	16.5	23.5	24.5	NA
954	#222222	16	23	1	938	15.5	16.5	22.5	23.5	NA
955	#525252	16	22	1	937	15.5	16.5	21.5	22.5	NA
956	#1F1F1F	16	21	1	936	15.5	16.5	20.5	21.5	NA
957	#1F1F1F	16	20	1	935	15.5	16.5	19.5	20.5	NA
958	#1F1F1F	16	19	1	934	15.5	16.5	18.5	19.5	NA
959	#CACACA	16	18	1	933	15.5	16.5	17.5	18.5	NA
960	#7C7C7C	16	17	1	932	15.5	16.5	16.5	17.5	NA
961	#BEBEBE	16	16	1	931	15.5	16.5	15.5	16.5	NA

962	#C6C6C6	16	15	1	930	15.5	16.5	14.5	15.5	NA
963	#636363	16	14	1	929	15.5	16.5	13.5	14.5	NA
964	#B2B2B2	16	13	1	928	15.5	16.5	12.5	13.5	NA
965	#7C7C7C	16	12	1	927	15.5	16.5	11.5	12.5	NA
966	black	16	11	1	926	15.5	16.5	10.5	11.5	NA
967	#5C5C5C	16	10	1	925	15.5	16.5	9.5	10.5	NA
968	#B6B6B6	16	9	1	924	15.5	16.5	8.5	9.5	NA
969	#9E9E9E	16	8	1	923	15.5	16.5	7.5	8.5	NA
970	#4B4B4B	16	7	1	922	15.5	16.5	6.5	7.5	NA
971	#717171	16	6	1	921	15.5	16.5	5.5	6.5	NA
972	#C2C2C2	16	5	1	920	15.5	16.5	4.5	5.5	NA
973	#676767	16	4	1	919	15.5	16.5	3.5	4.5	NA
974	#5C5C5C	16	3	1	918	15.5	16.5	2.5	3.5	NA
975	#595959	16	2	1	917	15.5	16.5	1.5	2.5	NA
976	#888888	16	1	1	916	15.5	16.5	0.5	1.5	NA
977	#595959	17	61	1	1037	16.5	17.5	60.5	61.5	NA
978	#757575	17	60	1	1036	16.5	17.5	59.5	60.5	NA
979	#AAAAAA	17	59	1	1035	16.5	17.5	58.5	59.5	NA
980	#D2D2D2	17	58	1	1034	16.5	17.5	57.5	58.5	NA
981	black	17	57	1	1033	16.5	17.5	56.5	57.5	NA
982	#717171	17	56	1	1032	16.5	17.5	55.5	56.5	NA
983	#9E9E9E	17	55	1	1031	16.5	17.5	54.5	55.5	NA
984	#1F1F1F	17	54	1	1030	16.5	17.5	53.5	54.5	NA
985	#797979	17	53	1	1029	16.5	17.5	52.5	53.5	NA
986	#C6C6C6	17	52	1	1028	16.5	17.5	51.5	52.5	NA
987	#888888	17	51	1	1027	16.5	17.5	50.5	51.5	NA
988	black	17	50	1	1026	16.5	17.5	49.5	50.5	NA
989	black	17	49	1	1025	16.5	17.5	48.5	49.5	NA
990	#808080	17	48	1	1024	16.5	17.5	47.5	48.5	NA
991	#5C5C5C	17	47	1	1023	16.5	17.5	46.5	47.5	NA
992	#3E3E3E	17	46	1	1022	16.5	17.5	45.5	46.5	NA
993	#939393	17	45	1	1021	16.5	17.5	44.5	45.5	NA
994	#808080	17	44	1	1020	16.5	17.5	43.5	44.5	NA
995	#A6A6A6	17	43	1	1019	16.5	17.5	42.5	43.5	NA
996	#888888	17	42	1	1018	16.5	17.5	41.5	42.5	NA
997	#191919	17	41	1	1017	16.5	17.5	40.5	41.5	NA
998	#A2A2A2	17	40	1	1016	16.5	17.5	39.5	40.5	NA
999	#979797	17	39	1	1015	16.5	17.5	38.5	39.5	NA
1000	#4B4B4B	17	38	1	1014	16.5	17.5	37.5	38.5	NA
1001	#808080	17	37	1	1013	16.5	17.5	36.5	37.5	NA
1002	#3E3E3E	17	36	1	1012	16.5	17.5	35.5	36.5	NA
1003	#676767	17	35	1	1011	16.5	17.5	34.5	35.5	NA
1004	#3E3E3E	17	34	1	1010	16.5	17.5	33.5	34.5	NA
1005	#3E3E3E	17	33	1	1009	16.5	17.5	32.5	33.5	NA
1006	#A6A6A6	17	32	1	1008	16.5	17.5	31.5	32.5	NA

1007	#595959	17	31	1	1007	16.5	17.5	30.5	31.5	NA
1008	#AAAAAA	17	30	1	1006	16.5	17.5	29.5	30.5	NA
1009	#CACACA	17	29	1	1005	16.5	17.5	28.5	29.5	NA
1010	#9A9A9A	17	28	1	1004	16.5	17.5	27.5	28.5	NA
1011	#797979	17	27	1	1003	16.5	17.5	26.5	27.5	NA
1012	#C2C2C2	17	26	1	1002	16.5	17.5	25.5	26.5	NA
1013	#1C1C1C	17	25	1	1001	16.5	17.5	24.5	25.5	NA
1014	black	17	24	1	1000	16.5	17.5	23.5	24.5	NA
1015	#252525	17	23	1	999	16.5	17.5	22.5	23.5	NA
1016	#7C7C7C	17	22	1	998	16.5	17.5	21.5	22.5	NA
1017	#1C1C1C	17	21	1	997	16.5	17.5	20.5	21.5	NA
1018	#3A3A3A	17	20	1	996	16.5	17.5	19.5	20.5	NA
1019	#1C1C1C	17	19	1	995	16.5	17.5	18.5	19.5	NA
1020	#CECECE	17	18	1	994	16.5	17.5	17.5	18.5	NA
1021	#8F8F8F	17	17	1	993	16.5	17.5	16.5	17.5	NA
1022	#C2C2C2	17	16	1	992	16.5	17.5	15.5	16.5	NA
1023	#E2E2E2	17	15	1	991	16.5	17.5	14.5	15.5	NA
1024	#595959	17	14	1	990	16.5	17.5	13.5	14.5	NA
1025	#C2C2C2	17	13	1	989	16.5	17.5	12.5	13.5	NA
1026	#AAAAAA	17	12	1	988	16.5	17.5	11.5	12.5	NA
1027	black	17	11	1	987	16.5	17.5	10.5	11.5	NA
1028	#606060	17	10	1	986	16.5	17.5	9.5	10.5	NA
1029	#AEAEAE	17	9	1	985	16.5	17.5	8.5	9.5	NA
1030	#8F8F8F	17	8	1	984	16.5	17.5	7.5	8.5	NA
1031	#000000	17	7	1	983	16.5	17.5	6.5	7.5	NA
1032	#A2A2A2	17	6	1	982	16.5	17.5	5.5	6.5	NA
1033	#CECECE	17	5	1	981	16.5	17.5	4.5	5.5	NA
1034	#6A6A6A	17	4	1	980	16.5	17.5	3.5	4.5	NA
1035	#636363	17	3	1	979	16.5	17.5	2.5	3.5	NA
1036	#595959	17	2	1	978	16.5	17.5	1.5	2.5	NA
1037	#9A9A9A	17	1	1	977	16.5	17.5	0.5	1.5	NA
1038	#9A9A9A	18	61	1	1098	17.5	18.5	60.5	61.5	NA
1039	#8F8F8F	18	60	1	1097	17.5	18.5	59.5	60.5	NA
1040	#888888	18	59	1	1096	17.5	18.5	58.5	59.5	NA
1041	#CECECE	18	58	1	1095	17.5	18.5	57.5	58.5	NA
1042	black	18	57	1	1094	17.5	18.5	56.5	57.5	NA
1043	#343434	18	56	1	1093	17.5	18.5	55.5	56.5	NA
1044	#B2B2B2	18	55	1	1092	17.5	18.5	54.5	55.5	NA
1045	#8B8B8B	18	54	1	1091	17.5	18.5	53.5	54.5	NA
1046	#AEAEAE	18	53	1	1090	17.5	18.5	52.5	53.5	NA
1047	#9A9A9A	18	52	1	1089	17.5	18.5	51.5	52.5	NA
1048	#808080	18	51	1	1088	17.5	18.5	50.5	51.5	NA
1049	black	18	50	1	1087	17.5	18.5	49.5	50.5	NA
1050	black	18	49	1	1086	17.5	18.5	48.5	49.5	NA
1051	#4B4B4B	18	48	1	1085	17.5	18.5	47.5	48.5	NA

1052	#979797	18	47	1	1084	17.5	18.5	46.5	47.5	NA
1053	#848484	18	46	1	1083	17.5	18.5	45.5	46.5	NA
1054	#A6A6A6	18	45	1	1082	17.5	18.5	44.5	45.5	NA
1055	#7C7C7C	18	44	1	1081	17.5	18.5	43.5	44.5	NA
1056	#9A9A9A	18	43	1	1080	17.5	18.5	42.5	43.5	NA
1057	#AAAAAA	18	42	1	1079	17.5	18.5	41.5	42.5	NA
1058	#A6A6A6	18	41	1	1078	17.5	18.5	40.5	41.5	NA
1059	#DADADA	18	40	1	1077	17.5	18.5	39.5	40.5	NA
1060	#939393	18	39	1	1076	17.5	18.5	38.5	39.5	NA
1061	#595959	18	38	1	1075	17.5	18.5	37.5	38.5	NA
1062	#9E9E9E	18	37	1	1074	17.5	18.5	36.5	37.5	NA
1063	#6E6E6E	18	36	1	1073	17.5	18.5	35.5	36.5	NA
1064	#8F8F8F	18	35	1	1072	17.5	18.5	34.5	35.5	NA
1065	#343434	18	34	1	1071	17.5	18.5	33.5	34.5	NA
1066	#757575	18	33	1	1070	17.5	18.5	32.5	33.5	NA
1067	#8F8F8F	18	32	1	1069	17.5	18.5	31.5	32.5	NA
1068	#6E6E6E	18	31	1	1068	17.5	18.5	30.5	31.5	NA
1069	#7C7C7C	18	30	1	1067	17.5	18.5	29.5	30.5	NA
1070	#9E9E9E	18	29	1	1066	17.5	18.5	28.5	29.5	NA
1071	#8B8B8B	18	28	1	1065	17.5	18.5	27.5	28.5	NA
1072	#6A6A6A	18	27	1	1064	17.5	18.5	26.5	27.5	NA
1073	#A6A6A6	18	26	1	1063	17.5	18.5	25.5	26.5	NA
1074	#676767	18	25	1	1062	17.5	18.5	24.5	25.5	NA
1075	black	18	24	1	1061	17.5	18.5	23.5	24.5	NA
1076	#A6A6A6	18	23	1	1060	17.5	18.5	22.5	23.5	NA
1077	#8B8B8B	18	22	1	1059	17.5	18.5	21.5	22.5	NA
1078	#2E2E2E	18	21	1	1058	17.5	18.5	20.5	21.5	NA
1079	#808080	18	20	1	1057	17.5	18.5	19.5	20.5	NA
1080	#595959	18	19	1	1056	17.5	18.5	18.5	19.5	NA
1081	#FBFBFB	18	18	1	1055	17.5	18.5	17.5	18.5	NA
1082	#676767	18	17	1	1054	17.5	18.5	16.5	17.5	NA
1083	#CACACA	18	16	1	1053	17.5	18.5	15.5	16.5	NA
1084	#C2C2C2	18	15	1	1052	17.5	18.5	14.5	15.5	NA
1085	#414141	18	14	1	1051	17.5	18.5	13.5	14.5	NA
1086	#A6A6A6	18	13	1	1050	17.5	18.5	12.5	13.5	NA
1087	#8B8B8B	18	12	1	1049	17.5	18.5	11.5	12.5	NA
1088	black	18	11	1	1048	17.5	18.5	10.5	11.5	NA
1089	#636363	18	10	1	1047	17.5	18.5	9.5	10.5	NA
1090	#AEAEAE	18	9	1	1046	17.5	18.5	8.5	9.5	NA
1091	#A6A6A6	18	8	1	1045	17.5	18.5	7.5	8.5	NA
1092	#A2A2A2	18	7	1	1044	17.5	18.5	6.5	7.5	NA
1093	#D2D2D2	18	6	1	1043	17.5	18.5	5.5	6.5	NA
1094	#C2C2C2	18	5	1	1042	17.5	18.5	4.5	5.5	NA
1095	#5C5C5C	18	4	1	1041	17.5	18.5	3.5	4.5	NA
1096	#444444	18	3	1	1040	17.5	18.5	2.5	3.5	NA

1097	#525252	18	2	1	1039	17.5	18.5	1.5	2.5	NA
1098	#AEAEAE	18	1	1	1038	17.5	18.5	0.5	1.5	NA
1099	#717171	19	61	1	1159	18.5	19.5	60.5	61.5	NA
1100	#6E6E6E	19	60	1	1158	18.5	19.5	59.5	60.5	NA
1101	#7C7C7C	19	59	1	1157	18.5	19.5	58.5	59.5	NA
1102	#7C7C7C	19	58	1	1156	18.5	19.5	57.5	58.5	NA
1103	black	19	57	1	1155	18.5	19.5	56.5	57.5	NA
1104	#676767	19	56	1	1154	18.5	19.5	55.5	56.5	NA
1105	#797979	19	55	1	1153	18.5	19.5	54.5	55.5	NA
1106	#606060	19	54	1	1152	18.5	19.5	53.5	54.5	NA
1107	#6E6E6E	19	53	1	1151	18.5	19.5	52.5	53.5	NA
1108	#808080	19	52	1	1150	18.5	19.5	51.5	52.5	NA
1109	#757575	19	51	1	1149	18.5	19.5	50.5	51.5	NA
1110	black	19	50	1	1148	18.5	19.5	49.5	50.5	NA
1111	black	19	49	1	1147	18.5	19.5	48.5	49.5	NA
1112	#797979	19	48	1	1146	18.5	19.5	47.5	48.5	NA
1113	#7C7C7C	19	47	1	1145	18.5	19.5	46.5	47.5	NA
1114	#7C7C7C	19	46	1	1144	18.5	19.5	45.5	46.5	NA
1115	#757575	19	45	1	1143	18.5	19.5	44.5	45.5	NA
1116	#6A6A6A	19	44	1	1142	18.5	19.5	43.5	44.5	NA
1117	#6A6A6A	19	43	1	1141	18.5	19.5	42.5	43.5	NA
1118	#636363	19	42	1	1140	18.5	19.5	41.5	42.5	NA
1119	#717171	19	41	1	1139	18.5	19.5	40.5	41.5	NA
1120	#595959	19	40	1	1138	18.5	19.5	39.5	40.5	NA
1121	#6E6E6E	19	39	1	1137	18.5	19.5	38.5	39.5	NA
1122	#6E6E6E	19	38	1	1136	18.5	19.5	37.5	38.5	NA
1123	#676767	19	37	1	1135	18.5	19.5	36.5	37.5	NA
1124	#6E6E6E	19	36	1	1134	18.5	19.5	35.5	36.5	NA
1125	#606060	19	35	1	1133	18.5	19.5	34.5	35.5	NA
1126	#757575	19	34	1	1132	18.5	19.5	33.5	34.5	NA
1127	#808080	19	33	1	1131	18.5	19.5	32.5	33.5	NA
1128	#6E6E6E	19	32	1	1130	18.5	19.5	31.5	32.5	NA
1129	#6A6A6A	19	31	1	1129	18.5	19.5	30.5	31.5	NA
1130	#7C7C7C	19	30	1	1128	18.5	19.5	29.5	30.5	NA
1131	#717171	19	29	1	1127	18.5	19.5	28.5	29.5	NA
1132	#7C7C7C	19	28	1	1126	18.5	19.5	27.5	28.5	NA
1133	#6E6E6E	19	27	1	1125	18.5	19.5	26.5	27.5	NA
1134	#636363	19	26	1	1124	18.5	19.5	25.5	26.5	NA
1135	#6A6A6A	19	25	1	1123	18.5	19.5	24.5	25.5	NA
1136	black	19	24	1	1122	18.5	19.5	23.5	24.5	NA
1137	#797979	19	23	1	1121	18.5	19.5	22.5	23.5	NA
1138	#6E6E6E	19	22	1	1120	18.5	19.5	21.5	22.5	NA
1139	#6E6E6E	19	21	1	1119	18.5	19.5	20.5	21.5	NA
1140	#6A6A6A	19	20	1	1118	18.5	19.5	19.5	20.5	NA
1141	#8B8B8B	19	19	1	1117	18.5	19.5	18.5	19.5	NA

1142	#B2B2B2	19	18	1	1116	18.5	19.5	17.5	18.5	NA
1143	#6E6E6E	19	17	1	1115	18.5	19.5	16.5	17.5	NA
1144	#606060	19	16	1	1114	18.5	19.5	15.5	16.5	NA
1145	#979797	19	15	1	1113	18.5	19.5	14.5	15.5	NA
1146	#595959	19	14	1	1112	18.5	19.5	13.5	14.5	NA
1147	#797979	19	13	1	1111	18.5	19.5	12.5	13.5	NA
1148	#757575	19	12	1	1110	18.5	19.5	11.5	12.5	NA
1149	black	19	11	1	1109	18.5	19.5	10.5	11.5	NA
1150	#555555	19	10	1	1108	18.5	19.5	9.5	10.5	NA
1151	#7C7C7C	19	9	1	1107	18.5	19.5	8.5	9.5	NA
1152	#8B8B8B	19	8	1	1106	18.5	19.5	7.5	8.5	NA
1153	#848484	19	7	1	1105	18.5	19.5	6.5	7.5	NA
1154	#9E9E9E	19	6	1	1104	18.5	19.5	5.5	6.5	NA
1155	#808080	19	5	1	1103	18.5	19.5	4.5	5.5	NA
1156	#606060	19	4	1	1102	18.5	19.5	3.5	4.5	NA
1157	#4B4B4B	19	3	1	1101	18.5	19.5	2.5	3.5	NA
1158	#4B4B4B	19	2	1	1100	18.5	19.5	1.5	2.5	NA
1159	#797979	19	1	1	1099	18.5	19.5	0.5	1.5	NA
1160	#6E6E6E	20	61	1	1220	19.5	20.5	60.5	61.5	NA
1161	#6A6A6A	20	60	1	1219	19.5	20.5	59.5	60.5	NA
1162	#808080	20	59	1	1218	19.5	20.5	58.5	59.5	NA
1163	#757575	20	58	1	1217	19.5	20.5	57.5	58.5	NA
1164	black	20	57	1	1216	19.5	20.5	56.5	57.5	NA
1165	#606060	20	56	1	1215	19.5	20.5	55.5	56.5	NA
1166	#676767	20	55	1	1214	19.5	20.5	54.5	55.5	NA
1167	#636363	20	54	1	1213	19.5	20.5	53.5	54.5	NA
1168	#676767	20	53	1	1212	19.5	20.5	52.5	53.5	NA
1169	#797979	20	52	1	1211	19.5	20.5	51.5	52.5	NA
1170	#6A6A6A	20	51	1	1210	19.5	20.5	50.5	51.5	NA
1171	black	20	50	1	1209	19.5	20.5	49.5	50.5	NA
1172	black	20	49	1	1208	19.5	20.5	48.5	49.5	NA
1173	#676767	20	48	1	1207	19.5	20.5	47.5	48.5	NA
1174	#717171	20	47	1	1206	19.5	20.5	46.5	47.5	NA
1175	#757575	20	46	1	1205	19.5	20.5	45.5	46.5	NA
1176	#717171	20	45	1	1204	19.5	20.5	44.5	45.5	NA
1177	#636363	20	44	1	1203	19.5	20.5	43.5	44.5	NA
1178	#6A6A6A	20	43	1	1202	19.5	20.5	42.5	43.5	NA
1179	#6E6E6E	20	42	1	1201	19.5	20.5	41.5	42.5	NA
1180	#6E6E6E	20	41	1	1200	19.5	20.5	40.5	41.5	NA
1181	#636363	20	40	1	1199	19.5	20.5	39.5	40.5	NA
1182	#676767	20	39	1	1198	19.5	20.5	38.5	39.5	NA
1183	#6E6E6E	20	38	1	1197	19.5	20.5	37.5	38.5	NA
1184	#717171	20	37	1	1196	19.5	20.5	36.5	37.5	NA
1185	#6E6E6E	20	36	1	1195	19.5	20.5	35.5	36.5	NA
1186	#676767	20	35	1	1194	19.5	20.5	34.5	35.5	NA

```

1187 #676767 20 34      1 1193 19.5 20.5 33.5 34.5    NA
1188 #717171 20 33      1 1192 19.5 20.5 32.5 33.5    NA
1189 #676767 20 32      1 1191 19.5 20.5 31.5 32.5    NA
1190 #636363 20 31      1 1190 19.5 20.5 30.5 31.5    NA
1191 #6A6A6A 20 30      1 1189 19.5 20.5 29.5 30.5    NA
1192 #808080 20 29      1 1188 19.5 20.5 28.5 29.5    NA
1193 #797979 20 28      1 1187 19.5 20.5 27.5 28.5    NA
1194 #636363 20 27      1 1186 19.5 20.5 26.5 27.5    NA
1195 #676767 20 26      1 1185 19.5 20.5 25.5 26.5    NA
1196 #6E6E6E 20 25      1 1184 19.5 20.5 24.5 25.5    NA
1197 black 20 24         1 1183 19.5 20.5 23.5 24.5    NA
1198 #676767 20 23      1 1182 19.5 20.5 22.5 23.5    NA
1199 #6E6E6E 20 22      1 1181 19.5 20.5 21.5 22.5    NA
1200 #636363 20 21      1 1180 19.5 20.5 20.5 21.5    NA
1201 #636363 20 20      1 1179 19.5 20.5 19.5 20.5    NA
1202 #8F8F8F 20 19      1 1178 19.5 20.5 18.5 19.5    NA
1203 #979797 20 18      1 1177 19.5 20.5 17.5 18.5    NA
1204 #606060 20 17      1 1176 19.5 20.5 16.5 17.5    NA
1205 #636363 20 16      1 1175 19.5 20.5 15.5 16.5    NA
1206 #9A9A9A 20 15      1 1174 19.5 20.5 14.5 15.5    NA
1207 #484848 20 14      1 1173 19.5 20.5 13.5 14.5    NA
1208 #757575 20 13      1 1172 19.5 20.5 12.5 13.5    NA
1209 #6E6E6E 20 12      1 1171 19.5 20.5 11.5 12.5    NA
1210 black 20 11         1 1170 19.5 20.5 10.5 11.5    NA
1211 #4B4B4B 20 10      1 1169 19.5 20.5 9.5 10.5    NA
1212 #797979 20 9       1 1168 19.5 20.5 8.5 9.5     NA
1213 #808080 20 8       1 1167 19.5 20.5 7.5 8.5     NA
1214 #7C7C7C 20 7       1 1166 19.5 20.5 6.5 7.5     NA
1215 #888888 20 6       1 1165 19.5 20.5 5.5 6.5     NA
1216 #757575 20 5       1 1164 19.5 20.5 4.5 5.5     NA
1217 #5C5C5C 20 4       1 1163 19.5 20.5 3.5 4.5     NA
1218 #484848 20 3       1 1162 19.5 20.5 2.5 3.5     NA
1219 #444444 20 2       1 1161 19.5 20.5 1.5 2.5     NA
1220 #7C7C7C 20 1       1 1160 19.5 20.5 0.5 1.5     NA

```

```
write.xlsx(g$data[[1]], "chapter2/mydatablack.xlsx")
```

```
##on colors
```

```
colorHeatPlot<-ggplot(docking.m, aes(x=variable, y=Enzima)) + labs(x = "Substrates", y =
ggsave("chapter2/colorHeatPlot.pdf", plot = colorHeatPlot, height = 36, width = 24)
```

```
gcolor <- ggplot_build(colorHeatPlot)
gcolor$data[[1]]["fill"]
```

```
        fill
1      #FEE695
2      #FEE695
3      #FEEA9C
4      #F9FCB6
5      gray
6      #FED481
7      #B6E1A1
8      #FDB063
9      #FEDB87
10     #92D2A4
11     #FDB063
12     gray
13     gray
14     #F46F43
15     #FA9554
16     #FEE695
17     #FEC575
18     #F2F9AB
19     #FEE28E
20     #D0EC9C
21     #F7834C
22     #C8E89E
23     #FDB063
24     #FFF8B3
25     #FEE695
26     #FFEEA4
27     #FEEA9C
28     #FA9554
29     #FEE28E
30     #FDDEBC
31     #FEEA9C
32     #FDDEBC
33     #FFF8B3
34     #FEE695
35     #FEEA9C
36     #FB9F59
37     #FCA75D
38     gray
39     #F88C50
40     #FB9F59
41     #FFEEA4
42     #FEBE6E
43     #FEC575
44     #68C2A4
```

```
45  #EOF299
46  #F6FBB1
47  #68C2A4
48  #FEE695
49  #B6E1A1
50  #FEEA9C
51      gray
52  #F6FBB1
53  #3E90B9
54  #73C6A4
55  #EC6147
56  #BFE4A0
57  #88CEA4
58  #F2F9AB
59  #F6FBB1
60  #FEDB87
61  #EBF79F
62  #FEE28E
63  #FEDB87
64  #FEEA9C
65  #FEE695
66      gray
67  #FFEEA4
68  #EOF299
69  #FEE28E
70  #FDB768
71  #4578B5
72  #FDB063
73      gray
74      gray
75  #F6FBB1
76  #FED481
77  #FDB768
78  #FEEA9C
79  #FFEEA4
80  #D9EF9B
81  #FDB063
82  #FEBE6E
83  #FEC575
84  #F6FBB1
85  #FEDB87
86  #FEBE6E
87  #FED481
88  #FDB768
89  #FEBE6E
```

```
90  #FECC7A
91  #FEE28E
92  #FECC7A
93  #FED481
94  #FEDB87
95  #FEC575
96  #FEC575
97  #FECC7A
98  #FEC575
99      gray
100 #FEBE6E
101 #FFF3AC
102 #FDB768
103 #FEE28E
104 #FEBE6E
105 #FFF8B3
106 #E7F59A
107 #FFFCBB
108 #4898B6
109 #FDDEBC
110 #FFF8B3
111 #FEC575
112      gray
113 #EBF79F
114 #ADDDA3
115 #BFE4A0
116 #F06744
117 #DE4D4B
118 #88CEA4
119 #D9EF9B
120 #FDDEBC
121 #D9EF9B
122 #E7F59A
123 #FEEA9C
124 #FECC7A
125 #FFFCBB
126 #FFEEA4
127      gray
128 #FEDB87
129 #FDB768
130 #FECC7A
131 #FEBE6E
132 #D0EC9C
133 #FEE28E
134      gray
```

```
135     gray
136 #FED481
137 #FEE695
138 #FEE695
139 #FFFCCB
140 #FEEA9C
141 #FEEA9C
142 #FDB768
143 #FEC575
144 #FED481
145 #FED481
146 #FFEEA4
147 #FED481
148 #FEEA9C
149 #FEBE6E
150 #FECC7A
151 #FEBE6E
152 #FEC575
153 #FEC575
154 #FDB768
155 #FFEEA4
156 #FEE28E
157 #FEBE6E
158 #FED481
159 #FEDB87
160     gray
161 #FEE695
162 #FEE695
163 #FED481
164 #FEC575
165 #FEEA9C
166 #D0EC9C
167 #92D2A4
168 #B6E1A1
169 #5E4EA1
170 #FFEEA4
171 #4578B5
172 #FEDB87
173     gray
174 #F9FCB6
175 #ADDDA3
176 #7ECAA4
177 #F67948
178 #FB9F59
179 #B6E1A1
```

```
180 #F6FBB1
181 #FEE695
182 #F6FBB1
183 #D9EF9B
184 #FED481
185 #FCA75D
186 #FECC7A
187 #FEC575
188     gray
189 #FEE28E
190 #FDB768
191 #FED481
192 #FCA75D
193 #FED481
194 #FEC575
195     gray
196     gray
197 #FDB063
198 #FEBE6E
199 #FEE28E
200 #FFF8B3
201 #FEBE6E
202 #FDB768
203 #FEBE6E
204 #FCA75D
205 #FEBE6E
206 #FB9F59
207 #FEE28E
208 #FEDB87
209 #FEE695
210 #FDB063
211 #FA9554
212 #FDB063
213 #FDB063
214 #FDB063
215 #FEC575
216 #FEDB87
217 #FEBE6E
218 #FEBE6E
219 #FDB768
220 #FED481
221     gray
222 #FCA75D
223 #FEDB87
224 #FEDB87
```

```
225 #FDB768
226 #FED481
227 #DE4D4B
228 #A4DAA4
229 #FEE695
230 #FB9F59
231 #FB9F59
232 #FEDB87
233 #FCA75D
234     gray
235 #FFFCCB
236 #FEDB87
237 #F9FCB6
238 #EC6147
239 #D53E4E
240 #F7834C
241 #FEBE6E
242 #FEDB87
243 #FEE28E
244 #FEE28E
245 #FCA75D
246 #FEE28E
247 #FECC7A
248 #FDB768
249     gray
250 #FEDB87
251 #FEE695
252 #FED481
253 #F88C50
254 #F67948
255 #FCA75D
256     gray
257     gray
258 #FEBE6E
259 #FFF3AC
260 #FFF3AC
261 #FEEA9C
262 #FB9F59
263 #FECC7A
264 #FEDB87
265 #FDB768
266 #FA9554
267 #FED481
268 #F88C50
269 #FEDB87
```

```
270 #F88C50
271 #FEBE6E
272 #FEC575
273 #FCA75D
274 #FEDB87
275 #FDB063
276 #FDB063
277 #FEE695
278 #FEE28E
279 #FCA75D
280 #FFF3AC
281 #FCA75D
282     gray
283 #FFF8B3
284 #FFEEA4
285 #FED481
286 #FDDEBC
287 #FFF8B3
288 #E7F59A
289 #FB9F59
290 #FFEEA4
291 #F6FBB1
292 #D53E4E
293 #FFEEA9C
294 #EEF8A5
295     gray
296 #EC6147
297 #FEDB87
298 #FEE695
299 #FDB768
300 #FDDEBC
301 #FEDB87
302 #F88C50
303 #F7834C
304 #F88C50
305 #FED481
306 #F88C50
307 #FB9F59
308 #F88C50
309 #FEBE6E
310     gray
311 #FEBE6E
312 #FFF3AC
313 #FED481
314 #FDB063
```

```
315 #F88C50
316 #FA9554
317     gray
318     gray
319 #FECC7A
320 #FEC575
321 #FCA75D
322 #FEE28E
323 #FECC7A
324 #FCA75D
325 #FEDB87
326 #FA9554
327 #FEDB87
328 #FEE695
329 #FCA75D
330 #FEE695
331 #FCA75D
332 #FECC7A
333 #FEC575
334 #FEE28E
335 #FDB768
336 #FDB768
337 #FEBE6E
338 #FEC575
339 #FDB063
340 #FDB063
341 #FA9554
342 #FEC575
343     gray
344 #FEBE6E
345 #FEEA9C
346 #FCA75D
347 #FFFCBB
348 #FEE28E
349 #FEE28E
350 #F46F43
351 #FEEA9C
352 #FEDB87
353 #DE4D4B
354 #FFEEA4
355 #FDDEBC
356     gray
357 #E2544A
358 #FEBE6E
359 #FED481
```

```
360 #F88C50
361 #FEE28E
362 #FDB063
363 #F7834C
364 #E2544A
365 #EC6147
366 #FED481
367 #FCA75D
368 #FECC7A
369 #FCA75D
370 #FED481
371     gray
372 #FEC575
373 #FEDB87
374 #FEBE6E
375 #F46F43
376 #FDB768
377 #FCA75D
378     gray
379     gray
380 #FFEEA4
381 #FDB063
382 #FEBE6E
383 #FFF3AC
384 #F88C50
385 #FCA75D
386 #F88C50
387 #FDB768
388 #FDB063
389 #FED481
390 #FEC575
391 #FFF8B3
392 #FEC575
393 #FDB768
394 #FDB063
395 #FDB063
396 #F7834C
397 #FEC575
398 #FDB768
399 #FEE695
400 #FFEEA9C
401 #FCA75D
402 #F88C50
403 #FB9F59
404     gray
```

```
405 #FDB768
406 #FEDB87
407 #FDB063
408 #FFF3AC
409 #FEDB87
410 #FFF8B3
411 #E75A48
412 #FFEEA4
413 #FECC7A
414 #D53E4E
415 #FFF3AC
416 #EBF79F
417     gray
418 #F46F43
419 #FEE28E
420 #FEE695
421 #F06744
422 #FEE695
423 #FEBE6E
424 #F67948
425 #DE4D4B
426 #EC6147
427 #FED481
428 #FFF3AC
429 #FEEA9C
430 #FFF8B3
431 #FFFCBB
432     gray
433 #F9FCB6
434 #FEEA9C
435 #FDDEBC
436 #FFF8B3
437 #F9FCB6
438 #F9FCB6
439     gray
440     gray
441 #FFFCBB
442 #FDDEBC
443 #EBF79F
444 #F9FCB6
445 #F6FBB1
446 #EOF299
447 #FFF3AC
448 #FEEA9C
449 #F9FCB6
```

```
450 #FEE695
451 #FDDEBC
452 #E7F59A
453 #FDDEBC
454 #FFF8B3
455 #FFF8B3
456 #E7F59A
457 #FFEEA4
458 #FFF3AC
459 #F6FB1
460 #EBF79F
461 #FDDEBC
462 #F2F9AB
463 #F9FCB6
464 #FEE28E
465     gray
466 #9BD6A4
467 #EBF79F
468 #FFF8B3
469 #EBF79F
470 #F2F9AB
471 #9BD6A4
472 #FED481
473 #EEF8A5
474 #92D2A4
475 #F7834C
476 #D0EC9C
477 #EOF299
478     gray
479 #FECC7A
480 #FFEEA9C
481 #FFF8B3
482 #FFEEA4
483 #D9EF9B
484 #E7F59A
485 #FEBE6E
486 #FCA75D
487 #FEC575
488 #FFEEA9C
489 #A4DAA4
490 #92D2A4
491 #D9EF9B
492 #BFE4A0
493     gray
494 #F6FB1
```

```
495 #7ECAA4
496 #B6E1A1
497 #EBF79F
498 #BFE4A0
499 #E7F59A
500     gray
501     gray
502 #EEF8A5
503 #92D2A4
504 #73C6A4
505 #68C2A4
506 #92D2A4
507 #68C2A4
508 #92D2A4
509 #92D2A4
510 #7ECAA4
511 #A4DAA4
512 #D9EF9B
513 #88CEA4
514 #D0EC9C
515 #73C6A4
516 #ADDDA3
517 #BFE4A0
518 #B6E1A1
519 #EEF8A5
520 #9BD6A4
521 #A4DAA4
522 #7ECAA4
523 #FDDEBC
524 #EBF79F
525 #FFF8B3
526     gray
527 #92D2A4
528 #62BBA8
529 #E7F59A
530 #9BD6A4
531 #B6E1A1
532 #4578B5
533 #FECC7A
534 #88CEA4
535 #5DB2AB
536 #FEBE6E
537 #C8E89E
538 #9BD6A4
539     gray
```

```
540 #FEEA9C
541 #9BD6A4
542 #B6E1A1
543 #B6E1A1
544 #3288BC
545 #9BD6A4
546 #FEE695
547 #FED481
548 #FDB063
549 #88CEA4
550 #ADDDA3
551 #EBF79F
552 #B6E1A1
553 #C8E89E
554 gray
555 #FEDB87
556 #D0EC9C
557 #EOF299
558 #FFF8B3
559 #D9EF9B
560 #BFE4A0
561 gray
562 gray
563 #F2F9AB
564 #D0EC9C
565 #7ECAA4
566 #88CEA4
567 #C8E89E
568 #88CEA4
569 #9BD6A4
570 #92D2A4
571 #ADDDA3
572 #EBF79F
573 #E7F59A
574 #ADDDA3
575 #EOF299
576 #88CEA4
577 #FEE695
578 #EOF299
579 #BFE4A0
580 #F6FBB1
581 #BFE4A0
582 #A4DAA4
583 #ADDDA3
584 #F9FCB6
```

```
585 #B6E1A1
586 #FFF3AC
587     gray
588 #A4DAA4
589 #68C2A4
590 #68C2A4
591 #7ECAA4
592 #F2F9AB
593 #57AAAF
594 #FEEA9C
595 #9BD6A4
596 #5DB2AB
597 #FB9F59
598 #7ECAA4
599 #92D2A4
600     gray
601 #FEDB87
602 #7ECAA4
603 #7ECAA4
604 #D9EF9B
605 #5DB2AB
606 #BFE4A0
607 #FFEEA4
608 #FED481
609 #FDB768
610 #A4DAA4
611 #FFFCBB
612 #FFFCBB
613 #FFF8B3
614 #F2F9AB
615     gray
616 #F6FBB1
617 #F6FBB1
618 #FFF8B3
619 #FFF8B3
620 #F2F9AB
621 #FDDEBC
622     gray
623     gray
624 #F6FBB1
625 #E7F59A
626 #F2F9AB
627 #E0F299
628 #FFFCBB
629 #D9EF9B
```

```
630 #EEF8A5
631 #E7F59A
632 #FFF3AC
633 #E7F59A
634 #FFF3AC
635 #D9EF9B
636 #FFF3AC
637 #F2F9AB
638 #EBF79F
639 #D0EC9C
640 #FFF8B3
641 #F6FBB1
642 #E7F59A
643 #E7F59A
644 #E0F299
645 #FFEEA4
646 #F2F9AB
647 #F2F9AB
648     gray
649 #E0F299
650 #E0F299
651 #E7F59A
652 #F9FCB6
653 #D0EC9C
654 #9BD6A4
655 #FEE28E
656 #ADDDA3
657 #73C6A4
658 #EC6147
659 #C8E89E
660 #A4DAA4
661     gray
662 #FED481
663 #FDDEBC
664 #F2F9AB
665 #FFF8B3
666 #E0F299
667 #E7F59A
668 #FFEEA9C
669 #FECC7A
670 #FEE28E
671 #FFF8B3
672 #FEDB87
673 #FFEEA4
674 #FFFCBB
```

```
675 #E7F59A
676     gray
677 #FEDB87
678 #FFF8B3
679 #FFEEA4
680 #FEDB87
681 #FFF8B3
682 #FFF8B3
683     gray
684     gray
685 #F9FCB6
686 #FFF8B3
687 #FFF8B3
688 #FFF8B3
689 #FEE695
690 #FFF3AC
691 #FEE695
692 #FFF8B3
693 #FDDEBC
694 #FEEA9C
695 #FED481
696 #FFF3AC
697 #FEE695
698 #FFF3AC
699 #FEE28E
700 #FFF3AC
701 #FEE695
702 #FEEA9C
703 #FDDEBC
704 #FFEEA4
705 #FFEEA4
706 #FEE695
707 #FFEEA4
708 #FEEA9C
709     gray
710 #F6FB1
711 #FFF8B3
712 #FEEA9C
713 #FFF8B3
714 #EEF8A5
715 #C8E89E
716 #FEBE6E
717 #FFF8B3
718 #EBF79F
719 #FB9F59
```

```
720 #F2F9AB
721 #D9EF9B
722 gray
723 #FDB768
724 #FFF8B3
725 #FFF8B3
726 #FEE695
727 #E0F299
728 #F6FBB1
729 #FEC575
730 #F88C50
731 #FDB768
732 #FFEEA4
733 #F2F9AB
734 #EEF8A5
735 #FDFEBC
736 #EBF79F
737 gray
738 #EEF8A5
739 #D9EF9B
740 #F2F9AB
741 #F6FBB1
742 #DOEC9C
743 #FDFEBC
744 gray
745 gray
746 #EEF8A5
747 #E7F59A
748 #F6FBB1
749 #D9EF9B
750 #F2F9AB
751 #F6FBB1
752 #EBF79F
753 #E0F299
754 #E0F299
755 #D9EF9B
756 #FFF3AC
757 #DOEC9C
758 #FFF3AC
759 #EBF79F
760 #FDFEBC
761 #DOEC9C
762 #F6FBB1
763 #F9FCB6
764 #EEF8A5
```

```
765 #EEF8A5
766 #EBF79F
767 #EOF299
768 #C8E89E
769 #FFFCBB
770     gray
771 #E7F59A
772 #D9EF9B
773 #F2F9AB
774 #EOF299
775 #D0EC9C
776 #7ECAA4
777 #FEE695
778 #E7F59A
779 #ADDDA3
780 #FA9554
781 #D9EF9B
782 #C8E89E
783     gray
784 #FED481
785 #ADDDA3
786 #ADDDA3
787 #F2F9AB
788 #92D2A4
789 #C8E89E
790 #FFEEA4
791 #FEBE6E
792 #FFEEA4
793 #92D2A4
794 #E7F59A
795 #EOF299
796 #D0EC9C
797 #C8E89E
798     gray
799 #F2F9AB
800 #EOF299
801 #EEF8A5
802 #FDDEBC
803 #ADDDA3
804 #EEF8A5
805     gray
806     gray
807 #EOF299
808 #EEF8A5
809 #EEF8A5
```

```
810 #D9EF9B
811 #E7F59A
812 #E7F59A
813 #F6FB1
814 #EOF299
815 #D9EF9B
816 #EEF8A5
817 #FFFCBB
818 #EOF299
819 #FFF8B3
820 #E7F59A
821 #EOF299
822 #C8E89E
823 #EBF79F
824 #FFF3AC
825 #EOF299
826 #E7F59A
827 #EEF8A5
828 #F9FCB6
829 #EBF79F
830 #EEF8A5
831     gray
832 #BFE4A0
833 #BFE4A0
834 #EBF79F
835 #88CEA4
836 #ADDDA3
837 #7ECAA4
838 #EEF8A5
839 #E7F59A
840 #92D2A4
841 #FA9554
842 #B6E1A1
843 #9BD6A4
844     gray
845 #FEE695
846 #D0EC9C
847 #C8E89E
848 #EEF8A5
849 #73C6A4
850 #E7F59A
851 #FEEA9C
852 #FEBE6E
853 #FEC575
854 #D9EF9B
```

```
855 #D0EC9C
856 #7ECAA4
857 #57AAAF
858 #3E90B9
859     gray
860 #EBF79F
861 #62BBA8
862 #BFE4A0
863 #92D2A4
864 #A4DAA4
865 #EBF79F
866     gray
867     gray
868 #FFF3AC
869 #BFE4A0
870 #4898B6
871 #3E90B9
872 #68C2A4
873 #4898B6
874 #88CEA4
875 #73C6A4
876 #4898B6
877 #92D2A4
878 #FEDB87
879 #5DB2AB
880 #FCA75D
881 #68C2A4
882 #EBF79F
883 #EOF299
884 #92D2A4
885 #F6FBB1
886 #BFE4A0
887 #BFE4A0
888 #3E90B9
889 #F9FCB6
890 #88CEA4
891 #9BD6A4
892     gray
893 #73C6A4
894 #5DB2AB
895 #D9EF9B
896 #68C2A4
897 #A4DAA4
898 #5A58A5
899 #FEEA9C
```

```
900 #5DB2AB
901 #4578B5
902 #FED481
903 #62BBA8
904 #ADDDA3
905     gray
906 #EEF8A5
907 #57AAAF
908 #73C6A4
909 #ADDDA3
910 #4578B5
911 #5DB2AB
912 #FFF3AC
913 #FEC575
914 #FEEA9C
915 #62BBA8
916 #C8E89E
917 #F2F9AB
918 #B6E1A1
919 #68C2A4
920     gray
921 #FFFCBB
922 #BFE4A0
923 #F06744
924 #F6FBB1
925 #7ECAA4
926 #FEDB87
927     gray
928     gray
929 #F6FBB1
930 #FEE695
931 #FED481
932 #FFF8B3
933 #F6FBB1
934 #F9FCB6
935 #EBF79F
936 #F88C50
937 #FFEEA4
938 #D9EF9B
939 #FED481
940 #FEBE6E
941 #FECC7A
942 #FFEEA4
943 #FEE695
944 #F67948
```

```
945 #B6E1A1
946 #FDB768
947 #9BD6A4
948 #68C2A4
949 #BFE4A0
950 #EBF79F
951 #9BD6A4
952 #FFEEA4
953     gray
954 #DE4D4B
955 #FEC575
956 #D9454D
957 #D9454D
958 #D9454D
959 #62BBA8
960 #F9FCB6
961 #7ECAA4
962 #68C2A4
963 #FEE695
964 #9BD6A4
965 #F9FCB6
966     gray
967 #FEDB87
968 #92D2A4
969 #C8E89E
970 #FDB768
971 #FFF8B3
972 #73C6A4
973 #FEEA9C
974 #FEDB87
975 #FED481
976 #EEF8A5
977 #FED481
978 #FFFCBB
979 #ADDDA3
980 #57AAAF
981     gray
982 #FFF8B3
983 #C8E89E
984 #D9454D
985 #FDDEBC
986 #68C2A4
987 #EEF8A5
988     gray
989     gray
```

```
990 #F6FBB1
991 #FEDB87
992 #FA9554
993 #E0F299
994 #F6FBB1
995 #B6E1A1
996 #EEF8A5
997 #CD374D
998 #BFE4A0
999 #D9EF9B
1000 #FDB768
1001 #F6FBB1
1002 #FA9554
1003 #FEEA9C
1004 #FA9554
1005 #FA9554
1006 #B6E1A1
1007 #FED481
1008 #ADDDA3
1009 #62BBA8
1010 #D0EC9C
1011 #FDFEBC
1012 #73C6A4
1013 #D53E4E
1014 gray
1015 #E2544A
1016 #F9FCB6
1017 #D53E4E
1018 #F88C50
1019 #D53E4E
1020 #5DB2AB
1021 #E7F59A
1022 #73C6A4
1023 #3288BC
1024 #FED481
1025 #73C6A4
1026 #ADDDA3
1027 gray
1028 #FEE28E
1029 #A4DAA4
1030 #E7F59A
1031 #9E0041
1032 #BFE4A0
1033 #5DB2AB
1034 #FFEEA4
```

```
1035 #FEE695
1036 #FED481
1037 #D0EC9C
1038 #D0EC9C
1039 #E7F59A
1040 #EEF8A5
1041 #5DB2AB
1042 gray
1043 #F67948
1044 #9BD6A4
1045 #EBF79F
1046 #A4DAA4
1047 #D0EC9C
1048 #F6FBB1
1049 gray
1050 gray
1051 #FDB768
1052 #D9EF9B
1053 #F2F9AB
1054 #B6E1A1
1055 #F9FCB6
1056 #D0EC9C
1057 #ADDDA3
1058 #B6E1A1
1059 #4898B6
1060 #EOF299
1061 #FED481
1062 #C8E89E
1063 #FFF3AC
1064 #E7F59A
1065 #F67948
1066 #FFFCBB
1067 #E7F59A
1068 #FFF3AC
1069 #F9FCB6
1070 #C8E89E
1071 #EBF79F
1072 #FFEEA4
1073 #B6E1A1
1074 #FEEA9C
1075 gray
1076 #B6E1A1
1077 #EBF79F
1078 #F06744
1079 #F6FBB1
```

```
1080 #FED481
1081 #5A58A5
1082 #FEEA9C
1083 #62BBA8
1084 #73C6A4
1085 #FB9F59
1086 #B6E1A1
1087 #EBF79F
1088 gray
1089 #FEE695
1090 #A4DAA4
1091 #B6E1A1
1092 #BFE4A0
1093 #57AAAF
1094 #73C6A4
1095 #FEDB87
1096 #FCA75D
1097 #FEC575
1098 #A4DAA4
1099 #FFF8B3
1100 #FFF3AC
1101 #F9FCB6
1102 #F9FCB6
1103 gray
1104 #FEEA9C
1105 #FDDEBC
1106 #FEE28E
1107 #FFF3AC
1108 #F6FBB1
1109 #FFFCCB
1110 gray
1111 gray
1112 #FDDEBC
1113 #F9FCB6
1114 #F9FCB6
1115 #FFFCCB
1116 #FFEEA4
1117 #FFEEA4
1118 #FEE695
1119 #FFF8B3
1120 #FED481
1121 #FFF3AC
1122 #FFF3AC
1123 #FEEA9C
1124 #FFF3AC
```

```
1125 #FEE28E
1126 #FFFCBB
1127 #F6FBB1
1128 #FFF3AC
1129 #FFEEA4
1130 #F9FCB6
1131 #FFF8B3
1132 #F9FCB6
1133 #FFF3AC
1134 #FEE695
1135 #FFEEA4
1136 gray
1137 #FDDEBC
1138 #FFF3AC
1139 #FFF3AC
1140 #FFEEA4
1141 #EBF79F
1142 #9BD6A4
1143 #FFF3AC
1144 #FEE28E
1145 #D9EF9B
1146 #FED481
1147 #FDDEBC
1148 #FFFCBB
1149 gray
1150 #FECC7A
1151 #F9FCB6
1152 #EBF79F
1153 #F2F9AB
1154 #C8E89E
1155 #F6FBB1
1156 #FEE28E
1157 #FDB768
1158 #FDB768
1159 #FDDEBC
1160 #FFF3AC
1161 #FFEEA4
1162 #F6FBB1
1163 #FFFCBB
1164 gray
1165 #FEE28E
1166 #FEEA9C
1167 #FEE695
1168 #FEEA9C
1169 #FDDEBC
```

```
1170 #FFEEA4
1171 gray
1172 gray
1173 #FEEA9C
1174 #FFF8B3
1175 #FFFCBB
1176 #FFF8B3
1177 #FEE695
1178 #FFEEA4
1179 #FFF3AC
1180 #FFF3AC
1181 #FEE695
1182 #FEEA9C
1183 #FFF3AC
1184 #FFF8B3
1185 #FFF3AC
1186 #FEEA9C
1187 #FEEA9C
1188 #FFF8B3
1189 #FEEA9C
1190 #FEE695
1191 #FFEEA4
1192 #F6FBB1
1193 #FDDEBC
1194 #FEE695
1195 #FEEA9C
1196 #FFF3AC
1197 gray
1198 #FEEA9C
1199 #FFF3AC
1200 #FEE695
1201 #FEE695
1202 #E7F59A
1203 #D9EF9B
1204 #FEE28E
1205 #FEE695
1206 #D0EC9C
1207 #FDB063
1208 #FFFCBB
1209 #FFF3AC
1210 gray
1211 #FDB768
1212 #FDDEBC
1213 #F6FBB1
1214 #F9FCB6
```

```

1215 #EEF8A5
1216 #FFFCBB
1217 #FEDB87
1218 #FDB063
1219 #FCA75D
1220 #F9FCB6

```

```
gcolor$data[[1]]
```

	fill	x	y	PANEL	group	xmin	xmax	ymin	ymax	alpha
1	#FEE695	1	61	1	61	0.5	1.5	60.5	61.5	NA
2	#FEE695	1	60	1	60	0.5	1.5	59.5	60.5	NA
3	#FEEA9C	1	59	1	59	0.5	1.5	58.5	59.5	NA
4	#F9FCB6	1	58	1	58	0.5	1.5	57.5	58.5	NA
5	gray	1	57	1	57	0.5	1.5	56.5	57.5	NA
6	#FED481	1	56	1	56	0.5	1.5	55.5	56.5	NA
7	#B6E1A1	1	55	1	55	0.5	1.5	54.5	55.5	NA
8	#FDB063	1	54	1	54	0.5	1.5	53.5	54.5	NA
9	#FEDB87	1	53	1	53	0.5	1.5	52.5	53.5	NA
10	#92D2A4	1	52	1	52	0.5	1.5	51.5	52.5	NA
11	#FDB063	1	51	1	51	0.5	1.5	50.5	51.5	NA
12	gray	1	50	1	50	0.5	1.5	49.5	50.5	NA
13	gray	1	49	1	49	0.5	1.5	48.5	49.5	NA
14	#F46F43	1	48	1	48	0.5	1.5	47.5	48.5	NA
15	#FA9554	1	47	1	47	0.5	1.5	46.5	47.5	NA
16	#FEE695	1	46	1	46	0.5	1.5	45.5	46.5	NA
17	#FEC575	1	45	1	45	0.5	1.5	44.5	45.5	NA
18	#F2F9AB	1	44	1	44	0.5	1.5	43.5	44.5	NA
19	#FEE28E	1	43	1	43	0.5	1.5	42.5	43.5	NA
20	#DOEC9C	1	42	1	42	0.5	1.5	41.5	42.5	NA
21	#F7834C	1	41	1	41	0.5	1.5	40.5	41.5	NA
22	#C8E89E	1	40	1	40	0.5	1.5	39.5	40.5	NA
23	#FDB063	1	39	1	39	0.5	1.5	38.5	39.5	NA
24	#FFF8B3	1	38	1	38	0.5	1.5	37.5	38.5	NA
25	#FEE695	1	37	1	37	0.5	1.5	36.5	37.5	NA
26	#FFEEA4	1	36	1	36	0.5	1.5	35.5	36.5	NA
27	#FEEA9C	1	35	1	35	0.5	1.5	34.5	35.5	NA
28	#FA9554	1	34	1	34	0.5	1.5	33.5	34.5	NA
29	#FEE28E	1	33	1	33	0.5	1.5	32.5	33.5	NA
30	#FDDEBC	1	32	1	32	0.5	1.5	31.5	32.5	NA
31	#FEEA9C	1	31	1	31	0.5	1.5	30.5	31.5	NA
32	#FDDEBC	1	30	1	30	0.5	1.5	29.5	30.5	NA
33	#FFF8B3	1	29	1	29	0.5	1.5	28.5	29.5	NA
34	#FEE695	1	28	1	28	0.5	1.5	27.5	28.5	NA
35	#FEEA9C	1	27	1	27	0.5	1.5	26.5	27.5	NA

36	#FB9F59	1	26	1	26	0.5	1.5	25.5	26.5	NA
37	#FCA75D	1	25	1	25	0.5	1.5	24.5	25.5	NA
38	gray	1	24	1	24	0.5	1.5	23.5	24.5	NA
39	#F88C50	1	23	1	23	0.5	1.5	22.5	23.5	NA
40	#FB9F59	1	22	1	22	0.5	1.5	21.5	22.5	NA
41	#FFEEA4	1	21	1	21	0.5	1.5	20.5	21.5	NA
42	#FEBE6E	1	20	1	20	0.5	1.5	19.5	20.5	NA
43	#FEC575	1	19	1	19	0.5	1.5	18.5	19.5	NA
44	#68C2A4	1	18	1	18	0.5	1.5	17.5	18.5	NA
45	#E0F299	1	17	1	17	0.5	1.5	16.5	17.5	NA
46	#F6FBB1	1	16	1	16	0.5	1.5	15.5	16.5	NA
47	#68C2A4	1	15	1	15	0.5	1.5	14.5	15.5	NA
48	#FEE695	1	14	1	14	0.5	1.5	13.5	14.5	NA
49	#B6E1A1	1	13	1	13	0.5	1.5	12.5	13.5	NA
50	#FEEA9C	1	12	1	12	0.5	1.5	11.5	12.5	NA
51	gray	1	11	1	11	0.5	1.5	10.5	11.5	NA
52	#F6FBB1	1	10	1	10	0.5	1.5	9.5	10.5	NA
53	#3E90B9	1	9	1	9	0.5	1.5	8.5	9.5	NA
54	#73C6A4	1	8	1	8	0.5	1.5	7.5	8.5	NA
55	#EC6147	1	7	1	7	0.5	1.5	6.5	7.5	NA
56	#BFE4A0	1	6	1	6	0.5	1.5	5.5	6.5	NA
57	#88CEA4	1	5	1	5	0.5	1.5	4.5	5.5	NA
58	#F2F9AB	1	4	1	4	0.5	1.5	3.5	4.5	NA
59	#F6FBB1	1	3	1	3	0.5	1.5	2.5	3.5	NA
60	#FEDB87	1	2	1	2	0.5	1.5	1.5	2.5	NA
61	#EBF79F	1	1	1	1	0.5	1.5	0.5	1.5	NA
62	#FEE28E	2	61	1	122	1.5	2.5	60.5	61.5	NA
63	#FEDB87	2	60	1	121	1.5	2.5	59.5	60.5	NA
64	#FEEA9C	2	59	1	120	1.5	2.5	58.5	59.5	NA
65	#FEE695	2	58	1	119	1.5	2.5	57.5	58.5	NA
66	gray	2	57	1	118	1.5	2.5	56.5	57.5	NA
67	#FFEEA4	2	56	1	117	1.5	2.5	55.5	56.5	NA
68	#E0F299	2	55	1	116	1.5	2.5	54.5	55.5	NA
69	#FEE28E	2	54	1	115	1.5	2.5	53.5	54.5	NA
70	#FDB768	2	53	1	114	1.5	2.5	52.5	53.5	NA
71	#4578B5	2	52	1	113	1.5	2.5	51.5	52.5	NA
72	#FDB063	2	51	1	112	1.5	2.5	50.5	51.5	NA
73	gray	2	50	1	111	1.5	2.5	49.5	50.5	NA
74	gray	2	49	1	110	1.5	2.5	48.5	49.5	NA
75	#F6FBB1	2	48	1	109	1.5	2.5	47.5	48.5	NA
76	#FED481	2	47	1	108	1.5	2.5	46.5	47.5	NA
77	#FDB768	2	46	1	107	1.5	2.5	45.5	46.5	NA
78	#FEEA9C	2	45	1	106	1.5	2.5	44.5	45.5	NA
79	#FFEEA4	2	44	1	105	1.5	2.5	43.5	44.5	NA
80	#D9EF9B	2	43	1	104	1.5	2.5	42.5	43.5	NA

81	#FDB063	2 42	1	103	1.5	2.5	41.5	42.5	NA
82	#FEBE6E	2 41	1	102	1.5	2.5	40.5	41.5	NA
83	#FEC575	2 40	1	101	1.5	2.5	39.5	40.5	NA
84	#F6FBB1	2 39	1	100	1.5	2.5	38.5	39.5	NA
85	#FEDB87	2 38	1	99	1.5	2.5	37.5	38.5	NA
86	#FEBE6E	2 37	1	98	1.5	2.5	36.5	37.5	NA
87	#FED481	2 36	1	97	1.5	2.5	35.5	36.5	NA
88	#FDB768	2 35	1	96	1.5	2.5	34.5	35.5	NA
89	#FEBE6E	2 34	1	95	1.5	2.5	33.5	34.5	NA
90	#FECC7A	2 33	1	94	1.5	2.5	32.5	33.5	NA
91	#FEE28E	2 32	1	93	1.5	2.5	31.5	32.5	NA
92	#FECC7A	2 31	1	92	1.5	2.5	30.5	31.5	NA
93	#FED481	2 30	1	91	1.5	2.5	29.5	30.5	NA
94	#FEDB87	2 29	1	90	1.5	2.5	28.5	29.5	NA
95	#FEC575	2 28	1	89	1.5	2.5	27.5	28.5	NA
96	#FEC575	2 27	1	88	1.5	2.5	26.5	27.5	NA
97	#FECC7A	2 26	1	87	1.5	2.5	25.5	26.5	NA
98	#FEC575	2 25	1	86	1.5	2.5	24.5	25.5	NA
99	gray	2 24	1	85	1.5	2.5	23.5	24.5	NA
100	#FEBE6E	2 23	1	84	1.5	2.5	22.5	23.5	NA
101	#FFF3AC	2 22	1	83	1.5	2.5	21.5	22.5	NA
102	#FDB768	2 21	1	82	1.5	2.5	20.5	21.5	NA
103	#FEE28E	2 20	1	81	1.5	2.5	19.5	20.5	NA
104	#FEBE6E	2 19	1	80	1.5	2.5	18.5	19.5	NA
105	#FFF8B3	2 18	1	79	1.5	2.5	17.5	18.5	NA
106	#E7F59A	2 17	1	78	1.5	2.5	16.5	17.5	NA
107	#FFFCBB	2 16	1	77	1.5	2.5	15.5	16.5	NA
108	#4898B6	2 15	1	76	1.5	2.5	14.5	15.5	NA
109	#FDDEBC	2 14	1	75	1.5	2.5	13.5	14.5	NA
110	#FFF8B3	2 13	1	74	1.5	2.5	12.5	13.5	NA
111	#FEC575	2 12	1	73	1.5	2.5	11.5	12.5	NA
112	gray	2 11	1	72	1.5	2.5	10.5	11.5	NA
113	#EBF79F	2 10	1	71	1.5	2.5	9.5	10.5	NA
114	#ADDDA3	2 9	1	70	1.5	2.5	8.5	9.5	NA
115	#BFE4A0	2 8	1	69	1.5	2.5	7.5	8.5	NA
116	#F06744	2 7	1	68	1.5	2.5	6.5	7.5	NA
117	#DE4D4B	2 6	1	67	1.5	2.5	5.5	6.5	NA
118	#88CEA4	2 5	1	66	1.5	2.5	4.5	5.5	NA
119	#D9EF9B	2 4	1	65	1.5	2.5	3.5	4.5	NA
120	#FDDEBC	2 3	1	64	1.5	2.5	2.5	3.5	NA
121	#D9EF9B	2 2	1	63	1.5	2.5	1.5	2.5	NA
122	#E7F59A	2 1	1	62	1.5	2.5	0.5	1.5	NA
123	#FEEA9C	3 61	1	183	2.5	3.5	60.5	61.5	NA
124	#FECC7A	3 60	1	182	2.5	3.5	59.5	60.5	NA
125	#FFFCBB	3 59	1	181	2.5	3.5	58.5	59.5	NA

126	#FFEEA4	3	58	1	180	2.5	3.5	57.5	58.5	NA
127	gray	3	57	1	179	2.5	3.5	56.5	57.5	NA
128	#FEDB87	3	56	1	178	2.5	3.5	55.5	56.5	NA
129	#FDB768	3	55	1	177	2.5	3.5	54.5	55.5	NA
130	#FECC7A	3	54	1	176	2.5	3.5	53.5	54.5	NA
131	#FEBE6E	3	53	1	175	2.5	3.5	52.5	53.5	NA
132	#D0EC9C	3	52	1	174	2.5	3.5	51.5	52.5	NA
133	#FEE28E	3	51	1	173	2.5	3.5	50.5	51.5	NA
134	gray	3	50	1	172	2.5	3.5	49.5	50.5	NA
135	gray	3	49	1	171	2.5	3.5	48.5	49.5	NA
136	#FED481	3	48	1	170	2.5	3.5	47.5	48.5	NA
137	#FEE695	3	47	1	169	2.5	3.5	46.5	47.5	NA
138	#FEE695	3	46	1	168	2.5	3.5	45.5	46.5	NA
139	#FFFCCB	3	45	1	167	2.5	3.5	44.5	45.5	NA
140	#FEEA9C	3	44	1	166	2.5	3.5	43.5	44.5	NA
141	#FEEA9C	3	43	1	165	2.5	3.5	42.5	43.5	NA
142	#FDB768	3	42	1	164	2.5	3.5	41.5	42.5	NA
143	#FEC575	3	41	1	163	2.5	3.5	40.5	41.5	NA
144	#FED481	3	40	1	162	2.5	3.5	39.5	40.5	NA
145	#FED481	3	39	1	161	2.5	3.5	38.5	39.5	NA
146	#FFEEA4	3	38	1	160	2.5	3.5	37.5	38.5	NA
147	#FED481	3	37	1	159	2.5	3.5	36.5	37.5	NA
148	#FEEA9C	3	36	1	158	2.5	3.5	35.5	36.5	NA
149	#FEBE6E	3	35	1	157	2.5	3.5	34.5	35.5	NA
150	#FECC7A	3	34	1	156	2.5	3.5	33.5	34.5	NA
151	#FEBE6E	3	33	1	155	2.5	3.5	32.5	33.5	NA
152	#FEC575	3	32	1	154	2.5	3.5	31.5	32.5	NA
153	#FEC575	3	31	1	153	2.5	3.5	30.5	31.5	NA
154	#FDB768	3	30	1	152	2.5	3.5	29.5	30.5	NA
155	#FFEEA4	3	29	1	151	2.5	3.5	28.5	29.5	NA
156	#FEE28E	3	28	1	150	2.5	3.5	27.5	28.5	NA
157	#FEBE6E	3	27	1	149	2.5	3.5	26.5	27.5	NA
158	#FED481	3	26	1	148	2.5	3.5	25.5	26.5	NA
159	#FEDB87	3	25	1	147	2.5	3.5	24.5	25.5	NA
160	gray	3	24	1	146	2.5	3.5	23.5	24.5	NA
161	#FEE695	3	23	1	145	2.5	3.5	22.5	23.5	NA
162	#FEE695	3	22	1	144	2.5	3.5	21.5	22.5	NA
163	#FED481	3	21	1	143	2.5	3.5	20.5	21.5	NA
164	#FEC575	3	20	1	142	2.5	3.5	19.5	20.5	NA
165	#FEEA9C	3	19	1	141	2.5	3.5	18.5	19.5	NA
166	#D0EC9C	3	18	1	140	2.5	3.5	17.5	18.5	NA
167	#92D2A4	3	17	1	139	2.5	3.5	16.5	17.5	NA
168	#B6E1A1	3	16	1	138	2.5	3.5	15.5	16.5	NA
169	#5E4EA1	3	15	1	137	2.5	3.5	14.5	15.5	NA
170	#FFEEA4	3	14	1	136	2.5	3.5	13.5	14.5	NA

171	#4578B5	3 13	1	135	2.5	3.5	12.5	13.5	NA
172	#FEDB87	3 12	1	134	2.5	3.5	11.5	12.5	NA
173	gray	3 11	1	133	2.5	3.5	10.5	11.5	NA
174	#F9FCB6	3 10	1	132	2.5	3.5	9.5	10.5	NA
175	#ADDDA3	3 9	1	131	2.5	3.5	8.5	9.5	NA
176	#7ECAA4	3 8	1	130	2.5	3.5	7.5	8.5	NA
177	#F67948	3 7	1	129	2.5	3.5	6.5	7.5	NA
178	#FB9F59	3 6	1	128	2.5	3.5	5.5	6.5	NA
179	#B6E1A1	3 5	1	127	2.5	3.5	4.5	5.5	NA
180	#F6FBB1	3 4	1	126	2.5	3.5	3.5	4.5	NA
181	#FEE695	3 3	1	125	2.5	3.5	2.5	3.5	NA
182	#F6FBB1	3 2	1	124	2.5	3.5	1.5	2.5	NA
183	#D9EF9B	3 1	1	123	2.5	3.5	0.5	1.5	NA
184	#FED481	4 61	1	244	3.5	4.5	60.5	61.5	NA
185	#FCA75D	4 60	1	243	3.5	4.5	59.5	60.5	NA
186	#FECC7A	4 59	1	242	3.5	4.5	58.5	59.5	NA
187	#FEC575	4 58	1	241	3.5	4.5	57.5	58.5	NA
188	gray	4 57	1	240	3.5	4.5	56.5	57.5	NA
189	#FEE28E	4 56	1	239	3.5	4.5	55.5	56.5	NA
190	#FDB768	4 55	1	238	3.5	4.5	54.5	55.5	NA
191	#FED481	4 54	1	237	3.5	4.5	53.5	54.5	NA
192	#FCA75D	4 53	1	236	3.5	4.5	52.5	53.5	NA
193	#FED481	4 52	1	235	3.5	4.5	51.5	52.5	NA
194	#FEC575	4 51	1	234	3.5	4.5	50.5	51.5	NA
195	gray	4 50	1	233	3.5	4.5	49.5	50.5	NA
196	gray	4 49	1	232	3.5	4.5	48.5	49.5	NA
197	#FDB063	4 48	1	231	3.5	4.5	47.5	48.5	NA
198	#FEBE6E	4 47	1	230	3.5	4.5	46.5	47.5	NA
199	#FEE28E	4 46	1	229	3.5	4.5	45.5	46.5	NA
200	#FFF8B3	4 45	1	228	3.5	4.5	44.5	45.5	NA
201	#FEBE6E	4 44	1	227	3.5	4.5	43.5	44.5	NA
202	#FDB768	4 43	1	226	3.5	4.5	42.5	43.5	NA
203	#FEBE6E	4 42	1	225	3.5	4.5	41.5	42.5	NA
204	#FCA75D	4 41	1	224	3.5	4.5	40.5	41.5	NA
205	#FEBE6E	4 40	1	223	3.5	4.5	39.5	40.5	NA
206	#FB9F59	4 39	1	222	3.5	4.5	38.5	39.5	NA
207	#FEE28E	4 38	1	221	3.5	4.5	37.5	38.5	NA
208	#FEDB87	4 37	1	220	3.5	4.5	36.5	37.5	NA
209	#FEE695	4 36	1	219	3.5	4.5	35.5	36.5	NA
210	#FDB063	4 35	1	218	3.5	4.5	34.5	35.5	NA
211	#FA9554	4 34	1	217	3.5	4.5	33.5	34.5	NA
212	#FDB063	4 33	1	216	3.5	4.5	32.5	33.5	NA
213	#FDB063	4 32	1	215	3.5	4.5	31.5	32.5	NA
214	#FDB063	4 31	1	214	3.5	4.5	30.5	31.5	NA
215	#FEC575	4 30	1	213	3.5	4.5	29.5	30.5	NA

216	#FEDB87	4	29	1	212	3.5	4.5	28.5	29.5	NA
217	#FEBE6E	4	28	1	211	3.5	4.5	27.5	28.5	NA
218	#FEBE6E	4	27	1	210	3.5	4.5	26.5	27.5	NA
219	#FDB768	4	26	1	209	3.5	4.5	25.5	26.5	NA
220	#FED481	4	25	1	208	3.5	4.5	24.5	25.5	NA
221	gray	4	24	1	207	3.5	4.5	23.5	24.5	NA
222	#FCA75D	4	23	1	206	3.5	4.5	22.5	23.5	NA
223	#FEDB87	4	22	1	205	3.5	4.5	21.5	22.5	NA
224	#FEDB87	4	21	1	204	3.5	4.5	20.5	21.5	NA
225	#FDB768	4	20	1	203	3.5	4.5	19.5	20.5	NA
226	#FED481	4	19	1	202	3.5	4.5	18.5	19.5	NA
227	#DE4D4B	4	18	1	201	3.5	4.5	17.5	18.5	NA
228	#A4DAA4	4	17	1	200	3.5	4.5	16.5	17.5	NA
229	#FEE695	4	16	1	199	3.5	4.5	15.5	16.5	NA
230	#FB9F59	4	15	1	198	3.5	4.5	14.5	15.5	NA
231	#FB9F59	4	14	1	197	3.5	4.5	13.5	14.5	NA
232	#FEDB87	4	13	1	196	3.5	4.5	12.5	13.5	NA
233	#FCA75D	4	12	1	195	3.5	4.5	11.5	12.5	NA
234	gray	4	11	1	194	3.5	4.5	10.5	11.5	NA
235	#FFFCBB	4	10	1	193	3.5	4.5	9.5	10.5	NA
236	#FEDB87	4	9	1	192	3.5	4.5	8.5	9.5	NA
237	#F9FCB6	4	8	1	191	3.5	4.5	7.5	8.5	NA
238	#EC6147	4	7	1	190	3.5	4.5	6.5	7.5	NA
239	#D53E4E	4	6	1	189	3.5	4.5	5.5	6.5	NA
240	#F7834C	4	5	1	188	3.5	4.5	4.5	5.5	NA
241	#FEBE6E	4	4	1	187	3.5	4.5	3.5	4.5	NA
242	#FEDB87	4	3	1	186	3.5	4.5	2.5	3.5	NA
243	#FEE28E	4	2	1	185	3.5	4.5	1.5	2.5	NA
244	#FEE28E	4	1	1	184	3.5	4.5	0.5	1.5	NA
245	#FCA75D	5	61	1	305	4.5	5.5	60.5	61.5	NA
246	#FEE28E	5	60	1	304	4.5	5.5	59.5	60.5	NA
247	#FECC7A	5	59	1	303	4.5	5.5	58.5	59.5	NA
248	#FDB768	5	58	1	302	4.5	5.5	57.5	58.5	NA
249	gray	5	57	1	301	4.5	5.5	56.5	57.5	NA
250	#FEDB87	5	56	1	300	4.5	5.5	55.5	56.5	NA
251	#FEE695	5	55	1	299	4.5	5.5	54.5	55.5	NA
252	#FED481	5	54	1	298	4.5	5.5	53.5	54.5	NA
253	#F88C50	5	53	1	297	4.5	5.5	52.5	53.5	NA
254	#F67948	5	52	1	296	4.5	5.5	51.5	52.5	NA
255	#FCA75D	5	51	1	295	4.5	5.5	50.5	51.5	NA
256	gray	5	50	1	294	4.5	5.5	49.5	50.5	NA
257	gray	5	49	1	293	4.5	5.5	48.5	49.5	NA
258	#FEBE6E	5	48	1	292	4.5	5.5	47.5	48.5	NA
259	#FFF3AC	5	47	1	291	4.5	5.5	46.5	47.5	NA
260	#FFF3AC	5	46	1	290	4.5	5.5	45.5	46.5	NA

261	#FEEA9C	5 45	1	289	4.5	5.5	44.5	45.5	NA
262	#FB9F59	5 44	1	288	4.5	5.5	43.5	44.5	NA
263	#FECC7A	5 43	1	287	4.5	5.5	42.5	43.5	NA
264	#FEDB87	5 42	1	286	4.5	5.5	41.5	42.5	NA
265	#FDB768	5 41	1	285	4.5	5.5	40.5	41.5	NA
266	#FA9554	5 40	1	284	4.5	5.5	39.5	40.5	NA
267	#FED481	5 39	1	283	4.5	5.5	38.5	39.5	NA
268	#F88C50	5 38	1	282	4.5	5.5	37.5	38.5	NA
269	#FEDB87	5 37	1	281	4.5	5.5	36.5	37.5	NA
270	#F88C50	5 36	1	280	4.5	5.5	35.5	36.5	NA
271	#FEBE6E	5 35	1	279	4.5	5.5	34.5	35.5	NA
272	#FEC575	5 34	1	278	4.5	5.5	33.5	34.5	NA
273	#FCA75D	5 33	1	277	4.5	5.5	32.5	33.5	NA
274	#FEDB87	5 32	1	276	4.5	5.5	31.5	32.5	NA
275	#FDB063	5 31	1	275	4.5	5.5	30.5	31.5	NA
276	#FDB063	5 30	1	274	4.5	5.5	29.5	30.5	NA
277	#FEE695	5 29	1	273	4.5	5.5	28.5	29.5	NA
278	#FEE28E	5 28	1	272	4.5	5.5	27.5	28.5	NA
279	#FCA75D	5 27	1	271	4.5	5.5	26.5	27.5	NA
280	#FFF3AC	5 26	1	270	4.5	5.5	25.5	26.5	NA
281	#FCA75D	5 25	1	269	4.5	5.5	24.5	25.5	NA
282	gray	5 24	1	268	4.5	5.5	23.5	24.5	NA
283	#FFF8B3	5 23	1	267	4.5	5.5	22.5	23.5	NA
284	#FFEEA4	5 22	1	266	4.5	5.5	21.5	22.5	NA
285	#FED481	5 21	1	265	4.5	5.5	20.5	21.5	NA
286	#FDDEBC	5 20	1	264	4.5	5.5	19.5	20.5	NA
287	#FFF8B3	5 19	1	263	4.5	5.5	18.5	19.5	NA
288	#E7F59A	5 18	1	262	4.5	5.5	17.5	18.5	NA
289	#FB9F59	5 17	1	261	4.5	5.5	16.5	17.5	NA
290	#FFEEA4	5 16	1	260	4.5	5.5	15.5	16.5	NA
291	#F6FBB1	5 15	1	259	4.5	5.5	14.5	15.5	NA
292	#D53E4E	5 14	1	258	4.5	5.5	13.5	14.5	NA
293	#FEEA9C	5 13	1	257	4.5	5.5	12.5	13.5	NA
294	#EEF8A5	5 12	1	256	4.5	5.5	11.5	12.5	NA
295	gray	5 11	1	255	4.5	5.5	10.5	11.5	NA
296	#EC6147	5 10	1	254	4.5	5.5	9.5	10.5	NA
297	#FEDB87	5 9	1	253	4.5	5.5	8.5	9.5	NA
298	#FEE695	5 8	1	252	4.5	5.5	7.5	8.5	NA
299	#FDB768	5 7	1	251	4.5	5.5	6.5	7.5	NA
300	#FDDEBC	5 6	1	250	4.5	5.5	5.5	6.5	NA
301	#FEDB87	5 5	1	249	4.5	5.5	4.5	5.5	NA
302	#F88C50	5 4	1	248	4.5	5.5	3.5	4.5	NA
303	#F7834C	5 3	1	247	4.5	5.5	2.5	3.5	NA
304	#F88C50	5 2	1	246	4.5	5.5	1.5	2.5	NA
305	#FED481	5 1	1	245	4.5	5.5	0.5	1.5	NA

306	#F88C50	6 61	1	366	5.5	6.5	60.5	61.5	NA
307	#FB9F59	6 60	1	365	5.5	6.5	59.5	60.5	NA
308	#F88C50	6 59	1	364	5.5	6.5	58.5	59.5	NA
309	#FEBE6E	6 58	1	363	5.5	6.5	57.5	58.5	NA
310	gray	6 57	1	362	5.5	6.5	56.5	57.5	NA
311	#FEBE6E	6 56	1	361	5.5	6.5	55.5	56.5	NA
312	#FFF3AC	6 55	1	360	5.5	6.5	54.5	55.5	NA
313	#FED481	6 54	1	359	5.5	6.5	53.5	54.5	NA
314	#FDB063	6 53	1	358	5.5	6.5	52.5	53.5	NA
315	#F88C50	6 52	1	357	5.5	6.5	51.5	52.5	NA
316	#FA9554	6 51	1	356	5.5	6.5	50.5	51.5	NA
317	gray	6 50	1	355	5.5	6.5	49.5	50.5	NA
318	gray	6 49	1	354	5.5	6.5	48.5	49.5	NA
319	#FECC7A	6 48	1	353	5.5	6.5	47.5	48.5	NA
320	#FEC575	6 47	1	352	5.5	6.5	46.5	47.5	NA
321	#FCA75D	6 46	1	351	5.5	6.5	45.5	46.5	NA
322	#FEE28E	6 45	1	350	5.5	6.5	44.5	45.5	NA
323	#FECC7A	6 44	1	349	5.5	6.5	43.5	44.5	NA
324	#FCA75D	6 43	1	348	5.5	6.5	42.5	43.5	NA
325	#FEDB87	6 42	1	347	5.5	6.5	41.5	42.5	NA
326	#FA9554	6 41	1	346	5.5	6.5	40.5	41.5	NA
327	#FEDB87	6 40	1	345	5.5	6.5	39.5	40.5	NA
328	#FEE695	6 39	1	344	5.5	6.5	38.5	39.5	NA
329	#FCA75D	6 38	1	343	5.5	6.5	37.5	38.5	NA
330	#FEE695	6 37	1	342	5.5	6.5	36.5	37.5	NA
331	#FCA75D	6 36	1	341	5.5	6.5	35.5	36.5	NA
332	#FECC7A	6 35	1	340	5.5	6.5	34.5	35.5	NA
333	#FEC575	6 34	1	339	5.5	6.5	33.5	34.5	NA
334	#FEE28E	6 33	1	338	5.5	6.5	32.5	33.5	NA
335	#FDB768	6 32	1	337	5.5	6.5	31.5	32.5	NA
336	#FDB768	6 31	1	336	5.5	6.5	30.5	31.5	NA
337	#FEBE6E	6 30	1	335	5.5	6.5	29.5	30.5	NA
338	#FEC575	6 29	1	334	5.5	6.5	28.5	29.5	NA
339	#FDB063	6 28	1	333	5.5	6.5	27.5	28.5	NA
340	#FDB063	6 27	1	332	5.5	6.5	26.5	27.5	NA
341	#FA9554	6 26	1	331	5.5	6.5	25.5	26.5	NA
342	#FEC575	6 25	1	330	5.5	6.5	24.5	25.5	NA
343	gray	6 24	1	329	5.5	6.5	23.5	24.5	NA
344	#FEBE6E	6 23	1	328	5.5	6.5	22.5	23.5	NA
345	#FEEA9C	6 22	1	327	5.5	6.5	21.5	22.5	NA
346	#FCA75D	6 21	1	326	5.5	6.5	20.5	21.5	NA
347	#FFFCBB	6 20	1	325	5.5	6.5	19.5	20.5	NA
348	#FEE28E	6 19	1	324	5.5	6.5	18.5	19.5	NA
349	#FEE28E	6 18	1	323	5.5	6.5	17.5	18.5	NA
350	#F46F43	6 17	1	322	5.5	6.5	16.5	17.5	NA

351	#FEEA9C	6	16	1	321	5.5	6.5	15.5	16.5	NA
352	#FEDB87	6	15	1	320	5.5	6.5	14.5	15.5	NA
353	#DE4D4B	6	14	1	319	5.5	6.5	13.5	14.5	NA
354	#FFEEA4	6	13	1	318	5.5	6.5	12.5	13.5	NA
355	#FDFEBC	6	12	1	317	5.5	6.5	11.5	12.5	NA
356	gray	6	11	1	316	5.5	6.5	10.5	11.5	NA
357	#E2544A	6	10	1	315	5.5	6.5	9.5	10.5	NA
358	#FEBE6E	6	9	1	314	5.5	6.5	8.5	9.5	NA
359	#FED481	6	8	1	313	5.5	6.5	7.5	8.5	NA
360	#F88C50	6	7	1	312	5.5	6.5	6.5	7.5	NA
361	#FEE28E	6	6	1	311	5.5	6.5	5.5	6.5	NA
362	#FDB063	6	5	1	310	5.5	6.5	4.5	5.5	NA
363	#F7834C	6	4	1	309	5.5	6.5	3.5	4.5	NA
364	#E2544A	6	3	1	308	5.5	6.5	2.5	3.5	NA
365	#EC6147	6	2	1	307	5.5	6.5	1.5	2.5	NA
366	#FED481	6	1	1	306	5.5	6.5	0.5	1.5	NA
367	#FCA75D	7	61	1	427	6.5	7.5	60.5	61.5	NA
368	#FECC7A	7	60	1	426	6.5	7.5	59.5	60.5	NA
369	#FCA75D	7	59	1	425	6.5	7.5	58.5	59.5	NA
370	#FED481	7	58	1	424	6.5	7.5	57.5	58.5	NA
371	gray	7	57	1	423	6.5	7.5	56.5	57.5	NA
372	#FEC575	7	56	1	422	6.5	7.5	55.5	56.5	NA
373	#FEDB87	7	55	1	421	6.5	7.5	54.5	55.5	NA
374	#FEBE6E	7	54	1	420	6.5	7.5	53.5	54.5	NA
375	#F46F43	7	53	1	419	6.5	7.5	52.5	53.5	NA
376	#FDB768	7	52	1	418	6.5	7.5	51.5	52.5	NA
377	#FCA75D	7	51	1	417	6.5	7.5	50.5	51.5	NA
378	gray	7	50	1	416	6.5	7.5	49.5	50.5	NA
379	gray	7	49	1	415	6.5	7.5	48.5	49.5	NA
380	#FFEEA4	7	48	1	414	6.5	7.5	47.5	48.5	NA
381	#FDB063	7	47	1	413	6.5	7.5	46.5	47.5	NA
382	#FEBE6E	7	46	1	412	6.5	7.5	45.5	46.5	NA
383	#FFF3AC	7	45	1	411	6.5	7.5	44.5	45.5	NA
384	#F88C50	7	44	1	410	6.5	7.5	43.5	44.5	NA
385	#FCA75D	7	43	1	409	6.5	7.5	42.5	43.5	NA
386	#F88C50	7	42	1	408	6.5	7.5	41.5	42.5	NA
387	#FDB768	7	41	1	407	6.5	7.5	40.5	41.5	NA
388	#FDB063	7	40	1	406	6.5	7.5	39.5	40.5	NA
389	#FED481	7	39	1	405	6.5	7.5	38.5	39.5	NA
390	#FEC575	7	38	1	404	6.5	7.5	37.5	38.5	NA
391	#FFF8B3	7	37	1	403	6.5	7.5	36.5	37.5	NA
392	#FEC575	7	36	1	402	6.5	7.5	35.5	36.5	NA
393	#FDB768	7	35	1	401	6.5	7.5	34.5	35.5	NA
394	#FDB063	7	34	1	400	6.5	7.5	33.5	34.5	NA
395	#FDB063	7	33	1	399	6.5	7.5	32.5	33.5	NA

396	#F7834C	7	32	1	398	6.5	7.5	31.5	32.5	NA
397	#FEC575	7	31	1	397	6.5	7.5	30.5	31.5	NA
398	#FDB768	7	30	1	396	6.5	7.5	29.5	30.5	NA
399	#FEE695	7	29	1	395	6.5	7.5	28.5	29.5	NA
400	#FEEA9C	7	28	1	394	6.5	7.5	27.5	28.5	NA
401	#FCA75D	7	27	1	393	6.5	7.5	26.5	27.5	NA
402	#F88C50	7	26	1	392	6.5	7.5	25.5	26.5	NA
403	#FB9F59	7	25	1	391	6.5	7.5	24.5	25.5	NA
404	gray	7	24	1	390	6.5	7.5	23.5	24.5	NA
405	#FDB768	7	23	1	389	6.5	7.5	22.5	23.5	NA
406	#FEDB87	7	22	1	388	6.5	7.5	21.5	22.5	NA
407	#FDB063	7	21	1	387	6.5	7.5	20.5	21.5	NA
408	#FFF3AC	7	20	1	386	6.5	7.5	19.5	20.5	NA
409	#FEDB87	7	19	1	385	6.5	7.5	18.5	19.5	NA
410	#FFF8B3	7	18	1	384	6.5	7.5	17.5	18.5	NA
411	#E75A48	7	17	1	383	6.5	7.5	16.5	17.5	NA
412	#FFEEA4	7	16	1	382	6.5	7.5	15.5	16.5	NA
413	#FECC7A	7	15	1	381	6.5	7.5	14.5	15.5	NA
414	#D53E4E	7	14	1	380	6.5	7.5	13.5	14.5	NA
415	#FFF3AC	7	13	1	379	6.5	7.5	12.5	13.5	NA
416	#EBF79F	7	12	1	378	6.5	7.5	11.5	12.5	NA
417	gray	7	11	1	377	6.5	7.5	10.5	11.5	NA
418	#F46F43	7	10	1	376	6.5	7.5	9.5	10.5	NA
419	#FEE28E	7	9	1	375	6.5	7.5	8.5	9.5	NA
420	#FEE695	7	8	1	374	6.5	7.5	7.5	8.5	NA
421	#F06744	7	7	1	373	6.5	7.5	6.5	7.5	NA
422	#FEE695	7	6	1	372	6.5	7.5	5.5	6.5	NA
423	#FEBE6E	7	5	1	371	6.5	7.5	4.5	5.5	NA
424	#F67948	7	4	1	370	6.5	7.5	3.5	4.5	NA
425	#DE4D4B	7	3	1	369	6.5	7.5	2.5	3.5	NA
426	#EC6147	7	2	1	368	6.5	7.5	1.5	2.5	NA
427	#FED481	7	1	1	367	6.5	7.5	0.5	1.5	NA
428	#FFF3AC	8	61	1	488	7.5	8.5	60.5	61.5	NA
429	#FEEA9C	8	60	1	487	7.5	8.5	59.5	60.5	NA
430	#FFF8B3	8	59	1	486	7.5	8.5	58.5	59.5	NA
431	#FFFCBB	8	58	1	485	7.5	8.5	57.5	58.5	NA
432	gray	8	57	1	484	7.5	8.5	56.5	57.5	NA
433	#F9FCB6	8	56	1	483	7.5	8.5	55.5	56.5	NA
434	#FEEA9C	8	55	1	482	7.5	8.5	54.5	55.5	NA
435	#FDDEBC	8	54	1	481	7.5	8.5	53.5	54.5	NA
436	#FFF8B3	8	53	1	480	7.5	8.5	52.5	53.5	NA
437	#F9FCB6	8	52	1	479	7.5	8.5	51.5	52.5	NA
438	#F9FCB6	8	51	1	478	7.5	8.5	50.5	51.5	NA
439	gray	8	50	1	477	7.5	8.5	49.5	50.5	NA
440	gray	8	49	1	476	7.5	8.5	48.5	49.5	NA

441	#FFFCBB	8 48	1	475	7.5	8.5	47.5	48.5	NA
442	#FDFEBC	8 47	1	474	7.5	8.5	46.5	47.5	NA
443	#EBF79F	8 46	1	473	7.5	8.5	45.5	46.5	NA
444	#F9FCB6	8 45	1	472	7.5	8.5	44.5	45.5	NA
445	#F6FBB1	8 44	1	471	7.5	8.5	43.5	44.5	NA
446	#EOF299	8 43	1	470	7.5	8.5	42.5	43.5	NA
447	#FFF3AC	8 42	1	469	7.5	8.5	41.5	42.5	NA
448	#FEEA9C	8 41	1	468	7.5	8.5	40.5	41.5	NA
449	#F9FCB6	8 40	1	467	7.5	8.5	39.5	40.5	NA
450	#FEE695	8 39	1	466	7.5	8.5	38.5	39.5	NA
451	#FDFEBC	8 38	1	465	7.5	8.5	37.5	38.5	NA
452	#E7F59A	8 37	1	464	7.5	8.5	36.5	37.5	NA
453	#FDFEBC	8 36	1	463	7.5	8.5	35.5	36.5	NA
454	#FFFCBB	8 35	1	462	7.5	8.5	34.5	35.5	NA
455	#FFF8B3	8 34	1	461	7.5	8.5	33.5	34.5	NA
456	#E7F59A	8 33	1	460	7.5	8.5	32.5	33.5	NA
457	#FFEEA4	8 32	1	459	7.5	8.5	31.5	32.5	NA
458	#FFF3AC	8 31	1	458	7.5	8.5	30.5	31.5	NA
459	#F6FBB1	8 30	1	457	7.5	8.5	29.5	30.5	NA
460	#EBF79F	8 29	1	456	7.5	8.5	28.5	29.5	NA
461	#FDFEBC	8 28	1	455	7.5	8.5	27.5	28.5	NA
462	#F2F9AB	8 27	1	454	7.5	8.5	26.5	27.5	NA
463	#F9FCB6	8 26	1	453	7.5	8.5	25.5	26.5	NA
464	#FEE28E	8 25	1	452	7.5	8.5	24.5	25.5	NA
465	gray	8 24	1	451	7.5	8.5	23.5	24.5	NA
466	#9BD6A4	8 23	1	450	7.5	8.5	22.5	23.5	NA
467	#EBF79F	8 22	1	449	7.5	8.5	21.5	22.5	NA
468	#FFF8B3	8 21	1	448	7.5	8.5	20.5	21.5	NA
469	#EBF79F	8 20	1	447	7.5	8.5	19.5	20.5	NA
470	#F2F9AB	8 19	1	446	7.5	8.5	18.5	19.5	NA
471	#9BD6A4	8 18	1	445	7.5	8.5	17.5	18.5	NA
472	#FED481	8 17	1	444	7.5	8.5	16.5	17.5	NA
473	#EEF8A5	8 16	1	443	7.5	8.5	15.5	16.5	NA
474	#92D2A4	8 15	1	442	7.5	8.5	14.5	15.5	NA
475	#F7834C	8 14	1	441	7.5	8.5	13.5	14.5	NA
476	#D0EC9C	8 13	1	440	7.5	8.5	12.5	13.5	NA
477	#EOF299	8 12	1	439	7.5	8.5	11.5	12.5	NA
478	gray	8 11	1	438	7.5	8.5	10.5	11.5	NA
479	#FECC7A	8 10	1	437	7.5	8.5	9.5	10.5	NA
480	#FEEA9C	8 9	1	436	7.5	8.5	8.5	9.5	NA
481	#FFF8B3	8 8	1	435	7.5	8.5	7.5	8.5	NA
482	#FFEEA4	8 7	1	434	7.5	8.5	6.5	7.5	NA
483	#D9EF9B	8 6	1	433	7.5	8.5	5.5	6.5	NA
484	#E7F59A	8 5	1	432	7.5	8.5	4.5	5.5	NA
485	#FEBE6E	8 4	1	431	7.5	8.5	3.5	4.5	NA

486	#FCA75D	8	3	1	430	7.5	8.5	2.5	3.5	NA
487	#FEC575	8	2	1	429	7.5	8.5	1.5	2.5	NA
488	#FEEA9C	8	1	1	428	7.5	8.5	0.5	1.5	NA
489	#A4DAA4	9	61	1	549	8.5	9.5	60.5	61.5	NA
490	#92D2A4	9	60	1	548	8.5	9.5	59.5	60.5	NA
491	#D9EF9B	9	59	1	547	8.5	9.5	58.5	59.5	NA
492	#BFE4A0	9	58	1	546	8.5	9.5	57.5	58.5	NA
493	gray	9	57	1	545	8.5	9.5	56.5	57.5	NA
494	#F6FBB1	9	56	1	544	8.5	9.5	55.5	56.5	NA
495	#7ECAA4	9	55	1	543	8.5	9.5	54.5	55.5	NA
496	#B6E1A1	9	54	1	542	8.5	9.5	53.5	54.5	NA
497	#EBF79F	9	53	1	541	8.5	9.5	52.5	53.5	NA
498	#BFE4A0	9	52	1	540	8.5	9.5	51.5	52.5	NA
499	#E7F59A	9	51	1	539	8.5	9.5	50.5	51.5	NA
500	gray	9	50	1	538	8.5	9.5	49.5	50.5	NA
501	gray	9	49	1	537	8.5	9.5	48.5	49.5	NA
502	#EEF8A5	9	48	1	536	8.5	9.5	47.5	48.5	NA
503	#92D2A4	9	47	1	535	8.5	9.5	46.5	47.5	NA
504	#73C6A4	9	46	1	534	8.5	9.5	45.5	46.5	NA
505	#68C2A4	9	45	1	533	8.5	9.5	44.5	45.5	NA
506	#92D2A4	9	44	1	532	8.5	9.5	43.5	44.5	NA
507	#68C2A4	9	43	1	531	8.5	9.5	42.5	43.5	NA
508	#92D2A4	9	42	1	530	8.5	9.5	41.5	42.5	NA
509	#92D2A4	9	41	1	529	8.5	9.5	40.5	41.5	NA
510	#7ECAA4	9	40	1	528	8.5	9.5	39.5	40.5	NA
511	#A4DAA4	9	39	1	527	8.5	9.5	38.5	39.5	NA
512	#D9EF9B	9	38	1	526	8.5	9.5	37.5	38.5	NA
513	#88CEA4	9	37	1	525	8.5	9.5	36.5	37.5	NA
514	#D0EC9C	9	36	1	524	8.5	9.5	35.5	36.5	NA
515	#73C6A4	9	35	1	523	8.5	9.5	34.5	35.5	NA
516	#ADDDA3	9	34	1	522	8.5	9.5	33.5	34.5	NA
517	#BFE4A0	9	33	1	521	8.5	9.5	32.5	33.5	NA
518	#B6E1A1	9	32	1	520	8.5	9.5	31.5	32.5	NA
519	#EEF8A5	9	31	1	519	8.5	9.5	30.5	31.5	NA
520	#9BD6A4	9	30	1	518	8.5	9.5	29.5	30.5	NA
521	#A4DAA4	9	29	1	517	8.5	9.5	28.5	29.5	NA
522	#7ECAA4	9	28	1	516	8.5	9.5	27.5	28.5	NA
523	#FDFEBC	9	27	1	515	8.5	9.5	26.5	27.5	NA
524	#EBF79F	9	26	1	514	8.5	9.5	25.5	26.5	NA
525	#FFF8B3	9	25	1	513	8.5	9.5	24.5	25.5	NA
526	gray	9	24	1	512	8.5	9.5	23.5	24.5	NA
527	#92D2A4	9	23	1	511	8.5	9.5	22.5	23.5	NA
528	#62BBA8	9	22	1	510	8.5	9.5	21.5	22.5	NA
529	#E7F59A	9	21	1	509	8.5	9.5	20.5	21.5	NA
530	#9BD6A4	9	20	1	508	8.5	9.5	19.5	20.5	NA

531	#B6E1A1	9	19	1	507	8.5	9.5	18.5	19.5	NA
532	#4578B5	9	18	1	506	8.5	9.5	17.5	18.5	NA
533	#FECC7A	9	17	1	505	8.5	9.5	16.5	17.5	NA
534	#88CEA4	9	16	1	504	8.5	9.5	15.5	16.5	NA
535	#5DB2AB	9	15	1	503	8.5	9.5	14.5	15.5	NA
536	#FEBE6E	9	14	1	502	8.5	9.5	13.5	14.5	NA
537	#C8E89E	9	13	1	501	8.5	9.5	12.5	13.5	NA
538	#9BD6A4	9	12	1	500	8.5	9.5	11.5	12.5	NA
539	gray	9	11	1	499	8.5	9.5	10.5	11.5	NA
540	#FEEA9C	9	10	1	498	8.5	9.5	9.5	10.5	NA
541	#9BD6A4	9	9	1	497	8.5	9.5	8.5	9.5	NA
542	#B6E1A1	9	8	1	496	8.5	9.5	7.5	8.5	NA
543	#B6E1A1	9	7	1	495	8.5	9.5	6.5	7.5	NA
544	#3288BC	9	6	1	494	8.5	9.5	5.5	6.5	NA
545	#9BD6A4	9	5	1	493	8.5	9.5	4.5	5.5	NA
546	#FEE695	9	4	1	492	8.5	9.5	3.5	4.5	NA
547	#FED481	9	3	1	491	8.5	9.5	2.5	3.5	NA
548	#FDB063	9	2	1	490	8.5	9.5	1.5	2.5	NA
549	#88CEA4	9	1	1	489	8.5	9.5	0.5	1.5	NA
550	#ADDDA3	10	61	1	610	9.5	10.5	60.5	61.5	NA
551	#EBF79F	10	60	1	609	9.5	10.5	59.5	60.5	NA
552	#B6E1A1	10	59	1	608	9.5	10.5	58.5	59.5	NA
553	#C8E89E	10	58	1	607	9.5	10.5	57.5	58.5	NA
554	gray	10	57	1	606	9.5	10.5	56.5	57.5	NA
555	#FEDB87	10	56	1	605	9.5	10.5	55.5	56.5	NA
556	#D0EC9C	10	55	1	604	9.5	10.5	54.5	55.5	NA
557	#EOF299	10	54	1	603	9.5	10.5	53.5	54.5	NA
558	#FFF8B3	10	53	1	602	9.5	10.5	52.5	53.5	NA
559	#D9EF9B	10	52	1	601	9.5	10.5	51.5	52.5	NA
560	#BFE4A0	10	51	1	600	9.5	10.5	50.5	51.5	NA
561	gray	10	50	1	599	9.5	10.5	49.5	50.5	NA
562	gray	10	49	1	598	9.5	10.5	48.5	49.5	NA
563	#F2F9AB	10	48	1	597	9.5	10.5	47.5	48.5	NA
564	#D0EC9C	10	47	1	596	9.5	10.5	46.5	47.5	NA
565	#7ECAA4	10	46	1	595	9.5	10.5	45.5	46.5	NA
566	#88CEA4	10	45	1	594	9.5	10.5	44.5	45.5	NA
567	#C8E89E	10	44	1	593	9.5	10.5	43.5	44.5	NA
568	#88CEA4	10	43	1	592	9.5	10.5	42.5	43.5	NA
569	#9BD6A4	10	42	1	591	9.5	10.5	41.5	42.5	NA
570	#92D2A4	10	41	1	590	9.5	10.5	40.5	41.5	NA
571	#ADDDA3	10	40	1	589	9.5	10.5	39.5	40.5	NA
572	#EBF79F	10	39	1	588	9.5	10.5	38.5	39.5	NA
573	#E7F59A	10	38	1	587	9.5	10.5	37.5	38.5	NA
574	#ADDDA3	10	37	1	586	9.5	10.5	36.5	37.5	NA
575	#EOF299	10	36	1	585	9.5	10.5	35.5	36.5	NA

576	#88CEA4	10	35	1	584	9.5	10.5	34.5	35.5	NA
577	#FEE695	10	34	1	583	9.5	10.5	33.5	34.5	NA
578	#E0F299	10	33	1	582	9.5	10.5	32.5	33.5	NA
579	#BFE4A0	10	32	1	581	9.5	10.5	31.5	32.5	NA
580	#F6FBB1	10	31	1	580	9.5	10.5	30.5	31.5	NA
581	#BFE4A0	10	30	1	579	9.5	10.5	29.5	30.5	NA
582	#A4DAA4	10	29	1	578	9.5	10.5	28.5	29.5	NA
583	#ADDDA3	10	28	1	577	9.5	10.5	27.5	28.5	NA
584	#F9FCB6	10	27	1	576	9.5	10.5	26.5	27.5	NA
585	#B6E1A1	10	26	1	575	9.5	10.5	25.5	26.5	NA
586	#FFF3AC	10	25	1	574	9.5	10.5	24.5	25.5	NA
587	gray	10	24	1	573	9.5	10.5	23.5	24.5	NA
588	#A4DAA4	10	23	1	572	9.5	10.5	22.5	23.5	NA
589	#68C2A4	10	22	1	571	9.5	10.5	21.5	22.5	NA
590	#68C2A4	10	21	1	570	9.5	10.5	20.5	21.5	NA
591	#7ECAA4	10	20	1	569	9.5	10.5	19.5	20.5	NA
592	#F2F9AB	10	19	1	568	9.5	10.5	18.5	19.5	NA
593	#57AAAF	10	18	1	567	9.5	10.5	17.5	18.5	NA
594	#FEEA9C	10	17	1	566	9.5	10.5	16.5	17.5	NA
595	#9BD6A4	10	16	1	565	9.5	10.5	15.5	16.5	NA
596	#5DB2AB	10	15	1	564	9.5	10.5	14.5	15.5	NA
597	#FB9F59	10	14	1	563	9.5	10.5	13.5	14.5	NA
598	#7ECAA4	10	13	1	562	9.5	10.5	12.5	13.5	NA
599	#92D2A4	10	12	1	561	9.5	10.5	11.5	12.5	NA
600	gray	10	11	1	560	9.5	10.5	10.5	11.5	NA
601	#FEDB87	10	10	1	559	9.5	10.5	9.5	10.5	NA
602	#7ECAA4	10	9	1	558	9.5	10.5	8.5	9.5	NA
603	#7ECAA4	10	8	1	557	9.5	10.5	7.5	8.5	NA
604	#D9EF9B	10	7	1	556	9.5	10.5	6.5	7.5	NA
605	#5DB2AB	10	6	1	555	9.5	10.5	5.5	6.5	NA
606	#BFE4A0	10	5	1	554	9.5	10.5	4.5	5.5	NA
607	#FFEEA4	10	4	1	553	9.5	10.5	3.5	4.5	NA
608	#FED481	10	3	1	552	9.5	10.5	2.5	3.5	NA
609	#FDB768	10	2	1	551	9.5	10.5	1.5	2.5	NA
610	#A4DAA4	10	1	1	550	9.5	10.5	0.5	1.5	NA
611	#FFF8B3	11	61	1	671	10.5	11.5	60.5	61.5	NA
612	#FFF8B3	11	60	1	670	10.5	11.5	59.5	60.5	NA
613	#FFF8B3	11	59	1	669	10.5	11.5	58.5	59.5	NA
614	#F2F9AB	11	58	1	668	10.5	11.5	57.5	58.5	NA
615	gray	11	57	1	667	10.5	11.5	56.5	57.5	NA
616	#F6FBB1	11	56	1	666	10.5	11.5	55.5	56.5	NA
617	#F6FBB1	11	55	1	665	10.5	11.5	54.5	55.5	NA
618	#FFF8B3	11	54	1	664	10.5	11.5	53.5	54.5	NA
619	#FFF8B3	11	53	1	663	10.5	11.5	52.5	53.5	NA
620	#F2F9AB	11	52	1	662	10.5	11.5	51.5	52.5	NA

621	#FDFEBC	11	51	1	661	10.5	11.5	50.5	51.5	NA
622	gray	11	50	1	660	10.5	11.5	49.5	50.5	NA
623	gray	11	49	1	659	10.5	11.5	48.5	49.5	NA
624	#F6FBB1	11	48	1	658	10.5	11.5	47.5	48.5	NA
625	#E7F59A	11	47	1	657	10.5	11.5	46.5	47.5	NA
626	#F2F9AB	11	46	1	656	10.5	11.5	45.5	46.5	NA
627	#EOF299	11	45	1	655	10.5	11.5	44.5	45.5	NA
628	#FFFCBB	11	44	1	654	10.5	11.5	43.5	44.5	NA
629	#D9EF9B	11	43	1	653	10.5	11.5	42.5	43.5	NA
630	#EEF8A5	11	42	1	652	10.5	11.5	41.5	42.5	NA
631	#E7F59A	11	41	1	651	10.5	11.5	40.5	41.5	NA
632	#FFF3AC	11	40	1	650	10.5	11.5	39.5	40.5	NA
633	#E7F59A	11	39	1	649	10.5	11.5	38.5	39.5	NA
634	#FFF3AC	11	38	1	648	10.5	11.5	37.5	38.5	NA
635	#D9EF9B	11	37	1	647	10.5	11.5	36.5	37.5	NA
636	#FFF3AC	11	36	1	646	10.5	11.5	35.5	36.5	NA
637	#F2F9AB	11	35	1	645	10.5	11.5	34.5	35.5	NA
638	#EBF79F	11	34	1	644	10.5	11.5	33.5	34.5	NA
639	#DOEC9C	11	33	1	643	10.5	11.5	32.5	33.5	NA
640	#FFF8B3	11	32	1	642	10.5	11.5	31.5	32.5	NA
641	#F6FBB1	11	31	1	641	10.5	11.5	30.5	31.5	NA
642	#E7F59A	11	30	1	640	10.5	11.5	29.5	30.5	NA
643	#E7F59A	11	29	1	639	10.5	11.5	28.5	29.5	NA
644	#EOF299	11	28	1	638	10.5	11.5	27.5	28.5	NA
645	#FFEEA4	11	27	1	637	10.5	11.5	26.5	27.5	NA
646	#F2F9AB	11	26	1	636	10.5	11.5	25.5	26.5	NA
647	#F2F9AB	11	25	1	635	10.5	11.5	24.5	25.5	NA
648	gray	11	24	1	634	10.5	11.5	23.5	24.5	NA
649	#EOF299	11	23	1	633	10.5	11.5	22.5	23.5	NA
650	#EOF299	11	22	1	632	10.5	11.5	21.5	22.5	NA
651	#E7F59A	11	21	1	631	10.5	11.5	20.5	21.5	NA
652	#F9FCB6	11	20	1	630	10.5	11.5	19.5	20.5	NA
653	#DOEC9C	11	19	1	629	10.5	11.5	18.5	19.5	NA
654	#9BD6A4	11	18	1	628	10.5	11.5	17.5	18.5	NA
655	#FEE28E	11	17	1	627	10.5	11.5	16.5	17.5	NA
656	#ADDDA3	11	16	1	626	10.5	11.5	15.5	16.5	NA
657	#73C6A4	11	15	1	625	10.5	11.5	14.5	15.5	NA
658	#EC6147	11	14	1	624	10.5	11.5	13.5	14.5	NA
659	#C8E89E	11	13	1	623	10.5	11.5	12.5	13.5	NA
660	#A4DAA4	11	12	1	622	10.5	11.5	11.5	12.5	NA
661	gray	11	11	1	621	10.5	11.5	10.5	11.5	NA
662	#FED481	11	10	1	620	10.5	11.5	9.5	10.5	NA
663	#FDFEBC	11	9	1	619	10.5	11.5	8.5	9.5	NA
664	#F2F9AB	11	8	1	618	10.5	11.5	7.5	8.5	NA
665	#FFF8B3	11	7	1	617	10.5	11.5	6.5	7.5	NA

666	#E0F299	11	6	1	616	10.5	11.5	5.5	6.5	NA
667	#E7F59A	11	5	1	615	10.5	11.5	4.5	5.5	NA
668	#FEEA9C	11	4	1	614	10.5	11.5	3.5	4.5	NA
669	#FECC7A	11	3	1	613	10.5	11.5	2.5	3.5	NA
670	#FEE28E	11	2	1	612	10.5	11.5	1.5	2.5	NA
671	#FFF8B3	11	1	1	611	10.5	11.5	0.5	1.5	NA
672	#FEDB87	12	61	1	732	11.5	12.5	60.5	61.5	NA
673	#FFEEA4	12	60	1	731	11.5	12.5	59.5	60.5	NA
674	#FFFCBB	12	59	1	730	11.5	12.5	58.5	59.5	NA
675	#E7F59A	12	58	1	729	11.5	12.5	57.5	58.5	NA
676	gray	12	57	1	728	11.5	12.5	56.5	57.5	NA
677	#FEDB87	12	56	1	727	11.5	12.5	55.5	56.5	NA
678	#FFF8B3	12	55	1	726	11.5	12.5	54.5	55.5	NA
679	#FFEEA4	12	54	1	725	11.5	12.5	53.5	54.5	NA
680	#FEDB87	12	53	1	724	11.5	12.5	52.5	53.5	NA
681	#FFFCBB	12	52	1	723	11.5	12.5	51.5	52.5	NA
682	#FFFCBB	12	51	1	722	11.5	12.5	50.5	51.5	NA
683	gray	12	50	1	721	11.5	12.5	49.5	50.5	NA
684	gray	12	49	1	720	11.5	12.5	48.5	49.5	NA
685	#F9FCB6	12	48	1	719	11.5	12.5	47.5	48.5	NA
686	#FFFCBB	12	47	1	718	11.5	12.5	46.5	47.5	NA
687	#FFF8B3	12	46	1	717	11.5	12.5	45.5	46.5	NA
688	#FFF8B3	12	45	1	716	11.5	12.5	44.5	45.5	NA
689	#FEE695	12	44	1	715	11.5	12.5	43.5	44.5	NA
690	#FFF3AC	12	43	1	714	11.5	12.5	42.5	43.5	NA
691	#FEE695	12	42	1	713	11.5	12.5	41.5	42.5	NA
692	#FFF8B3	12	41	1	712	11.5	12.5	40.5	41.5	NA
693	#FDDEBC	12	40	1	711	11.5	12.5	39.5	40.5	NA
694	#FEEA9C	12	39	1	710	11.5	12.5	38.5	39.5	NA
695	#FED481	12	38	1	709	11.5	12.5	37.5	38.5	NA
696	#FFF3AC	12	37	1	708	11.5	12.5	36.5	37.5	NA
697	#FEE695	12	36	1	707	11.5	12.5	35.5	36.5	NA
698	#FFF3AC	12	35	1	706	11.5	12.5	34.5	35.5	NA
699	#FEE28E	12	34	1	705	11.5	12.5	33.5	34.5	NA
700	#FFF3AC	12	33	1	704	11.5	12.5	32.5	33.5	NA
701	#FEE695	12	32	1	703	11.5	12.5	31.5	32.5	NA
702	#FEEA9C	12	31	1	702	11.5	12.5	30.5	31.5	NA
703	#FDDEBC	12	30	1	701	11.5	12.5	29.5	30.5	NA
704	#FFEEA4	12	29	1	700	11.5	12.5	28.5	29.5	NA
705	#FFEEA4	12	28	1	699	11.5	12.5	27.5	28.5	NA
706	#FEE695	12	27	1	698	11.5	12.5	26.5	27.5	NA
707	#FFEEA4	12	26	1	697	11.5	12.5	25.5	26.5	NA
708	#FEEA9C	12	25	1	696	11.5	12.5	24.5	25.5	NA
709	gray	12	24	1	695	11.5	12.5	23.5	24.5	NA
710	#F6FB81	12	23	1	694	11.5	12.5	22.5	23.5	NA

711	#FFFCBB	12	22	1	693	11.5	12.5	21.5	22.5	NA
712	#FEEA9C	12	21	1	692	11.5	12.5	20.5	21.5	NA
713	#FFF8B3	12	20	1	691	11.5	12.5	19.5	20.5	NA
714	#EEF8A5	12	19	1	690	11.5	12.5	18.5	19.5	NA
715	#C8E89E	12	18	1	689	11.5	12.5	17.5	18.5	NA
716	#FEBE6E	12	17	1	688	11.5	12.5	16.5	17.5	NA
717	#FFF8B3	12	16	1	687	11.5	12.5	15.5	16.5	NA
718	#EBF79F	12	15	1	686	11.5	12.5	14.5	15.5	NA
719	#FB9F59	12	14	1	685	11.5	12.5	13.5	14.5	NA
720	#F2F9AB	12	13	1	684	11.5	12.5	12.5	13.5	NA
721	#D9EF9B	12	12	1	683	11.5	12.5	11.5	12.5	NA
722	gray	12	11	1	682	11.5	12.5	10.5	11.5	NA
723	#FDB768	12	10	1	681	11.5	12.5	9.5	10.5	NA
724	#FFF8B3	12	9	1	680	11.5	12.5	8.5	9.5	NA
725	#FFF8B3	12	8	1	679	11.5	12.5	7.5	8.5	NA
726	#FEE695	12	7	1	678	11.5	12.5	6.5	7.5	NA
727	#EOF299	12	6	1	677	11.5	12.5	5.5	6.5	NA
728	#F6FBB1	12	5	1	676	11.5	12.5	4.5	5.5	NA
729	#FEC575	12	4	1	675	11.5	12.5	3.5	4.5	NA
730	#F88C50	12	3	1	674	11.5	12.5	2.5	3.5	NA
731	#FDB768	12	2	1	673	11.5	12.5	1.5	2.5	NA
732	#FFEEA4	12	1	1	672	11.5	12.5	0.5	1.5	NA
733	#F2F9AB	13	61	1	793	12.5	13.5	60.5	61.5	NA
734	#EEF8A5	13	60	1	792	12.5	13.5	59.5	60.5	NA
735	#FDDEBC	13	59	1	791	12.5	13.5	58.5	59.5	NA
736	#EBF79F	13	58	1	790	12.5	13.5	57.5	58.5	NA
737	gray	13	57	1	789	12.5	13.5	56.5	57.5	NA
738	#EEF8A5	13	56	1	788	12.5	13.5	55.5	56.5	NA
739	#D9EF9B	13	55	1	787	12.5	13.5	54.5	55.5	NA
740	#F2F9AB	13	54	1	786	12.5	13.5	53.5	54.5	NA
741	#F6FBB1	13	53	1	785	12.5	13.5	52.5	53.5	NA
742	#D0EC9C	13	52	1	784	12.5	13.5	51.5	52.5	NA
743	#FDDEBC	13	51	1	783	12.5	13.5	50.5	51.5	NA
744	gray	13	50	1	782	12.5	13.5	49.5	50.5	NA
745	gray	13	49	1	781	12.5	13.5	48.5	49.5	NA
746	#EEF8A5	13	48	1	780	12.5	13.5	47.5	48.5	NA
747	#E7F59A	13	47	1	779	12.5	13.5	46.5	47.5	NA
748	#F6FBB1	13	46	1	778	12.5	13.5	45.5	46.5	NA
749	#D9EF9B	13	45	1	777	12.5	13.5	44.5	45.5	NA
750	#F2F9AB	13	44	1	776	12.5	13.5	43.5	44.5	NA
751	#F6FBB1	13	43	1	775	12.5	13.5	42.5	43.5	NA
752	#EBF79F	13	42	1	774	12.5	13.5	41.5	42.5	NA
753	#EOF299	13	41	1	773	12.5	13.5	40.5	41.5	NA
754	#EOF299	13	40	1	772	12.5	13.5	39.5	40.5	NA
755	#D9EF9B	13	39	1	771	12.5	13.5	38.5	39.5	NA

756	#FFF3AC	13	38	1	770	12.5	13.5	37.5	38.5	NA
757	#D0EC9C	13	37	1	769	12.5	13.5	36.5	37.5	NA
758	#FFF3AC	13	36	1	768	12.5	13.5	35.5	36.5	NA
759	#EBF79F	13	35	1	767	12.5	13.5	34.5	35.5	NA
760	#FDFEBC	13	34	1	766	12.5	13.5	33.5	34.5	NA
761	#D0EC9C	13	33	1	765	12.5	13.5	32.5	33.5	NA
762	#F6FB1	13	32	1	764	12.5	13.5	31.5	32.5	NA
763	#F9FCB6	13	31	1	763	12.5	13.5	30.5	31.5	NA
764	#EEF8A5	13	30	1	762	12.5	13.5	29.5	30.5	NA
765	#EEF8A5	13	29	1	761	12.5	13.5	28.5	29.5	NA
766	#EBF79F	13	28	1	760	12.5	13.5	27.5	28.5	NA
767	#EOF299	13	27	1	759	12.5	13.5	26.5	27.5	NA
768	#C8E89E	13	26	1	758	12.5	13.5	25.5	26.5	NA
769	#FFFCBB	13	25	1	757	12.5	13.5	24.5	25.5	NA
770	gray	13	24	1	756	12.5	13.5	23.5	24.5	NA
771	#E7F59A	13	23	1	755	12.5	13.5	22.5	23.5	NA
772	#D9EF9B	13	22	1	754	12.5	13.5	21.5	22.5	NA
773	#F2F9AB	13	21	1	753	12.5	13.5	20.5	21.5	NA
774	#EOF299	13	20	1	752	12.5	13.5	19.5	20.5	NA
775	#D0EC9C	13	19	1	751	12.5	13.5	18.5	19.5	NA
776	#7ECAA4	13	18	1	750	12.5	13.5	17.5	18.5	NA
777	#FEE695	13	17	1	749	12.5	13.5	16.5	17.5	NA
778	#E7F59A	13	16	1	748	12.5	13.5	15.5	16.5	NA
779	#ADDDA3	13	15	1	747	12.5	13.5	14.5	15.5	NA
780	#FA9554	13	14	1	746	12.5	13.5	13.5	14.5	NA
781	#D9EF9B	13	13	1	745	12.5	13.5	12.5	13.5	NA
782	#C8E89E	13	12	1	744	12.5	13.5	11.5	12.5	NA
783	gray	13	11	1	743	12.5	13.5	10.5	11.5	NA
784	#FED481	13	10	1	742	12.5	13.5	9.5	10.5	NA
785	#ADDDA3	13	9	1	741	12.5	13.5	8.5	9.5	NA
786	#ADDDA3	13	8	1	740	12.5	13.5	7.5	8.5	NA
787	#F2F9AB	13	7	1	739	12.5	13.5	6.5	7.5	NA
788	#92D2A4	13	6	1	738	12.5	13.5	5.5	6.5	NA
789	#C8E89E	13	5	1	737	12.5	13.5	4.5	5.5	NA
790	#FFEEA4	13	4	1	736	12.5	13.5	3.5	4.5	NA
791	#FEBE6E	13	3	1	735	12.5	13.5	2.5	3.5	NA
792	#FFEEA4	13	2	1	734	12.5	13.5	1.5	2.5	NA
793	#92D2A4	13	1	1	733	12.5	13.5	0.5	1.5	NA
794	#E7F59A	14	61	1	854	13.5	14.5	60.5	61.5	NA
795	#EOF299	14	60	1	853	13.5	14.5	59.5	60.5	NA
796	#D0EC9C	14	59	1	852	13.5	14.5	58.5	59.5	NA
797	#C8E89E	14	58	1	851	13.5	14.5	57.5	58.5	NA
798	gray	14	57	1	850	13.5	14.5	56.5	57.5	NA
799	#F2F9AB	14	56	1	849	13.5	14.5	55.5	56.5	NA
800	#EOF299	14	55	1	848	13.5	14.5	54.5	55.5	NA

801	#EEF8A5	14	54	1	847	13.5	14.5	53.5	54.5	NA
802	#FDFEBC	14	53	1	846	13.5	14.5	52.5	53.5	NA
803	#ADDDA3	14	52	1	845	13.5	14.5	51.5	52.5	NA
804	#EEF8A5	14	51	1	844	13.5	14.5	50.5	51.5	NA
805	gray	14	50	1	843	13.5	14.5	49.5	50.5	NA
806	gray	14	49	1	842	13.5	14.5	48.5	49.5	NA
807	#EOF299	14	48	1	841	13.5	14.5	47.5	48.5	NA
808	#EEF8A5	14	47	1	840	13.5	14.5	46.5	47.5	NA
809	#EEF8A5	14	46	1	839	13.5	14.5	45.5	46.5	NA
810	#D9EF9B	14	45	1	838	13.5	14.5	44.5	45.5	NA
811	#E7F59A	14	44	1	837	13.5	14.5	43.5	44.5	NA
812	#E7F59A	14	43	1	836	13.5	14.5	42.5	43.5	NA
813	#F6FBB1	14	42	1	835	13.5	14.5	41.5	42.5	NA
814	#EOF299	14	41	1	834	13.5	14.5	40.5	41.5	NA
815	#D9EF9B	14	40	1	833	13.5	14.5	39.5	40.5	NA
816	#EEF8A5	14	39	1	832	13.5	14.5	38.5	39.5	NA
817	#FFFCBB	14	38	1	831	13.5	14.5	37.5	38.5	NA
818	#EOF299	14	37	1	830	13.5	14.5	36.5	37.5	NA
819	#FFF8B3	14	36	1	829	13.5	14.5	35.5	36.5	NA
820	#E7F59A	14	35	1	828	13.5	14.5	34.5	35.5	NA
821	#EOF299	14	34	1	827	13.5	14.5	33.5	34.5	NA
822	#C8E89E	14	33	1	826	13.5	14.5	32.5	33.5	NA
823	#EBF79F	14	32	1	825	13.5	14.5	31.5	32.5	NA
824	#FFF3AC	14	31	1	824	13.5	14.5	30.5	31.5	NA
825	#EOF299	14	30	1	823	13.5	14.5	29.5	30.5	NA
826	#E7F59A	14	29	1	822	13.5	14.5	28.5	29.5	NA
827	#EEF8A5	14	28	1	821	13.5	14.5	27.5	28.5	NA
828	#F9FCB6	14	27	1	820	13.5	14.5	26.5	27.5	NA
829	#EBF79F	14	26	1	819	13.5	14.5	25.5	26.5	NA
830	#EEF8A5	14	25	1	818	13.5	14.5	24.5	25.5	NA
831	gray	14	24	1	817	13.5	14.5	23.5	24.5	NA
832	#BFE4A0	14	23	1	816	13.5	14.5	22.5	23.5	NA
833	#BFE4A0	14	22	1	815	13.5	14.5	21.5	22.5	NA
834	#EBF79F	14	21	1	814	13.5	14.5	20.5	21.5	NA
835	#88CEA4	14	20	1	813	13.5	14.5	19.5	20.5	NA
836	#ADDDA3	14	19	1	812	13.5	14.5	18.5	19.5	NA
837	#7ECAA4	14	18	1	811	13.5	14.5	17.5	18.5	NA
838	#EEF8A5	14	17	1	810	13.5	14.5	16.5	17.5	NA
839	#E7F59A	14	16	1	809	13.5	14.5	15.5	16.5	NA
840	#92D2A4	14	15	1	808	13.5	14.5	14.5	15.5	NA
841	#FA9554	14	14	1	807	13.5	14.5	13.5	14.5	NA
842	#B6E1A1	14	13	1	806	13.5	14.5	12.5	13.5	NA
843	#9BD6A4	14	12	1	805	13.5	14.5	11.5	12.5	NA
844	gray	14	11	1	804	13.5	14.5	10.5	11.5	NA
845	#FEE695	14	10	1	803	13.5	14.5	9.5	10.5	NA

846	#D0EC9C	14	9	1	802	13.5	14.5	8.5	9.5	NA
847	#C8E89E	14	8	1	801	13.5	14.5	7.5	8.5	NA
848	#EEF8A5	14	7	1	800	13.5	14.5	6.5	7.5	NA
849	#73C6A4	14	6	1	799	13.5	14.5	5.5	6.5	NA
850	#E7F59A	14	5	1	798	13.5	14.5	4.5	5.5	NA
851	#FEEA9C	14	4	1	797	13.5	14.5	3.5	4.5	NA
852	#FEBE6E	14	3	1	796	13.5	14.5	2.5	3.5	NA
853	#FEC575	14	2	1	795	13.5	14.5	1.5	2.5	NA
854	#D9EF9B	14	1	1	794	13.5	14.5	0.5	1.5	NA
855	#D0EC9C	15	61	1	915	14.5	15.5	60.5	61.5	NA
856	#7ECAA4	15	60	1	914	14.5	15.5	59.5	60.5	NA
857	#57AAAF	15	59	1	913	14.5	15.5	58.5	59.5	NA
858	#3E90B9	15	58	1	912	14.5	15.5	57.5	58.5	NA
859	gray	15	57	1	911	14.5	15.5	56.5	57.5	NA
860	#EBF79F	15	56	1	910	14.5	15.5	55.5	56.5	NA
861	#62BBA8	15	55	1	909	14.5	15.5	54.5	55.5	NA
862	#BFE4A0	15	54	1	908	14.5	15.5	53.5	54.5	NA
863	#92D2A4	15	53	1	907	14.5	15.5	52.5	53.5	NA
864	#A4DAA4	15	52	1	906	14.5	15.5	51.5	52.5	NA
865	#EBF79F	15	51	1	905	14.5	15.5	50.5	51.5	NA
866	gray	15	50	1	904	14.5	15.5	49.5	50.5	NA
867	gray	15	49	1	903	14.5	15.5	48.5	49.5	NA
868	#FFF3AC	15	48	1	902	14.5	15.5	47.5	48.5	NA
869	#BFE4A0	15	47	1	901	14.5	15.5	46.5	47.5	NA
870	#4898B6	15	46	1	900	14.5	15.5	45.5	46.5	NA
871	#3E90B9	15	45	1	899	14.5	15.5	44.5	45.5	NA
872	#68C2A4	15	44	1	898	14.5	15.5	43.5	44.5	NA
873	#4898B6	15	43	1	897	14.5	15.5	42.5	43.5	NA
874	#88CEA4	15	42	1	896	14.5	15.5	41.5	42.5	NA
875	#73C6A4	15	41	1	895	14.5	15.5	40.5	41.5	NA
876	#4898B6	15	40	1	894	14.5	15.5	39.5	40.5	NA
877	#92D2A4	15	39	1	893	14.5	15.5	38.5	39.5	NA
878	#FEDB87	15	38	1	892	14.5	15.5	37.5	38.5	NA
879	#5DB2AB	15	37	1	891	14.5	15.5	36.5	37.5	NA
880	#FCA75D	15	36	1	890	14.5	15.5	35.5	36.5	NA
881	#68C2A4	15	35	1	889	14.5	15.5	34.5	35.5	NA
882	#EBF79F	15	34	1	888	14.5	15.5	33.5	34.5	NA
883	#E0F299	15	33	1	887	14.5	15.5	32.5	33.5	NA
884	#92D2A4	15	32	1	886	14.5	15.5	31.5	32.5	NA
885	#F6FBB1	15	31	1	885	14.5	15.5	30.5	31.5	NA
886	#BFE4A0	15	30	1	884	14.5	15.5	29.5	30.5	NA
887	#BFE4A0	15	29	1	883	14.5	15.5	28.5	29.5	NA
888	#3E90B9	15	28	1	882	14.5	15.5	27.5	28.5	NA
889	#F9FCB6	15	27	1	881	14.5	15.5	26.5	27.5	NA
890	#88CEA4	15	26	1	880	14.5	15.5	25.5	26.5	NA

891	#9BD6A4	15	25	1	879	14.5	15.5	24.5	25.5	NA
892	gray	15	24	1	878	14.5	15.5	23.5	24.5	NA
893	#73C6A4	15	23	1	877	14.5	15.5	22.5	23.5	NA
894	#5DB2AB	15	22	1	876	14.5	15.5	21.5	22.5	NA
895	#D9EF9B	15	21	1	875	14.5	15.5	20.5	21.5	NA
896	#68C2A4	15	20	1	874	14.5	15.5	19.5	20.5	NA
897	#A4DAA4	15	19	1	873	14.5	15.5	18.5	19.5	NA
898	#5A58A5	15	18	1	872	14.5	15.5	17.5	18.5	NA
899	#FEEA9C	15	17	1	871	14.5	15.5	16.5	17.5	NA
900	#5DB2AB	15	16	1	870	14.5	15.5	15.5	16.5	NA
901	#4578B5	15	15	1	869	14.5	15.5	14.5	15.5	NA
902	#FED481	15	14	1	868	14.5	15.5	13.5	14.5	NA
903	#62BBA8	15	13	1	867	14.5	15.5	12.5	13.5	NA
904	#ADDDA3	15	12	1	866	14.5	15.5	11.5	12.5	NA
905	gray	15	11	1	865	14.5	15.5	10.5	11.5	NA
906	#EEF8A5	15	10	1	864	14.5	15.5	9.5	10.5	NA
907	#57AAAF	15	9	1	863	14.5	15.5	8.5	9.5	NA
908	#73C6A4	15	8	1	862	14.5	15.5	7.5	8.5	NA
909	#ADDDA3	15	7	1	861	14.5	15.5	6.5	7.5	NA
910	#4578B5	15	6	1	860	14.5	15.5	5.5	6.5	NA
911	#5DB2AB	15	5	1	859	14.5	15.5	4.5	5.5	NA
912	#FFF3AC	15	4	1	858	14.5	15.5	3.5	4.5	NA
913	#FEC575	15	3	1	857	14.5	15.5	2.5	3.5	NA
914	#FEEA9C	15	2	1	856	14.5	15.5	1.5	2.5	NA
915	#62BBA8	15	1	1	855	14.5	15.5	0.5	1.5	NA
916	#C8E89E	16	61	1	976	15.5	16.5	60.5	61.5	NA
917	#F2F9AB	16	60	1	975	15.5	16.5	59.5	60.5	NA
918	#B6E1A1	16	59	1	974	15.5	16.5	58.5	59.5	NA
919	#68C2A4	16	58	1	973	15.5	16.5	57.5	58.5	NA
920	gray	16	57	1	972	15.5	16.5	56.5	57.5	NA
921	#FFFCBB	16	56	1	971	15.5	16.5	55.5	56.5	NA
922	#BFE4A0	16	55	1	970	15.5	16.5	54.5	55.5	NA
923	#F06744	16	54	1	969	15.5	16.5	53.5	54.5	NA
924	#F6FBB1	16	53	1	968	15.5	16.5	52.5	53.5	NA
925	#7ECAA4	16	52	1	967	15.5	16.5	51.5	52.5	NA
926	#FEDB87	16	51	1	966	15.5	16.5	50.5	51.5	NA
927	gray	16	50	1	965	15.5	16.5	49.5	50.5	NA
928	gray	16	49	1	964	15.5	16.5	48.5	49.5	NA
929	#F6FBB1	16	48	1	963	15.5	16.5	47.5	48.5	NA
930	#FEE695	16	47	1	962	15.5	16.5	46.5	47.5	NA
931	#FED481	16	46	1	961	15.5	16.5	45.5	46.5	NA
932	#FFF8B3	16	45	1	960	15.5	16.5	44.5	45.5	NA
933	#F6FBB1	16	44	1	959	15.5	16.5	43.5	44.5	NA
934	#F9FCB6	16	43	1	958	15.5	16.5	42.5	43.5	NA
935	#EBF79F	16	42	1	957	15.5	16.5	41.5	42.5	NA

936	#F88C50	16	41	1	956	15.5	16.5	40.5	41.5	NA
937	#FFEEA4	16	40	1	955	15.5	16.5	39.5	40.5	NA
938	#D9EF9B	16	39	1	954	15.5	16.5	38.5	39.5	NA
939	#FED481	16	38	1	953	15.5	16.5	37.5	38.5	NA
940	#FEBE6E	16	37	1	952	15.5	16.5	36.5	37.5	NA
941	#FECC7A	16	36	1	951	15.5	16.5	35.5	36.5	NA
942	#FFEEA4	16	35	1	950	15.5	16.5	34.5	35.5	NA
943	#FEE695	16	34	1	949	15.5	16.5	33.5	34.5	NA
944	#F67948	16	33	1	948	15.5	16.5	32.5	33.5	NA
945	#B6E1A1	16	32	1	947	15.5	16.5	31.5	32.5	NA
946	#FDB768	16	31	1	946	15.5	16.5	30.5	31.5	NA
947	#9BD6A4	16	30	1	945	15.5	16.5	29.5	30.5	NA
948	#68C2A4	16	29	1	944	15.5	16.5	28.5	29.5	NA
949	#BFE4A0	16	28	1	943	15.5	16.5	27.5	28.5	NA
950	#EBF79F	16	27	1	942	15.5	16.5	26.5	27.5	NA
951	#9BD6A4	16	26	1	941	15.5	16.5	25.5	26.5	NA
952	#FFEEA4	16	25	1	940	15.5	16.5	24.5	25.5	NA
953	gray	16	24	1	939	15.5	16.5	23.5	24.5	NA
954	#DE4D4B	16	23	1	938	15.5	16.5	22.5	23.5	NA
955	#FEC575	16	22	1	937	15.5	16.5	21.5	22.5	NA
956	#D9454D	16	21	1	936	15.5	16.5	20.5	21.5	NA
957	#D9454D	16	20	1	935	15.5	16.5	19.5	20.5	NA
958	#D9454D	16	19	1	934	15.5	16.5	18.5	19.5	NA
959	#62BBA8	16	18	1	933	15.5	16.5	17.5	18.5	NA
960	#F9FCB6	16	17	1	932	15.5	16.5	16.5	17.5	NA
961	#7ECAA4	16	16	1	931	15.5	16.5	15.5	16.5	NA
962	#68C2A4	16	15	1	930	15.5	16.5	14.5	15.5	NA
963	#FEE695	16	14	1	929	15.5	16.5	13.5	14.5	NA
964	#9BD6A4	16	13	1	928	15.5	16.5	12.5	13.5	NA
965	#F9FCB6	16	12	1	927	15.5	16.5	11.5	12.5	NA
966	gray	16	11	1	926	15.5	16.5	10.5	11.5	NA
967	#FEDB87	16	10	1	925	15.5	16.5	9.5	10.5	NA
968	#92D2A4	16	9	1	924	15.5	16.5	8.5	9.5	NA
969	#C8E89E	16	8	1	923	15.5	16.5	7.5	8.5	NA
970	#FDB768	16	7	1	922	15.5	16.5	6.5	7.5	NA
971	#FFF8B3	16	6	1	921	15.5	16.5	5.5	6.5	NA
972	#73C6A4	16	5	1	920	15.5	16.5	4.5	5.5	NA
973	#FEEA9C	16	4	1	919	15.5	16.5	3.5	4.5	NA
974	#FEDB87	16	3	1	918	15.5	16.5	2.5	3.5	NA
975	#FED481	16	2	1	917	15.5	16.5	1.5	2.5	NA
976	#EEF8A5	16	1	1	916	15.5	16.5	0.5	1.5	NA
977	#FED481	17	61	1	1037	16.5	17.5	60.5	61.5	NA
978	#FFFCBB	17	60	1	1036	16.5	17.5	59.5	60.5	NA
979	#ADDDA3	17	59	1	1035	16.5	17.5	58.5	59.5	NA
980	#57AAAF	17	58	1	1034	16.5	17.5	57.5	58.5	NA

981	gray	17	57	1	1033	16.5	17.5	56.5	57.5	NA
982	#FFF8B3	17	56	1	1032	16.5	17.5	55.5	56.5	NA
983	#C8E89E	17	55	1	1031	16.5	17.5	54.5	55.5	NA
984	#D9454D	17	54	1	1030	16.5	17.5	53.5	54.5	NA
985	#FDFEBC	17	53	1	1029	16.5	17.5	52.5	53.5	NA
986	#68C2A4	17	52	1	1028	16.5	17.5	51.5	52.5	NA
987	#EEF8A5	17	51	1	1027	16.5	17.5	50.5	51.5	NA
988	gray	17	50	1	1026	16.5	17.5	49.5	50.5	NA
989	gray	17	49	1	1025	16.5	17.5	48.5	49.5	NA
990	#F6FBB1	17	48	1	1024	16.5	17.5	47.5	48.5	NA
991	#FEDB87	17	47	1	1023	16.5	17.5	46.5	47.5	NA
992	#FA9554	17	46	1	1022	16.5	17.5	45.5	46.5	NA
993	#E0F299	17	45	1	1021	16.5	17.5	44.5	45.5	NA
994	#F6FBB1	17	44	1	1020	16.5	17.5	43.5	44.5	NA
995	#B6E1A1	17	43	1	1019	16.5	17.5	42.5	43.5	NA
996	#EEF8A5	17	42	1	1018	16.5	17.5	41.5	42.5	NA
997	#CD374D	17	41	1	1017	16.5	17.5	40.5	41.5	NA
998	#BFE4A0	17	40	1	1016	16.5	17.5	39.5	40.5	NA
999	#D9EF9B	17	39	1	1015	16.5	17.5	38.5	39.5	NA
1000	#FDB768	17	38	1	1014	16.5	17.5	37.5	38.5	NA
1001	#F6FBB1	17	37	1	1013	16.5	17.5	36.5	37.5	NA
1002	#FA9554	17	36	1	1012	16.5	17.5	35.5	36.5	NA
1003	#FEEA9C	17	35	1	1011	16.5	17.5	34.5	35.5	NA
1004	#FA9554	17	34	1	1010	16.5	17.5	33.5	34.5	NA
1005	#FA9554	17	33	1	1009	16.5	17.5	32.5	33.5	NA
1006	#B6E1A1	17	32	1	1008	16.5	17.5	31.5	32.5	NA
1007	#FED481	17	31	1	1007	16.5	17.5	30.5	31.5	NA
1008	#ADDDA3	17	30	1	1006	16.5	17.5	29.5	30.5	NA
1009	#62BBA8	17	29	1	1005	16.5	17.5	28.5	29.5	NA
1010	#D0EC9C	17	28	1	1004	16.5	17.5	27.5	28.5	NA
1011	#FDFEBC	17	27	1	1003	16.5	17.5	26.5	27.5	NA
1012	#73C6A4	17	26	1	1002	16.5	17.5	25.5	26.5	NA
1013	#D53E4E	17	25	1	1001	16.5	17.5	24.5	25.5	NA
1014	gray	17	24	1	1000	16.5	17.5	23.5	24.5	NA
1015	#E2544A	17	23	1	999	16.5	17.5	22.5	23.5	NA
1016	#F9FCB6	17	22	1	998	16.5	17.5	21.5	22.5	NA
1017	#D53E4E	17	21	1	997	16.5	17.5	20.5	21.5	NA
1018	#F88C50	17	20	1	996	16.5	17.5	19.5	20.5	NA
1019	#D53E4E	17	19	1	995	16.5	17.5	18.5	19.5	NA
1020	#5DB2AB	17	18	1	994	16.5	17.5	17.5	18.5	NA
1021	#E7F59A	17	17	1	993	16.5	17.5	16.5	17.5	NA
1022	#73C6A4	17	16	1	992	16.5	17.5	15.5	16.5	NA
1023	#3288BC	17	15	1	991	16.5	17.5	14.5	15.5	NA
1024	#FED481	17	14	1	990	16.5	17.5	13.5	14.5	NA
1025	#73C6A4	17	13	1	989	16.5	17.5	12.5	13.5	NA

1026	#ADDDA3	17	12	1	988	16.5	17.5	11.5	12.5	NA
1027	gray	17	11	1	987	16.5	17.5	10.5	11.5	NA
1028	#FEE28E	17	10	1	986	16.5	17.5	9.5	10.5	NA
1029	#A4DAA4	17	9	1	985	16.5	17.5	8.5	9.5	NA
1030	#E7F59A	17	8	1	984	16.5	17.5	7.5	8.5	NA
1031	#9E0041	17	7	1	983	16.5	17.5	6.5	7.5	NA
1032	#BFE4A0	17	6	1	982	16.5	17.5	5.5	6.5	NA
1033	#5DB2AB	17	5	1	981	16.5	17.5	4.5	5.5	NA
1034	#FFEEA4	17	4	1	980	16.5	17.5	3.5	4.5	NA
1035	#FEE695	17	3	1	979	16.5	17.5	2.5	3.5	NA
1036	#FED481	17	2	1	978	16.5	17.5	1.5	2.5	NA
1037	#DOEC9C	17	1	1	977	16.5	17.5	0.5	1.5	NA
1038	#D0EC9C	18	61	1	1098	17.5	18.5	60.5	61.5	NA
1039	#E7F59A	18	60	1	1097	17.5	18.5	59.5	60.5	NA
1040	#EEF8A5	18	59	1	1096	17.5	18.5	58.5	59.5	NA
1041	#5DB2AB	18	58	1	1095	17.5	18.5	57.5	58.5	NA
1042	gray	18	57	1	1094	17.5	18.5	56.5	57.5	NA
1043	#F67948	18	56	1	1093	17.5	18.5	55.5	56.5	NA
1044	#9BD6A4	18	55	1	1092	17.5	18.5	54.5	55.5	NA
1045	#EBF79F	18	54	1	1091	17.5	18.5	53.5	54.5	NA
1046	#A4DAA4	18	53	1	1090	17.5	18.5	52.5	53.5	NA
1047	#D0EC9C	18	52	1	1089	17.5	18.5	51.5	52.5	NA
1048	#F6FB81	18	51	1	1088	17.5	18.5	50.5	51.5	NA
1049	gray	18	50	1	1087	17.5	18.5	49.5	50.5	NA
1050	gray	18	49	1	1086	17.5	18.5	48.5	49.5	NA
1051	#FDB768	18	48	1	1085	17.5	18.5	47.5	48.5	NA
1052	#D9EF9B	18	47	1	1084	17.5	18.5	46.5	47.5	NA
1053	#F2F9AB	18	46	1	1083	17.5	18.5	45.5	46.5	NA
1054	#B6E1A1	18	45	1	1082	17.5	18.5	44.5	45.5	NA
1055	#F9FCB6	18	44	1	1081	17.5	18.5	43.5	44.5	NA
1056	#D0EC9C	18	43	1	1080	17.5	18.5	42.5	43.5	NA
1057	#ADDDA3	18	42	1	1079	17.5	18.5	41.5	42.5	NA
1058	#B6E1A1	18	41	1	1078	17.5	18.5	40.5	41.5	NA
1059	#4898B6	18	40	1	1077	17.5	18.5	39.5	40.5	NA
1060	#EOF299	18	39	1	1076	17.5	18.5	38.5	39.5	NA
1061	#FED481	18	38	1	1075	17.5	18.5	37.5	38.5	NA
1062	#C8E89E	18	37	1	1074	17.5	18.5	36.5	37.5	NA
1063	#FFF3AC	18	36	1	1073	17.5	18.5	35.5	36.5	NA
1064	#E7F59A	18	35	1	1072	17.5	18.5	34.5	35.5	NA
1065	#F67948	18	34	1	1071	17.5	18.5	33.5	34.5	NA
1066	#FFF3AC	18	33	1	1070	17.5	18.5	32.5	33.5	NA
1067	#E7F59A	18	32	1	1069	17.5	18.5	31.5	32.5	NA
1068	#FFF3AC	18	31	1	1068	17.5	18.5	30.5	31.5	NA
1069	#F9FCB6	18	30	1	1067	17.5	18.5	29.5	30.5	NA
1070	#C8E89E	18	29	1	1066	17.5	18.5	28.5	29.5	NA

1071	#EBF79F	18	28	1	1065	17.5	18.5	27.5	28.5	NA
1072	#FFEEA4	18	27	1	1064	17.5	18.5	26.5	27.5	NA
1073	#B6E1A1	18	26	1	1063	17.5	18.5	25.5	26.5	NA
1074	#FEEA9C	18	25	1	1062	17.5	18.5	24.5	25.5	NA
1075	gray	18	24	1	1061	17.5	18.5	23.5	24.5	NA
1076	#B6E1A1	18	23	1	1060	17.5	18.5	22.5	23.5	NA
1077	#EBF79F	18	22	1	1059	17.5	18.5	21.5	22.5	NA
1078	#F06744	18	21	1	1058	17.5	18.5	20.5	21.5	NA
1079	#F6FBB1	18	20	1	1057	17.5	18.5	19.5	20.5	NA
1080	#FED481	18	19	1	1056	17.5	18.5	18.5	19.5	NA
1081	#5A58A5	18	18	1	1055	17.5	18.5	17.5	18.5	NA
1082	#FEEA9C	18	17	1	1054	17.5	18.5	16.5	17.5	NA
1083	#62BBA8	18	16	1	1053	17.5	18.5	15.5	16.5	NA
1084	#73C6A4	18	15	1	1052	17.5	18.5	14.5	15.5	NA
1085	#FB9F59	18	14	1	1051	17.5	18.5	13.5	14.5	NA
1086	#B6E1A1	18	13	1	1050	17.5	18.5	12.5	13.5	NA
1087	#EBF79F	18	12	1	1049	17.5	18.5	11.5	12.5	NA
1088	gray	18	11	1	1048	17.5	18.5	10.5	11.5	NA
1089	#FEE695	18	10	1	1047	17.5	18.5	9.5	10.5	NA
1090	#A4DAA4	18	9	1	1046	17.5	18.5	8.5	9.5	NA
1091	#B6E1A1	18	8	1	1045	17.5	18.5	7.5	8.5	NA
1092	#BFE4A0	18	7	1	1044	17.5	18.5	6.5	7.5	NA
1093	#57AAAF	18	6	1	1043	17.5	18.5	5.5	6.5	NA
1094	#73C6A4	18	5	1	1042	17.5	18.5	4.5	5.5	NA
1095	#FEDB87	18	4	1	1041	17.5	18.5	3.5	4.5	NA
1096	#FCA75D	18	3	1	1040	17.5	18.5	2.5	3.5	NA
1097	#FEC575	18	2	1	1039	17.5	18.5	1.5	2.5	NA
1098	#A4DAA4	18	1	1	1038	17.5	18.5	0.5	1.5	NA
1099	#FFF8B3	19	61	1	1159	18.5	19.5	60.5	61.5	NA
1100	#FFF3AC	19	60	1	1158	18.5	19.5	59.5	60.5	NA
1101	#F9FCB6	19	59	1	1157	18.5	19.5	58.5	59.5	NA
1102	#F9FCB6	19	58	1	1156	18.5	19.5	57.5	58.5	NA
1103	gray	19	57	1	1155	18.5	19.5	56.5	57.5	NA
1104	#FEEA9C	19	56	1	1154	18.5	19.5	55.5	56.5	NA
1105	#FDDEBC	19	55	1	1153	18.5	19.5	54.5	55.5	NA
1106	#FEE28E	19	54	1	1152	18.5	19.5	53.5	54.5	NA
1107	#FFF3AC	19	53	1	1151	18.5	19.5	52.5	53.5	NA
1108	#F6FBB1	19	52	1	1150	18.5	19.5	51.5	52.5	NA
1109	#FFFCBB	19	51	1	1149	18.5	19.5	50.5	51.5	NA
1110	gray	19	50	1	1148	18.5	19.5	49.5	50.5	NA
1111	gray	19	49	1	1147	18.5	19.5	48.5	49.5	NA
1112	#FDDEBC	19	48	1	1146	18.5	19.5	47.5	48.5	NA
1113	#F9FCB6	19	47	1	1145	18.5	19.5	46.5	47.5	NA
1114	#F9FCB6	19	46	1	1144	18.5	19.5	45.5	46.5	NA
1115	#FFFCBB	19	45	1	1143	18.5	19.5	44.5	45.5	NA

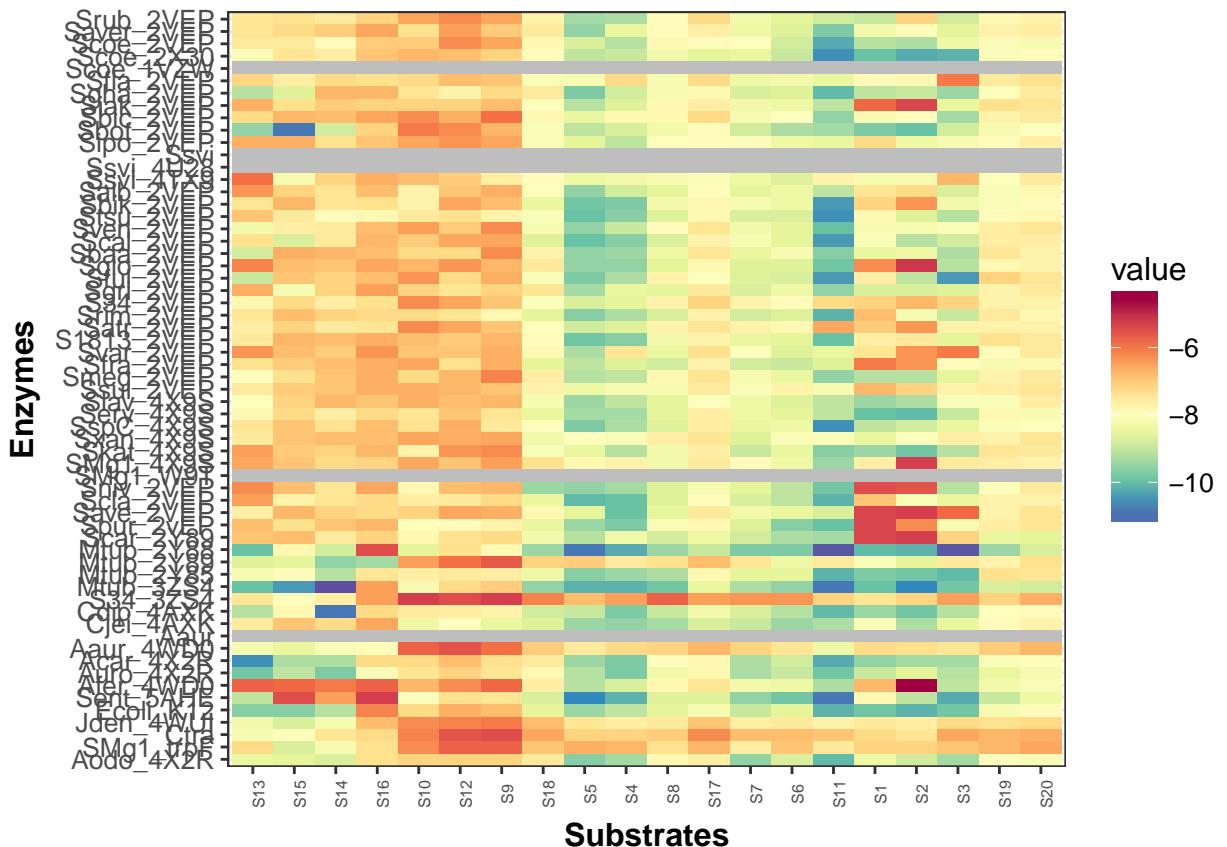
1116 #FFEEA4 19 44	1	1142	18.5	19.5	43.5	44.5	NA
1117 #FFEEA4 19 43	1	1141	18.5	19.5	42.5	43.5	NA
1118 #FEE695 19 42	1	1140	18.5	19.5	41.5	42.5	NA
1119 #FFF8B3 19 41	1	1139	18.5	19.5	40.5	41.5	NA
1120 #FED481 19 40	1	1138	18.5	19.5	39.5	40.5	NA
1121 #FFF3AC 19 39	1	1137	18.5	19.5	38.5	39.5	NA
1122 #FFF3AC 19 38	1	1136	18.5	19.5	37.5	38.5	NA
1123 #FEEA9C 19 37	1	1135	18.5	19.5	36.5	37.5	NA
1124 #FFF3AC 19 36	1	1134	18.5	19.5	35.5	36.5	NA
1125 #FEE28E 19 35	1	1133	18.5	19.5	34.5	35.5	NA
1126 #FFFCBB 19 34	1	1132	18.5	19.5	33.5	34.5	NA
1127 #F6FBB1 19 33	1	1131	18.5	19.5	32.5	33.5	NA
1128 #FFF3AC 19 32	1	1130	18.5	19.5	31.5	32.5	NA
1129 #FFEEA4 19 31	1	1129	18.5	19.5	30.5	31.5	NA
1130 #F9FCB6 19 30	1	1128	18.5	19.5	29.5	30.5	NA
1131 #FFF8B3 19 29	1	1127	18.5	19.5	28.5	29.5	NA
1132 #F9FCB6 19 28	1	1126	18.5	19.5	27.5	28.5	NA
1133 #FFF3AC 19 27	1	1125	18.5	19.5	26.5	27.5	NA
1134 #FEE695 19 26	1	1124	18.5	19.5	25.5	26.5	NA
1135 #FFEEA4 19 25	1	1123	18.5	19.5	24.5	25.5	NA
1136 gray 19 24	1	1122	18.5	19.5	23.5	24.5	NA
1137 #FDFEBC 19 23	1	1121	18.5	19.5	22.5	23.5	NA
1138 #FFF3AC 19 22	1	1120	18.5	19.5	21.5	22.5	NA
1139 #FFF3AC 19 21	1	1119	18.5	19.5	20.5	21.5	NA
1140 #FFEEA4 19 20	1	1118	18.5	19.5	19.5	20.5	NA
1141 #EBF79F 19 19	1	1117	18.5	19.5	18.5	19.5	NA
1142 #9BD6A4 19 18	1	1116	18.5	19.5	17.5	18.5	NA
1143 #FFF3AC 19 17	1	1115	18.5	19.5	16.5	17.5	NA
1144 #FEE28E 19 16	1	1114	18.5	19.5	15.5	16.5	NA
1145 #D9EF9B 19 15	1	1113	18.5	19.5	14.5	15.5	NA
1146 #FED481 19 14	1	1112	18.5	19.5	13.5	14.5	NA
1147 #FDFEBC 19 13	1	1111	18.5	19.5	12.5	13.5	NA
1148 #FFFCBB 19 12	1	1110	18.5	19.5	11.5	12.5	NA
1149 gray 19 11	1	1109	18.5	19.5	10.5	11.5	NA
1150 #FECC7A 19 10	1	1108	18.5	19.5	9.5	10.5	NA
1151 #F9FCB6 19 9	1	1107	18.5	19.5	8.5	9.5	NA
1152 #EBF79F 19 8	1	1106	18.5	19.5	7.5	8.5	NA
1153 #F2F9AB 19 7	1	1105	18.5	19.5	6.5	7.5	NA
1154 #C8E89E 19 6	1	1104	18.5	19.5	5.5	6.5	NA
1155 #F6FBB1 19 5	1	1103	18.5	19.5	4.5	5.5	NA
1156 #FEE28E 19 4	1	1102	18.5	19.5	3.5	4.5	NA
1157 #FDB768 19 3	1	1101	18.5	19.5	2.5	3.5	NA
1158 #FDB768 19 2	1	1100	18.5	19.5	1.5	2.5	NA
1159 #FDFEBC 19 1	1	1099	18.5	19.5	0.5	1.5	NA
1160 #FFF3AC 20 61	1	1220	19.5	20.5	60.5	61.5	NA

1161	#FFEEA4	20	60	1	1219	19.5	20.5	59.5	60.5	NA
1162	#F6FBB1	20	59	1	1218	19.5	20.5	58.5	59.5	NA
1163	#FFFCCB	20	58	1	1217	19.5	20.5	57.5	58.5	NA
1164	gray	20	57	1	1216	19.5	20.5	56.5	57.5	NA
1165	#FEE28E	20	56	1	1215	19.5	20.5	55.5	56.5	NA
1166	#FEEA9C	20	55	1	1214	19.5	20.5	54.5	55.5	NA
1167	#FEE695	20	54	1	1213	19.5	20.5	53.5	54.5	NA
1168	#FEEA9C	20	53	1	1212	19.5	20.5	52.5	53.5	NA
1169	#FDDEBC	20	52	1	1211	19.5	20.5	51.5	52.5	NA
1170	#FFEEA4	20	51	1	1210	19.5	20.5	50.5	51.5	NA
1171	gray	20	50	1	1209	19.5	20.5	49.5	50.5	NA
1172	gray	20	49	1	1208	19.5	20.5	48.5	49.5	NA
1173	#FEEA9C	20	48	1	1207	19.5	20.5	47.5	48.5	NA
1174	#FFF8B3	20	47	1	1206	19.5	20.5	46.5	47.5	NA
1175	#FFFCCB	20	46	1	1205	19.5	20.5	45.5	46.5	NA
1176	#FFF8B3	20	45	1	1204	19.5	20.5	44.5	45.5	NA
1177	#FEE695	20	44	1	1203	19.5	20.5	43.5	44.5	NA
1178	#FFEEA4	20	43	1	1202	19.5	20.5	42.5	43.5	NA
1179	#FFF3AC	20	42	1	1201	19.5	20.5	41.5	42.5	NA
1180	#FFF3AC	20	41	1	1200	19.5	20.5	40.5	41.5	NA
1181	#FEE695	20	40	1	1199	19.5	20.5	39.5	40.5	NA
1182	#FEEA9C	20	39	1	1198	19.5	20.5	38.5	39.5	NA
1183	#FFF3AC	20	38	1	1197	19.5	20.5	37.5	38.5	NA
1184	#FFF8B3	20	37	1	1196	19.5	20.5	36.5	37.5	NA
1185	#FFF3AC	20	36	1	1195	19.5	20.5	35.5	36.5	NA
1186	#FEEA9C	20	35	1	1194	19.5	20.5	34.5	35.5	NA
1187	#FEEA9C	20	34	1	1193	19.5	20.5	33.5	34.5	NA
1188	#FFF8B3	20	33	1	1192	19.5	20.5	32.5	33.5	NA
1189	#FEEA9C	20	32	1	1191	19.5	20.5	31.5	32.5	NA
1190	#FEE695	20	31	1	1190	19.5	20.5	30.5	31.5	NA
1191	#FFEEA4	20	30	1	1189	19.5	20.5	29.5	30.5	NA
1192	#F6FBB1	20	29	1	1188	19.5	20.5	28.5	29.5	NA
1193	#FDDEBC	20	28	1	1187	19.5	20.5	27.5	28.5	NA
1194	#FEE695	20	27	1	1186	19.5	20.5	26.5	27.5	NA
1195	#FEEA9C	20	26	1	1185	19.5	20.5	25.5	26.5	NA
1196	#FFF3AC	20	25	1	1184	19.5	20.5	24.5	25.5	NA
1197	gray	20	24	1	1183	19.5	20.5	23.5	24.5	NA
1198	#FEEA9C	20	23	1	1182	19.5	20.5	22.5	23.5	NA
1199	#FFF3AC	20	22	1	1181	19.5	20.5	21.5	22.5	NA
1200	#FEE695	20	21	1	1180	19.5	20.5	20.5	21.5	NA
1201	#FEE695	20	20	1	1179	19.5	20.5	19.5	20.5	NA
1202	#E7F59A	20	19	1	1178	19.5	20.5	18.5	19.5	NA
1203	#D9EF9B	20	18	1	1177	19.5	20.5	17.5	18.5	NA
1204	#FEE28E	20	17	1	1176	19.5	20.5	16.5	17.5	NA
1205	#FEE695	20	16	1	1175	19.5	20.5	15.5	16.5	NA

1206	#D0EC9C	20	15	1	1174	19.5	20.5	14.5	15.5	NA
1207	#FDB063	20	14	1	1173	19.5	20.5	13.5	14.5	NA
1208	#FFFCBB	20	13	1	1172	19.5	20.5	12.5	13.5	NA
1209	#FFF3AC	20	12	1	1171	19.5	20.5	11.5	12.5	NA
1210	gray	20	11	1	1170	19.5	20.5	10.5	11.5	NA
1211	#FDB768	20	10	1	1169	19.5	20.5	9.5	10.5	NA
1212	#FDFEBC	20	9	1	1168	19.5	20.5	8.5	9.5	NA
1213	#F6FBB1	20	8	1	1167	19.5	20.5	7.5	8.5	NA
1214	#F9FCB6	20	7	1	1166	19.5	20.5	6.5	7.5	NA
1215	#EEF8A5	20	6	1	1165	19.5	20.5	5.5	6.5	NA
1216	#FFFCBB	20	5	1	1164	19.5	20.5	4.5	5.5	NA
1217	#FEDB87	20	4	1	1163	19.5	20.5	3.5	4.5	NA
1218	#FDB063	20	3	1	1162	19.5	20.5	2.5	3.5	NA
1219	#FCA75D	20	2	1	1161	19.5	20.5	1.5	2.5	NA
1220	#F9FCB6	20	1	1	1160	19.5	20.5	0.5	1.5	NA

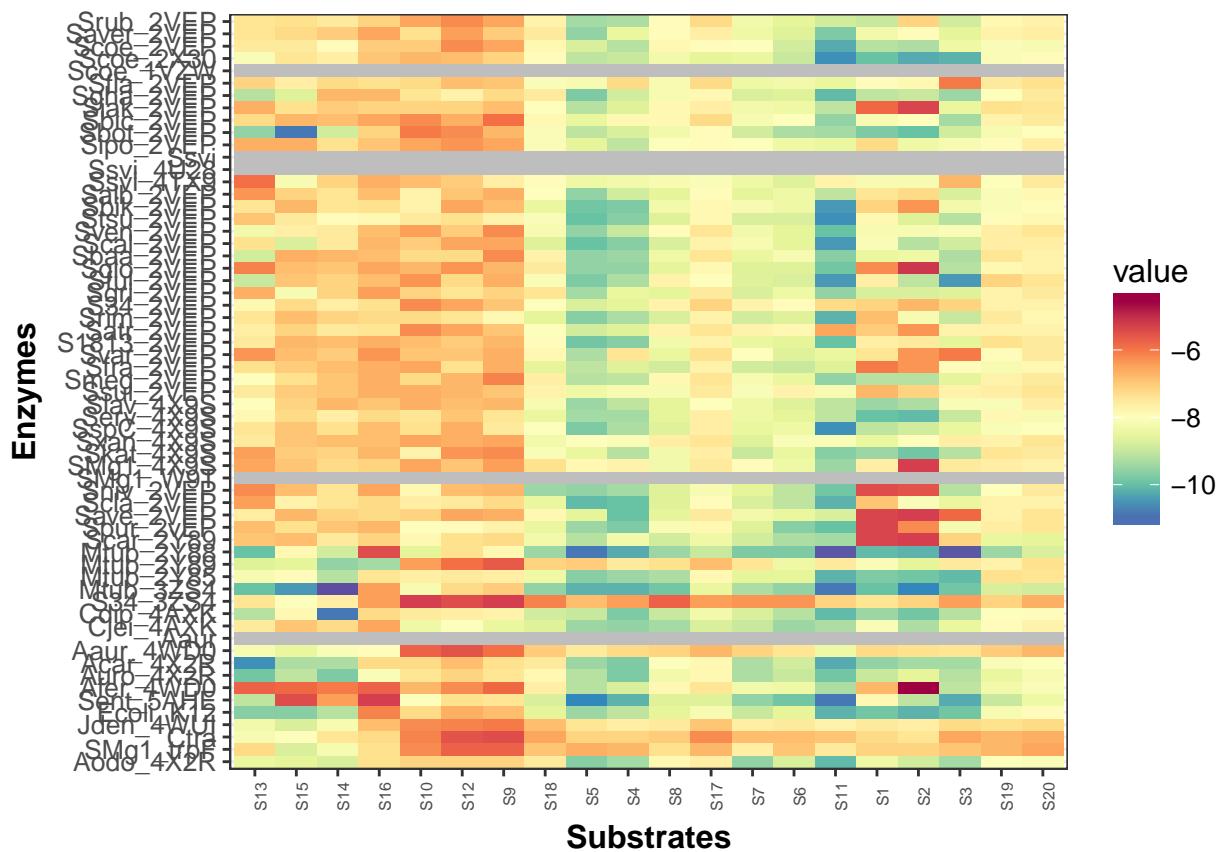
```
write.xlsx(gcolor$data[[1]], "chapter2/mydataColor.xlsx")
```

```
ggplot(docking.m, aes(x=variable, y=Enzima)) + labs(x = "Substrates", y = "Enzymes")
```



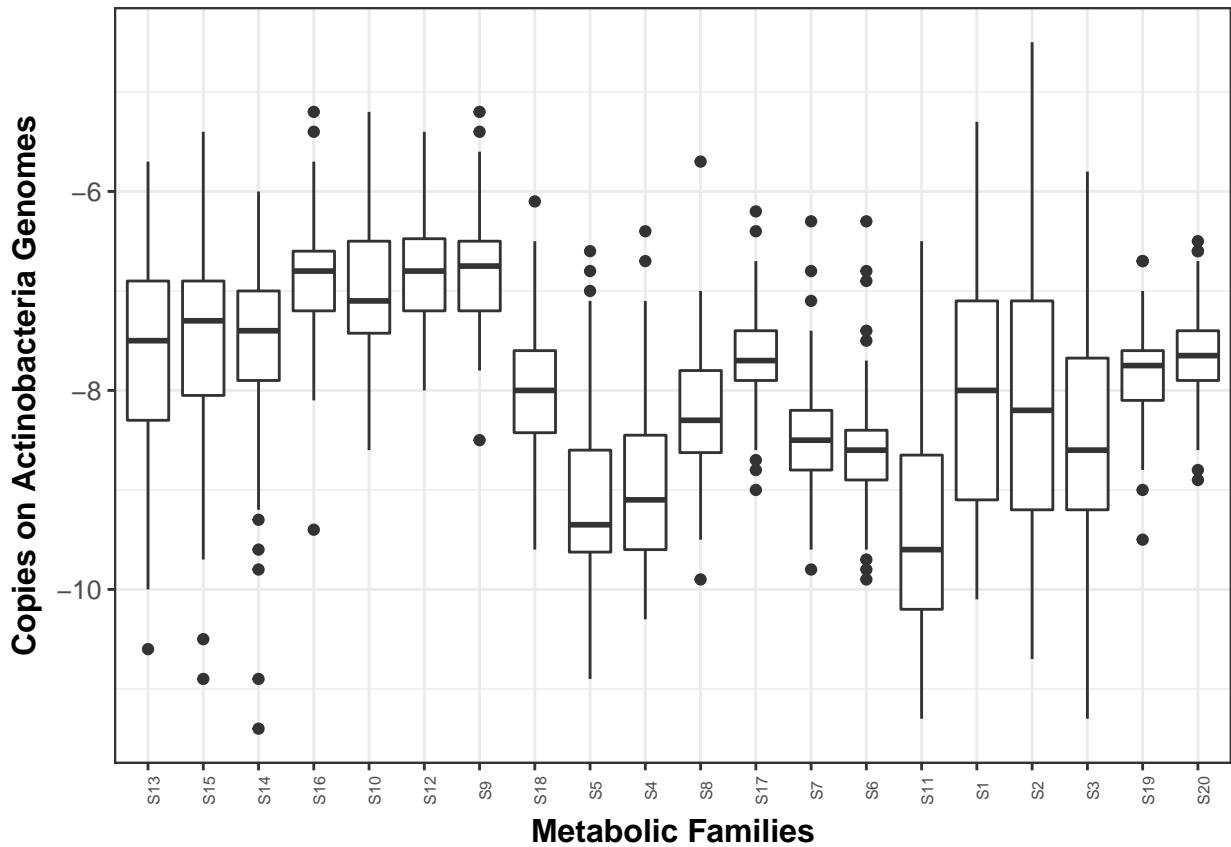
```
## boxplot de los sustratos
```

```
ggplot(docking.m, aes(x=variable, y=Enzima)) + labs(x = "Substrates", y = "Enzymes")
```



```
ggplot(docking.m, aes(x=variable, y=value)) + labs(x = "Metabolic Families", y = "Copies")
```

Warning: Removed 100 rows containing non-finite values (stat_boxplot).



We next introduce a useful function in the `knitr` package for making nice tables in *R Markdown* called `kable`. It produces the *L^AT_EX* code required to make the table and is much easier to use than manually entering values into a table by copying and pasting values into Excel or *L^AT_EX*. This again goes to show how nice reproducible documents can be! There is no need to copy-and-paste values to create a table. (Note the use of `results = "asis"` here which will produce the table instead of the code to create the table. You'll learn more about the `\label{tab:docking}` later.) The `caption.short` argument is used to include a shorter version of the title to appear in the List of Tables at the beginning of the document.

```
kable(docking,  caption = "Enzymes docking \label{tab:docking}",caption.short = "
```

Table 2.2: Enzymes docking

Enzima	S13	S15	S14	S16	S10	S12	S9	S18	S5	S4	S8	S17	S7
Srub_2VEP	-7.4	-7.3	-7.5	-7.1	-6.5	-6.2	-6.5	-7.7	-9.4	-9.3	-7.9	-7.2	-8.3
Saver_2VEP	-7.4	-7.2	-7.0	-6.5	-7.3	-6.4	-7.0	-7.5	-9.6	-8.5	-7.9	-7.6	-8.4
Scoe_2VEP	-7.5	-7.5	-7.9	-7.0	-7.0	-6.2	-6.5	-7.8	-8.8	-9.2	-7.8	-7.9	-8.0
Scoe_2X30	-8.1	-7.4	-7.6	-6.9	-6.7	-6.8	-7.1	-7.9	-9.1	-9.0	-8.3	-8.6	-8.5
Scoe_1VZW	NA												
Sfla_2VEP	-7.1	-7.6	-7.2	-7.3	-7.2	-6.8	-6.9	-8.1	-8.2	-7.2	-8.2	-7.2	-8.4
Sgha_2VEP	-9.2	-8.7	-6.7	-6.7	-7.4	-7.7	-7.2	-7.5	-9.8	-8.9	-8.2	-7.8	-8.8

Enzima	S13	S15	S14	S16	S10	S12	S9	S18	S5	S4	S8	S17	S7	S6
Siak_2VEP	-6.6	-7.3	-7.0	-7.1	-7.1	-7.1	-6.8	-8.0	-9.2	-8.7	-7.8	-7.6	-8.3	-8.4
Sbic_2VEP	-7.2	-6.7	-6.8	-6.5	-6.2	-6.6	-5.9	-7.8	-8.5	-7.8	-7.8	-7.2	-8.2	-8.0
Sbot_2VEP	-9.6	-10.9	-8.9	-7.1	-6.0	-6.2	-6.7	-8.1	-9.1	-8.8	-8.3	-7.9	-8.9	-9.3
Sipo_2VEP	-6.6	-6.6	-7.3	-6.9	-6.5	-6.3	-6.5	-8.1	-8.6	-9.1	-8.0	-7.9	-8.0	-8.4
Ssvi	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ssvi_4U28	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ssvi_4TX9	-5.9	-8.2	-7.1	-6.6	-6.8	-7.0	-7.6	-7.9	-8.4	-8.3	-8.2	-8.1	-8.4	-8.7
Salb_2VEP	-6.3	-7.1	-7.4	-6.8	-7.7	-6.9	-6.6	-8.0	-9.6	-8.9	-8.6	-7.9	-8.6	-8.4
Sbik_2VEP	-7.4	-6.7	-7.4	-7.3	-7.7	-6.5	-6.8	-8.5	-9.9	-9.8	-8.3	-7.8	-8.2	-8.4
Stsu_2VEP	-6.9	-7.5	-7.9	-7.8	-7.5	-7.3	-7.7	-8.1	-10.0	-9.7	-8.7	-7.8	-8.8	-8.8
Sven_2VEP	-8.3	-7.6	-7.5	-6.8	-6.4	-7.0	-6.2	-8.2	-9.6	-9.0	-7.9	-7.4	-8.3	-8.6
Scal_2VEP	-7.3	-8.8	-7.5	-6.7	-7.0	-6.5	-6.5	-8.7	-10.0	-9.7	-8.8	-7.7	-8.2	-8.6
Sbaa_2VEP	-8.9	-6.6	-6.7	-6.8	-7.2	-7.2	-6.2	-7.7	-9.6	-9.5	-8.4	-7.4	-8.5	-8.2
Sglo_2VEP	-6.1	-6.8	-6.9	-6.5	-6.7	-6.3	-6.7	-7.5	-9.6	-9.6	-8.6	-7.8	-8.7	-8.7
Sful_2VEP	-9.0	-6.9	-7.1	-6.8	-6.3	-7.2	-6.6	-8.1	-9.8	-9.3	-7.7	-8.0	-8.7	-8.8
Sgri_2VEP	-6.6	-8.2	-7.1	-6.4	-7.1	-7.4	-7.1	-7.4	-9.4	-8.5	-8.6	-7.5	-8.8	-8.4
S34_2VEP	-7.8	-7.2	-7.6	-7.3	-6.2	-6.5	-6.9	-8.0	-8.8	-8.6	-7.7	-7.1	-7.7	-7.9
Srim_2VEP	-7.4	-6.8	-7.1	-7.2	-7.2	-7.4	-7.8	-8.6	-9.7	-9.3	-8.8	-7.7	-8.9	-8.7
Satr_2VEP	-7.6	-7.1	-7.5	-7.4	-6.2	-6.5	-6.9	-8.0	-8.9	-8.7	-7.7	-7.4	-7.7	-7.8
S1813_2VEP	-7.5	-6.7	-6.8	-6.6	-6.8	-7.0	-6.7	-7.9	-9.9	-9.7	-8.3	-7.7	-8.5	-8.6
Svar_2VEP	-6.3	-6.8	-7.0	-6.3	-6.9	-6.9	-6.6	-7.8	-9.3	-7.4	-8.5	-7.3	-8.0	-8.7
Sfra_2VEP	-7.3	-7.0	-6.8	-6.6	-6.5	-7.3	-6.6	-8.6	-9.1	-8.7	-8.9	-7.7	-8.9	-9.0
Smeg_2VEP	-8.0	-7.3	-6.9	-6.6	-7.2	-6.7	-6.1	-7.6	-9.2	-9.1	-7.8	-7.4	-8.2	-8.5
Ssul_2VEP	-7.5	-7.0	-6.9	-6.6	-6.6	-6.7	-6.9	-7.7	-8.4	-8.2	-8.2	-7.5	-8.1	-7.7
Slav_4X9S	-8.0	-7.1	-6.7	-6.9	-6.6	-6.8	-6.7	-8.2	-9.5	-9.1	-8.6	-8.0	-8.4	-8.7
Sery_4X9S	-7.8	-7.2	-7.6	-7.2	-7.4	-6.9	-7.4	-8.5	-9.4	-9.4	-8.6	-7.6	-8.4	-8.6
SspC_4X9S	-7.4	-6.9	-7.3	-6.8	-7.3	-6.6	-7.5	-8.0	-9.8	-9.3	-8.7	-7.6	-8.5	-8.4
Sxan_4X9S	-7.5	-6.9	-6.8	-6.8	-6.5	-6.6	-6.5	-8.3	-8.0	-8.1	-7.6	-7.4	-8.7	-8.1
Skat_4X9S	-6.4	-7.0	-7.1	-6.7	-7.7	-6.3	-6.2	-8.1	-8.5	-9.2	-8.3	-7.6	-9.0	-8.5
SMg1_4X9S	-6.5	-6.9	-7.2	-7.1	-6.5	-6.9	-6.4	-7.3	-7.8	-7.7	-8.3	-7.5	-7.9	-8.4
SMg1_W9T	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sniv_2VEP	-6.2	-6.8	-7.4	-6.5	-7.8	-6.8	-6.7	-9.5	-9.6	-9.4	-8.7	-8.2	-8.6	-9.1
Scla_2VEP	-6.4	-7.7	-7.4	-7.2	-7.6	-7.5	-7.2	-8.5	-10.1	-10.0	-8.7	-7.9	-8.8	-9.1
Save_2VEP	-7.6	-6.7	-7.1	-7.2	-7.1	-6.5	-6.6	-7.8	-8.6	-10.0	-8.6	-7.5	-8.3	-8.5
Spur_2vEP	-6.8	-7.3	-6.9	-6.7	-8.0	-7.9	-7.7	-8.5	-9.5	-9.8	-8.1	-7.8	-8.7	-9.7
Scar_2Y89	-6.9	-6.8	-7.5	-7.1	-7.8	-7.3	-7.2	-8.3	-9.2	-8.3	-8.9	-8.4	-8.9	-9.3
Mtub_2Y88	-10.0	-7.8	-8.9	-5.4	-8.6	-7.3	-7.8	-9.5	-10.9	-10.3	-9.5	-9.0	-9.8	-9.8
Mtub_2Y89	-8.7	-8.6	-9.6	-9.4	-6.4	-5.9	-5.6	-7.1	-7.0	-7.5	-7.3	-6.8	-7.4	-8.4
Mtub_2Y85	-8.2	-7.9	-9.2	-7.4	-7.6	-7.5	-7.6	-8.4	-9.7	-9.5	-9.3	-7.8	-8.6	-8.6
Mtub_3ZS4	-10.0	-10.5	-11.4	-6.4	-8.2	-7.2	-7.0	-9.6	-10.2	-10.2	-9.9	-8.5	-9.3	-9.6
S34_3ZS4	-7.4	-8.0	-7.6	-6.4	-5.2	-5.4	-5.2	-6.1	-6.8	-6.4	-5.7	-6.4	-6.3	-6.3
Cdip_4AXK	-9.2	-7.8	-10.9	-7.2	-7.5	-7.6	-7.7	-8.9	-9.0	-9.8	-9.0	-8.3	-8.8	-9.2
Cjei_4AXK	-7.5	-6.9	-7.2	-6.5	-8.4	-8.0	-8.5	-8.7	-9.5	-9.6	-9.4	-8.8	-9.0	-9.5

Enzima	S13	S15	S14	S16	S10	S12	S9	S18	S5	S4	S8	S17	S7
Aaur	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Aaur_4WD0	-8.2	-8.5	-8.1	-7.9	-5.7	-5.5	-5.9	-7.0	-7.5	-7.2	-7.1	-6.7	-7.1
Acar_4X2R	-10.6	-9.3	-9.3	-7.2	-7.2	-6.8	-7.3	-7.5	-9.5	-9.8	-8.0	-7.8	-9.3
Auro_4X2R	-9.9	-9.1	-9.8	-8.1	-7.4	-7.1	-7.4	-7.8	-9.2	-9.8	-8.3	-7.8	-9.3
Afer_4WD0	-5.7	-5.8	-6.0	-5.7	-6.7	-6.2	-5.8	-7.6	-9.2	-8.8	-7.8	-7.4	-8.3
Sent_5AHE	-9.1	-5.4	-6.4	-5.2	-8.0	-7.3	-7.4	-8.8	-10.7	-10.2	-8.7	-8.7	-9.6
Ecoli_K12	-9.7	-9.7	-9.2	-6.1	-7.2	-6.6	-6.8	-8.6	-9.5	-9.1	-8.6	-8.2	-9.0
Jden_4WUI	-8.3	-8.8	-8.2	-6.8	-6.2	-6.1	-6.0	-6.8	-7.4	-7.6	-7.5	-6.9	-7.6
Ctra	-8.2	-8.0	-7.4	-7.2	-6.1	-5.5	-5.4	-6.5	-7.1	-7.1	-7.0	-6.2	-6.8
SMg1_trpF	-7.2	-8.8	-8.2	-7.3	-6.2	-5.7	-5.7	-6.9	-6.6	-6.7	-7.3	-6.7	-7.6
Aodo_4X2R	-8.5	-8.6	-8.8	-7.3	-7.1	-7.1	-7.1	-7.5	-9.7	-9.4	-7.8	-7.6	-9.6

We can further look into the properties of the largest value here for American Airlines Inc. To do so, we can isolate the row corresponding to the arrival delay of 1539 minutes for American in our original `flights` dataset.

```
#flights %>% dplyr::filter(arr_delay == 1539, carrier_name == "American Airlines"
#dplyr::select(-c(month, day, carrier, dest_name, hour, minute, carrier_name,
```

We see that the flight occurred on March 3rd and departed a little after 2 PM on its way to Dallas/Fort Worth. Lastly, we show how we can visualize the arrival delay of all departing flights from Portland on March 3rd against time of departure.

```
#flights %>% dplyr::filter(month == 3, day == 3) %>%
# ggplot(aes(x = dep_time, y = arr_delay)) +geom_point()
```

Genome size vs Total antimash cluster coloured by order

Docker simulation were calculated for Streptomyces enzymes
Genome size vs Total antimash cluster coloured by order

T_EX is the best way to typeset mathematics. Donald Knuth designed T_EX when he got frustrated at how long it was taking the typesetters to finish his book, which contained a lot of mathematics. One nice feature of *R Markdown* is its ability to read L_AT_EX code directly.

If you are doing a thesis that will involve lots of math, you will want to read the following section which has been commented out. If you're not going to use math, skip over or delete this next commented section.

2.2 Chemistry 101: Symbols

Chemical formulas will look best if they are not italicized. Get around math mode's automatic italicizing in L_AT_EX by using the argument `\mathrm{formula here}`,

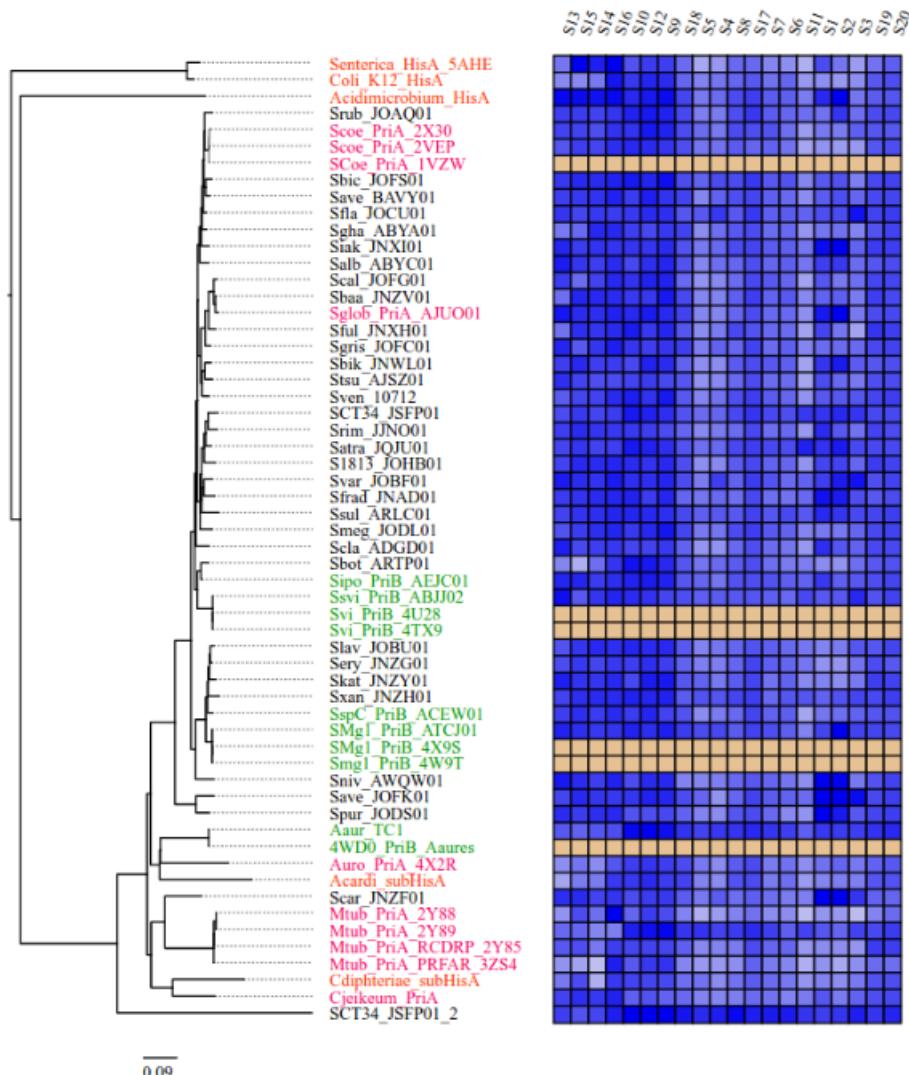


Figure 2.1: Heat Plot PriA Streptomyces vs other substrates



Figure 2.2: Heat Plot TrpF Streptomyces vs other substrates

with your formula inside the curly brackets. (Notice the use of the backticks here which enclose text that acts as code.)

So, $\text{Fe}_2^{2+}\text{Cr}_2\text{O}_4$ is written `$\backslash\mathrm{Fe_2^{2+}Cr_2O_4}$`.

Exponent or Superscript: O^-

Subscript: CH_4

To stack numbers or letters as in Fe_2^{2+} , the subscript is defined first, and then the superscript is defined.

Angstrom: \AA

Bullet: $\text{CuCl} \bullet 7\text{H}_2\text{O}$

Double Dagger: \ddagger

Delta: Δ

Reaction Arrows: \longrightarrow or $\xrightarrow{\text{solution}}$

Resonance Arrows: \leftrightarrow

Reversible Reaction Arrows: \rightleftharpoons or $\xrightleftharpoons{\text{solution}}$ (the latter requires the `chemarr` L^AT_EX package which is automatically loaded in this template)

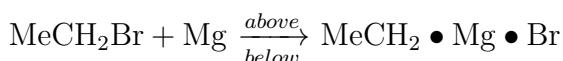
2.2.1 Typesetting reactions

You may wish to put your reaction in a figure environment, which means that L^AT_EX will place the reaction where it fits and you can have a figure caption. You'll see further description of this `R label` function in . (Note the use of the double backslash here as well as the `echo = FALSE` which hides the code from the output.)



Figure 2.3: Combustion of glucose

2.2.2 Other examples of reactions



2.3 Physics

Many of the symbols you will need can be found on the math page <http://web.reed.edu/cis/help/latex/math.html> and the Comprehensive L^AT_EX Symbol Guide

(<http://mirror.utexas.edu/ctan/info/symbols/comprehensive/symbols-letter.pdf>).

2.4 Biology

You will probably find the resources at <http://www.lecb.ncifcrf.gov/~toms/latex.html> helpful, particularly the links to bsts for various journals. You may also be interested in TeXShade for nucleotide typesetting (<http://homepages.uni-tuebingen.de/beitz/txe.html>). Be sure to read the proceeding chapter on graphics and tables.

```
sessionInfo()
```

```
R version 3.3.2 (2016-10-31)
Platform: x86_64-pc-linux-gnu (64-bit)
Running under: Ubuntu 14.04.5 LTS

locale:
[1] LC_CTYPE=en_US.UTF-8          LC_NUMERIC=C
[3] LC_TIME=es_MX.UTF-8          LC_COLLATE=en_US.UTF-8
[5] LC_MONETARY=es_MX.UTF-8       LC_MESSAGES=en_US.UTF-8
[7] LC_PAPER=es_MX.UTF-8          LC_NAME=es_MX.UTF-8
[9] LC_ADDRESS=es_MX.UTF-8         LC_TELEPHONE=es_MX.UTF-8
[11] LC_MEASUREMENT=es_MX.UTF-8    LC_IDENTIFICATION=es_MX.UTF-8

attached base packages:
[1] parallel   stats      graphics   grDevices  utils      datasets   methods
[8] base

other attached packages:
[1] xlsx_0.5.7           xlsxjars_0.6.1      rJava_0.9-8
[4] scales_0.4.1          Biobase_2.34.0       BiocGenerics_0.20.0
[7] genstats_0.1.02       RColorBrewer_1.1-2   reshape_0.8.6
[10] plyr_1.8.4            knitr_1.15.1        ggplot2_2.2.1
[13] dplyr_0.5.0            ape_4.0              reedtemplates_0.1
[16] devtools_1.12.0

loaded via a namespace (and not attached):
[1] Rcpp_0.12.9      highr_0.6       tools_3.3.2      digest_0.6.12
[5] evaluate_0.10    memoise_1.0.0    tibble_1.2       gtable_0.2.0
[9] nlme_3.1-131     lattice_0.20-34   DBI_0.5-1       yaml_2.1.14
[13] withr_1.0.2      stringr_1.1.0    rprojroot_1.2   grid_3.3.2
[17] R6_2.2.0          rmarkdown_1.3     magrittr_1.5     backports_1.0.5
[21] htmltools_0.3.5   assertthat_0.1    colorspace_1.3-2 labeling_0.3
```

```
[25] stringi_1.1.2     lazyeval_0.2.0    munsell_0.4.3
```


Chapter 3

Archaea EvoMining Results

During the decade between 1970 and 1980, Archaea was recognized as new life domain, a kingdom different from Bacteria and Eucarya in an exciting first great application of 16S phylogeny[115] . Main differences between this kingdoms are that Archaeal DNA is not arranged in a nucleus as in Eucarya and Archaeal cellular walls are not composed from peptidoglycans as in Bacteria. Archaeal proteins may be highly valuable to biotechnology industry for their great stability due to extreme temperature, PH and salt content conditions on Archeal habitats. Despite no Archaeal Natural products biosynthetic gene clusters (BGC's) has been reported on MiBIG, Archaea do have BGC's, some of them seems to be acquired by horizontal gene transfer (HGT) like methano nrps {search reference}. Other Archeal natural products known are archaeosins, Diketopiperazines, Acyl Homoserine Lactones, Exopolysaccharides, Carotenoids, Biosurfactants, Phenazines and Organic Solutes but this knowledge is not comparable to Bacterial BGC's knowledge[99].

Natural products biosynthetic gene clusters search is actually performed using either *high-confidence/low-novelty or low-confidence/high-novelty* bioinformatic approaches [50]. High confidence methods compares query sequences with previously known BGC's such as nrps or PKS, examples of this algorithms are antiSMASH and clusterfinder [????]. EvoMining searches on expansions from central metabolic pathways enzyme families, it has been classified as low confidence/high novelty method. EvoMining has proved useful on Actinobacteria phylum where its use lead to Arseno-compounds discovery [65]. Also on Actinobacteria antiSMASH analysis on 1245 genomes found 774 different classes of natural products, the same analysis on 876 Archaeal genomes, a full kingdom, identifies only 35 BGC's classes. So either Archaea does not have natural products BGC's or this are not yet known. Next paragraph deals with a possible approach about how natural products BGC's can be find.

Archaea resembled Bacteria in that Archaea uses horizontal gene transfer as a genic interchange mechanism, Archaeal genomes contains operons [118] and in general there is introns absence{Reference to Computational Methods for Understanding Bacterial and Archaeal Genomes}. Archaeas do have introns, but they are mainly located on

genes that encodes ribosomal and transfer RNA [118]. General lack of introns allows automatic genome annotation, operons gene organization permits functional inference to a certain degree and HGT contribute to expansions on Archaeal genomes. Some phylum on Archaea has an open pangenome, and as we will show on this chapter some Archaea has central pathway expansions. Enzyme families from central pathways expansions, open pangenome and operon organization made EvoMining succesful on Actinobacteria, this lead us to think that evoMining is suitable to analize Archaeal genomes, even more since EvoMining is a method oriented to use evolution and its not entirelyy based on previous knowledge of BGC's sequences if evolutionary logic behave on Archaea as on bacteria, new BGC's classes may be found on Archaea.

EvoMining is a trade off between conserved known central metabolic function and enough expansions divergence on sequence and on clusters to divergence

3.1 Tables

Table 3.1: Families on Archaeabacteria

Factors	Correlation between Parents & Child
GenomeDB	876
Phylum	12
Order	23

First lets investigate if Archaea has expansions on families within central metabolic routes. Since main metabolic pathways are shared between Bacteria and Archaea makes sense to assemble Archeal EvoMining central database by using orthologous from Actinobacteria evoMining central pathways.

3.1.1 Expansions BoxPlot by metabolic family

```
label(path = "chapter3/expansion_plotArchaeas.pdf", caption = "Expansions Boxplot")
```

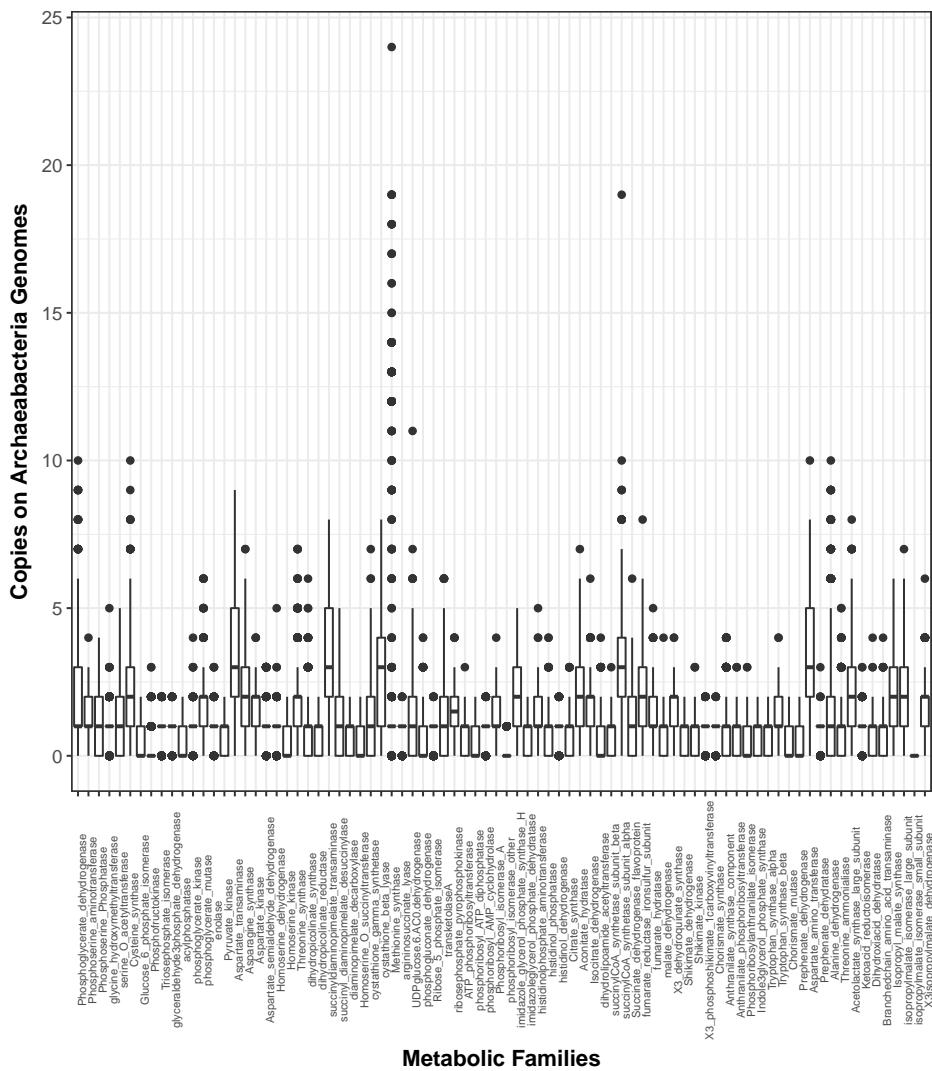


Figure 3.1: Expansions Boxplot

Here is a reference to the expansion boxplot: Figure 3.1.

3.1.2 Expansions BoxPlot by metabolic family by phylum

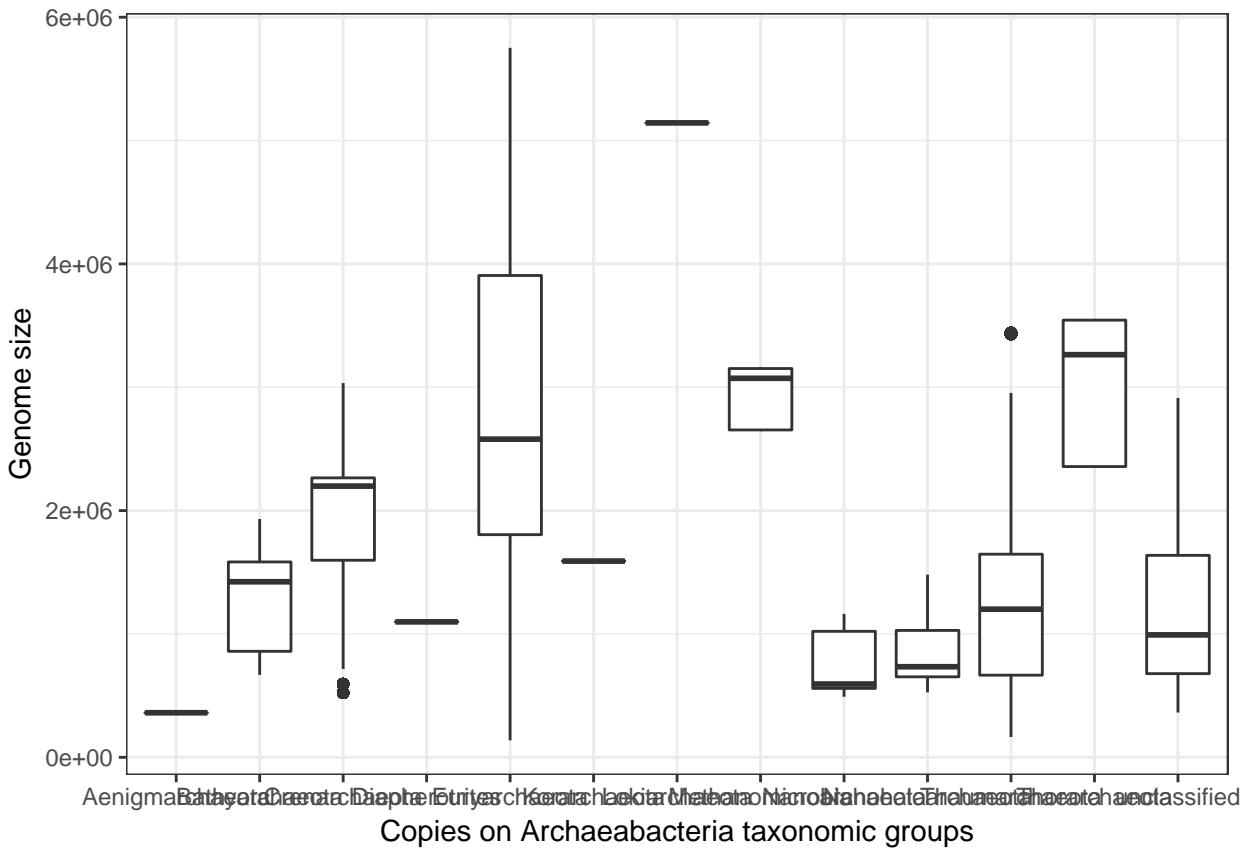
```
#+ geom_jitter()
#aes(fill = factor(vs))

ArchaeasTotalBP.m<-merge(ArchaeasHeatPlot,ArchaeasTaxa,by.x="RastId",by.y="RastId") ## w
ArchaeasHeatPlotBP.m <- melt(ArchaeasTotalBP.m,id =c("RastId","Name","SuperPhylum","Phyl
ArchaeasHeatPlotBP.m<-subset(ArchaeasHeatPlotBP.m,variable!="TOTAL") ## works as expected
ArchaeasHeatPlotBP.m<-subset(ArchaeasHeatPlotBP.m,variable!="TOTAL") ## works as expected

## Each metabolic pathway se parte por phylum coloreado por order

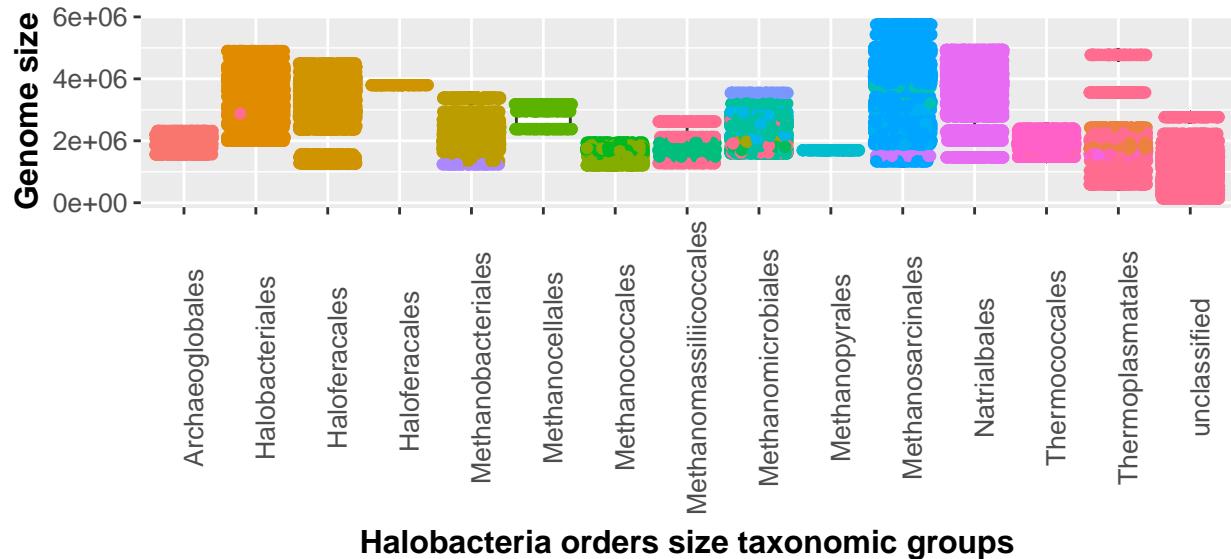
#3PGA_AMINOACIDS
#Glycolysis
#OXALACETATE_AMINOACIDS
#R5P_AMINOACIDS
#TCA
#E4P_AMINO_ACIDS
#PYR_THR_AA

## Genome size
ggplot(ArchaeasHeatPlotBP.m, aes(x=ArchaeasHeatPlotBP.m$Phylum, y=ArchaeasHeatPlotBP.m$S
```



```
#+ geom_jitter(aes(color=ArchaeaHeatPlotBP.m$Phylum))

## Halobacteria
MetFam_BP.m=subset(ArchaeaHeatPlotBP.m, Phylum=="Euryarchaeota")
ggplot(MetFam_BP.m, aes(x=MetFam_BP.m$Order, y=MetFam_BP.m$Size))+ geom_boxplot()
```

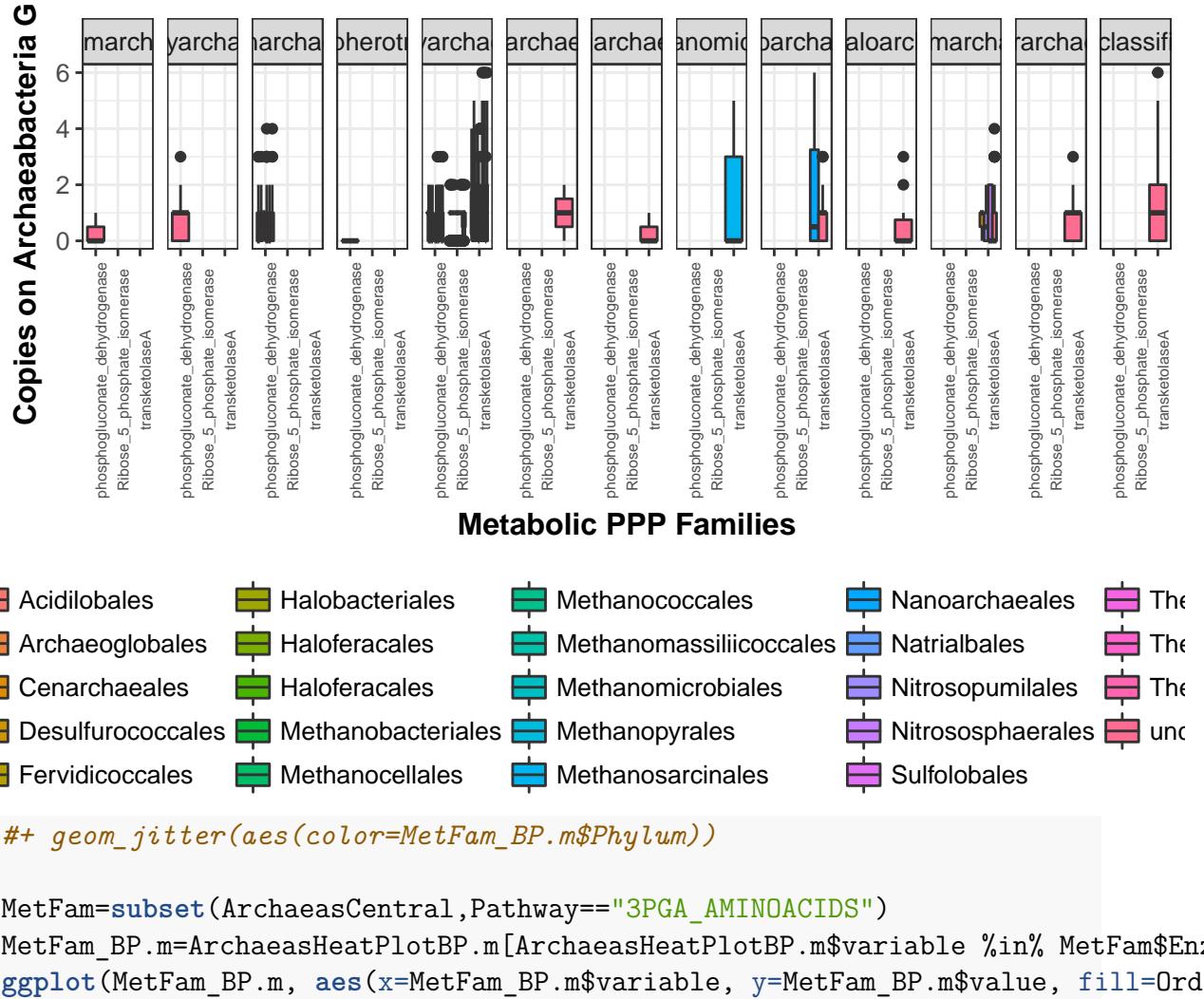


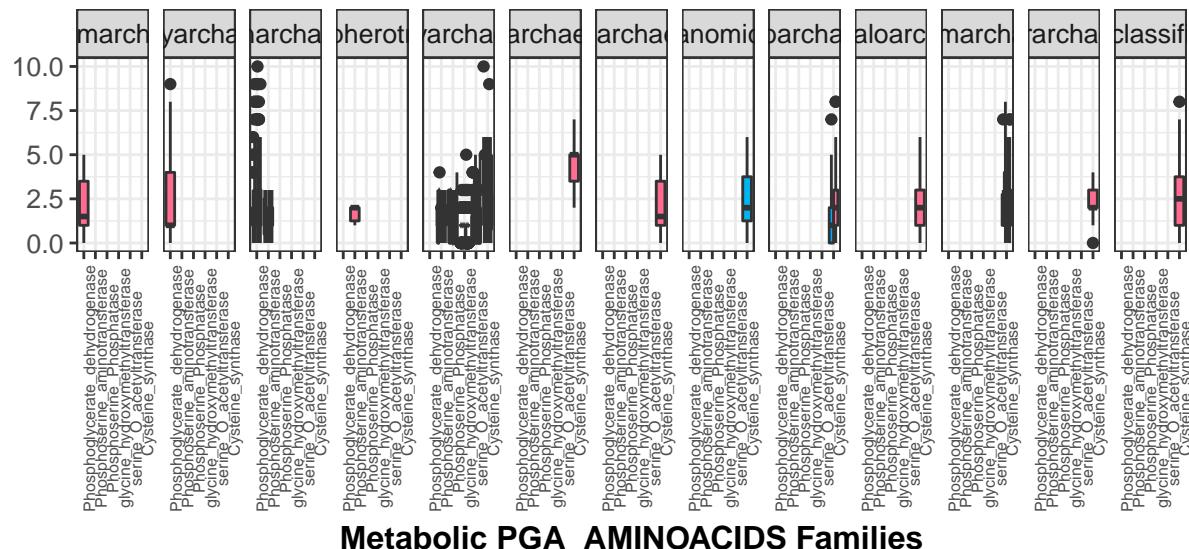
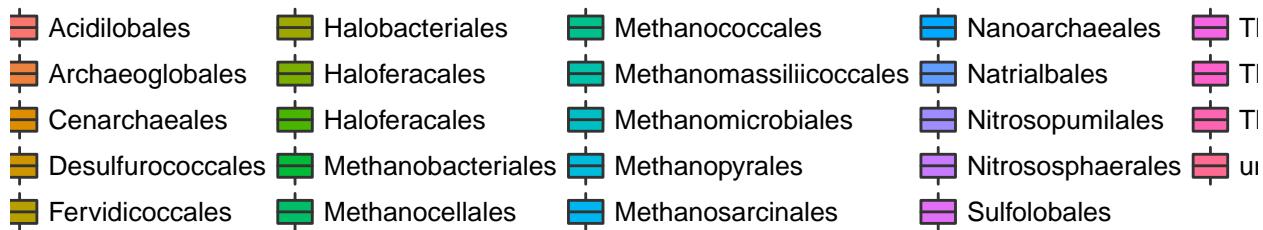
haeoglobaceae	● Methanocalculaceae	● Methanomassiliicoccaceae	● Methanosaetaceae
roplasmaceae	● Methanocaldococcaceae	● Methanomicrobiaceae	● Methanosarcinaceae
obacteriaceae	● Methanocellaceae	● Methanoperedenaceae	● Methanospirillaceae
oferacaceae	● Methanococcaceae	● Methanopyraceae	● Methanothermaceae
thanobacteriaceae	● Methanocorpusculaceae	● Methanoregulaceae	● Methermicoccaceae

```
#MetFam_BP.m=subset(ArchaeaHeatPlotBP.m,Family=="Methanosaetaceae")
#ggplot(MetFam_BP.m, aes(x=MetFam_BP.m$Size, y=MetFam_BP.m$value))
#+theme(plot.title = element_text(size = 14, face = "bold"), text = element_text(size = 12))

#geom_jitter(aes(color=ArchaeaHeatPlotBP.m$Phylum))# + facet_grid(. ~ Phylum)+theme

## Metabolic Pathways
MetFam=subset(ArchaeaCentral,Pathway=="PPP")
MetFam_BP.m=ArchaeaHeatPlotBP.m[ArchaeaHeatPlotBP.m$variable %in% MetFam$Enzyme,]
ggplot(MetFam_BP.m, aes(x=MetFam_BP.m$variable, y=MetFam_BP.m$value, fill=Order))+ labs(x="Metabolic Pathways", y="Number of Enzymes")+
  theme_minimal()+
  scale_fill_brewer(palette="Set1")+
  geom_bar(stat="identity")+
  facet_grid(~ Phylum)+theme
```

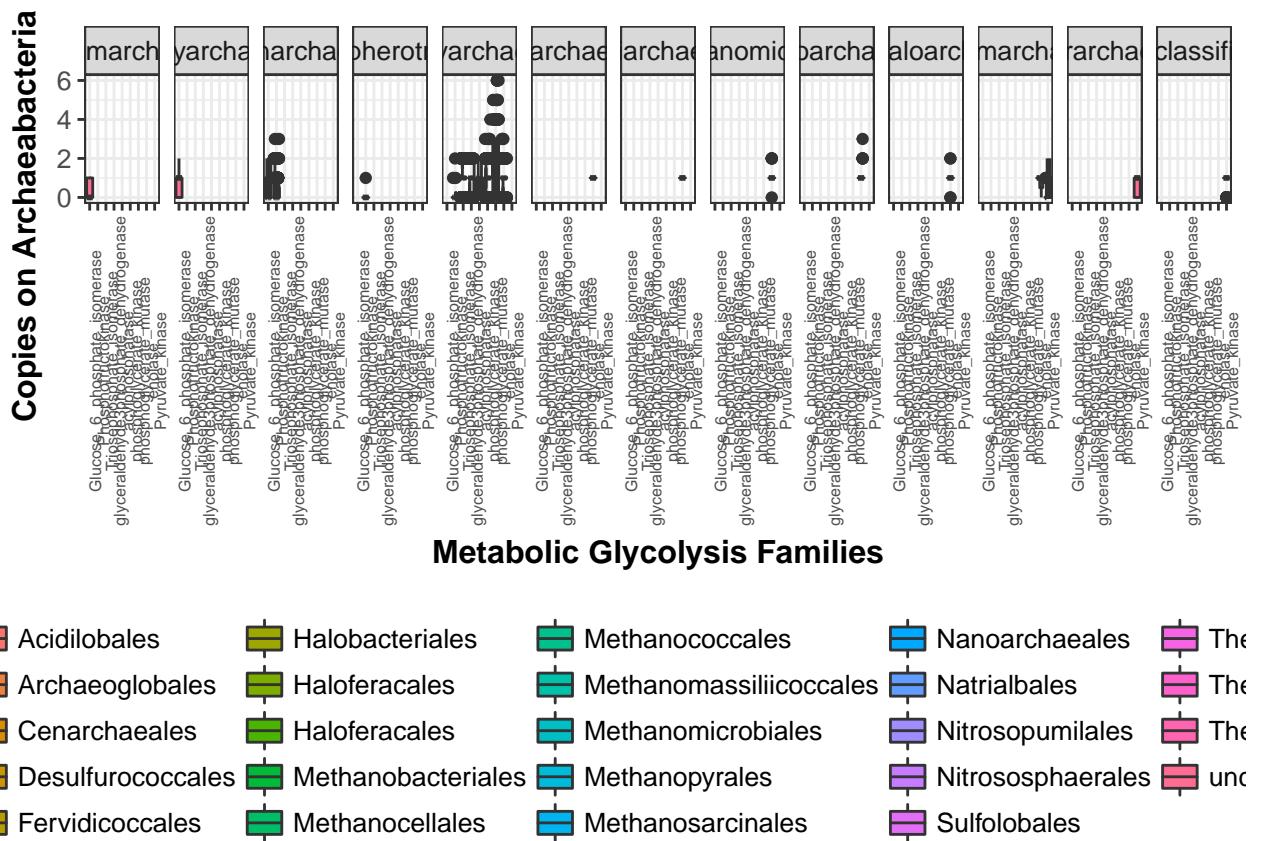


Copies on Archaeabacteria G**Metabolic PGA_AMINOACIDS Families**

```
#+ geom_jitter(aes(color=MetFam_BP.m$Phylum))
```

```
MetFam=subset(ArchaeaCentral,Pathway=="Glycolysis")
```

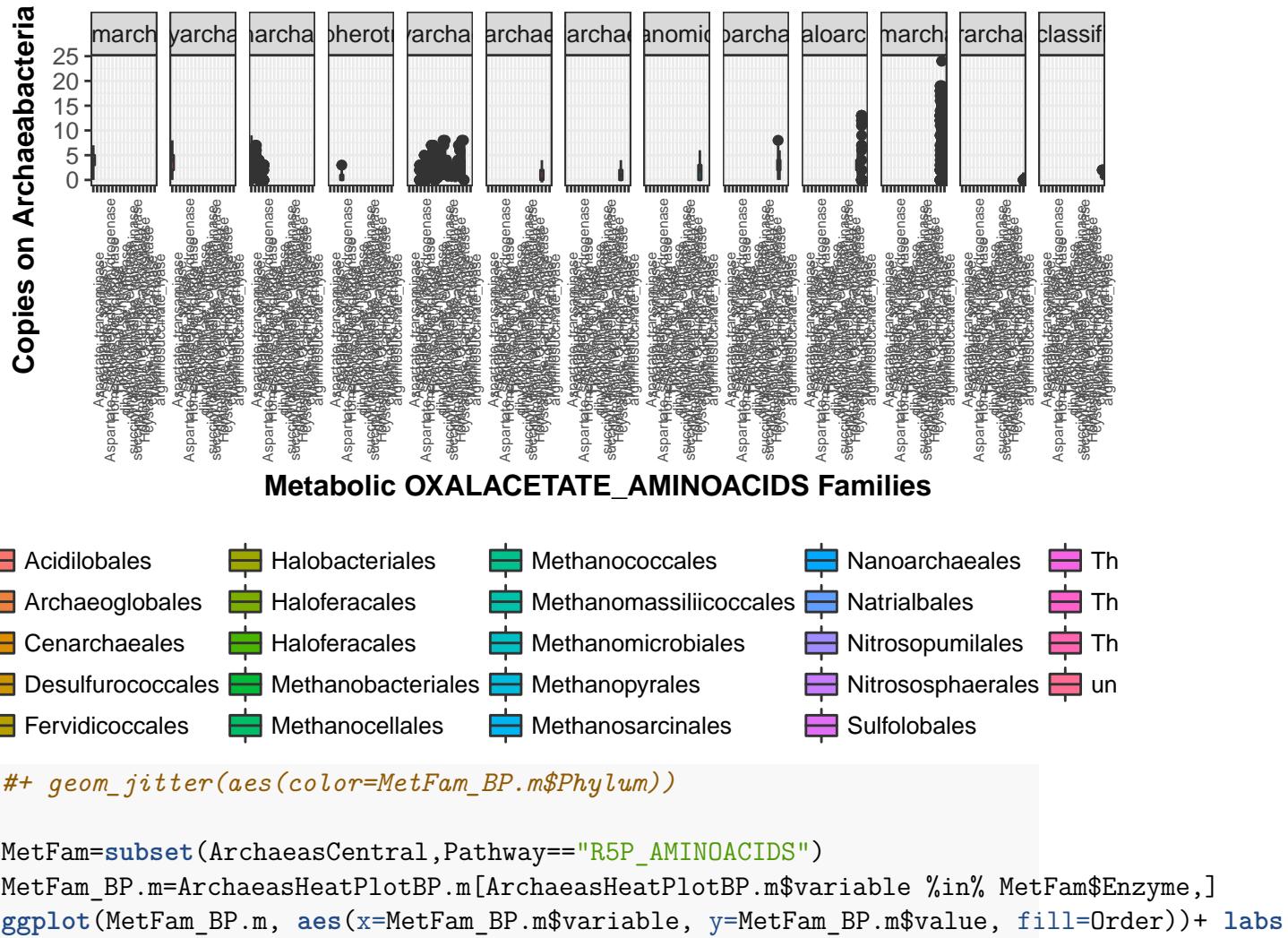
```
MetFam_BP.m=ArchaeaHeatPlotBP.m[ArchaeaHeatPlotBP.m$variable %in% MetFam$Enzyme,]
ggplot(MetFam_BP.m, aes(x=MetFam_BP.m$variable, y=MetFam_BP.m$value, fill=Order))+ labs(
```

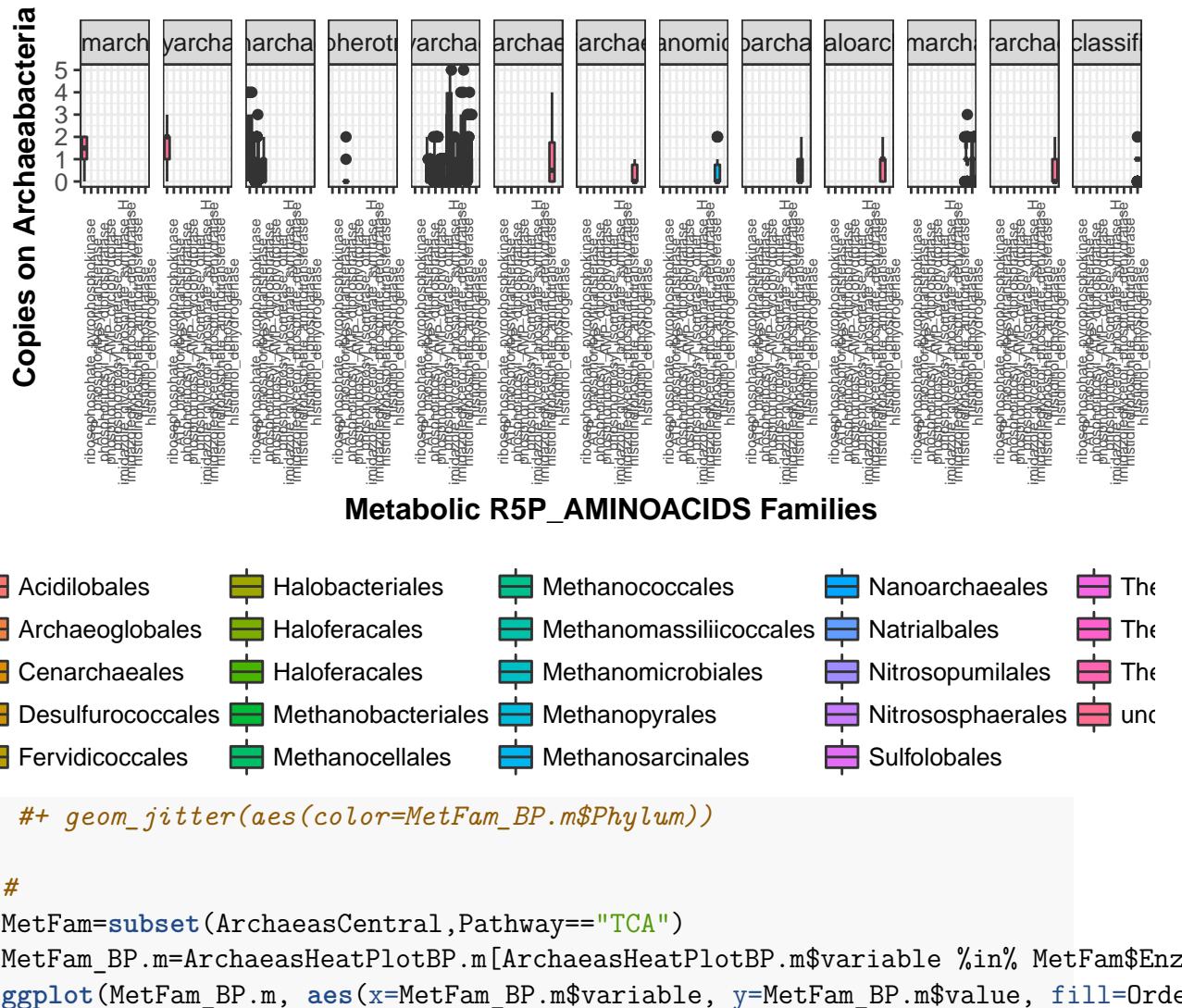


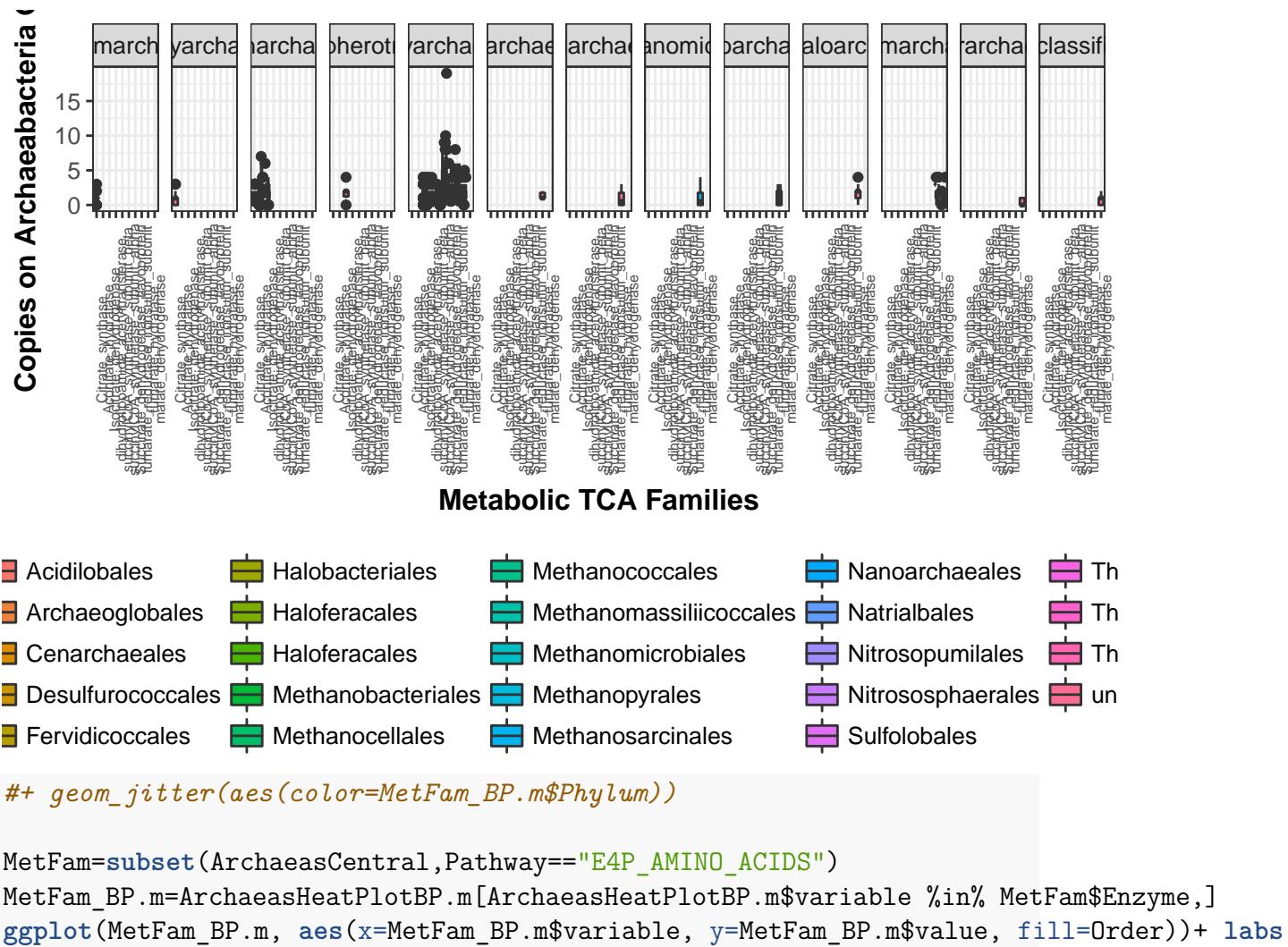
```

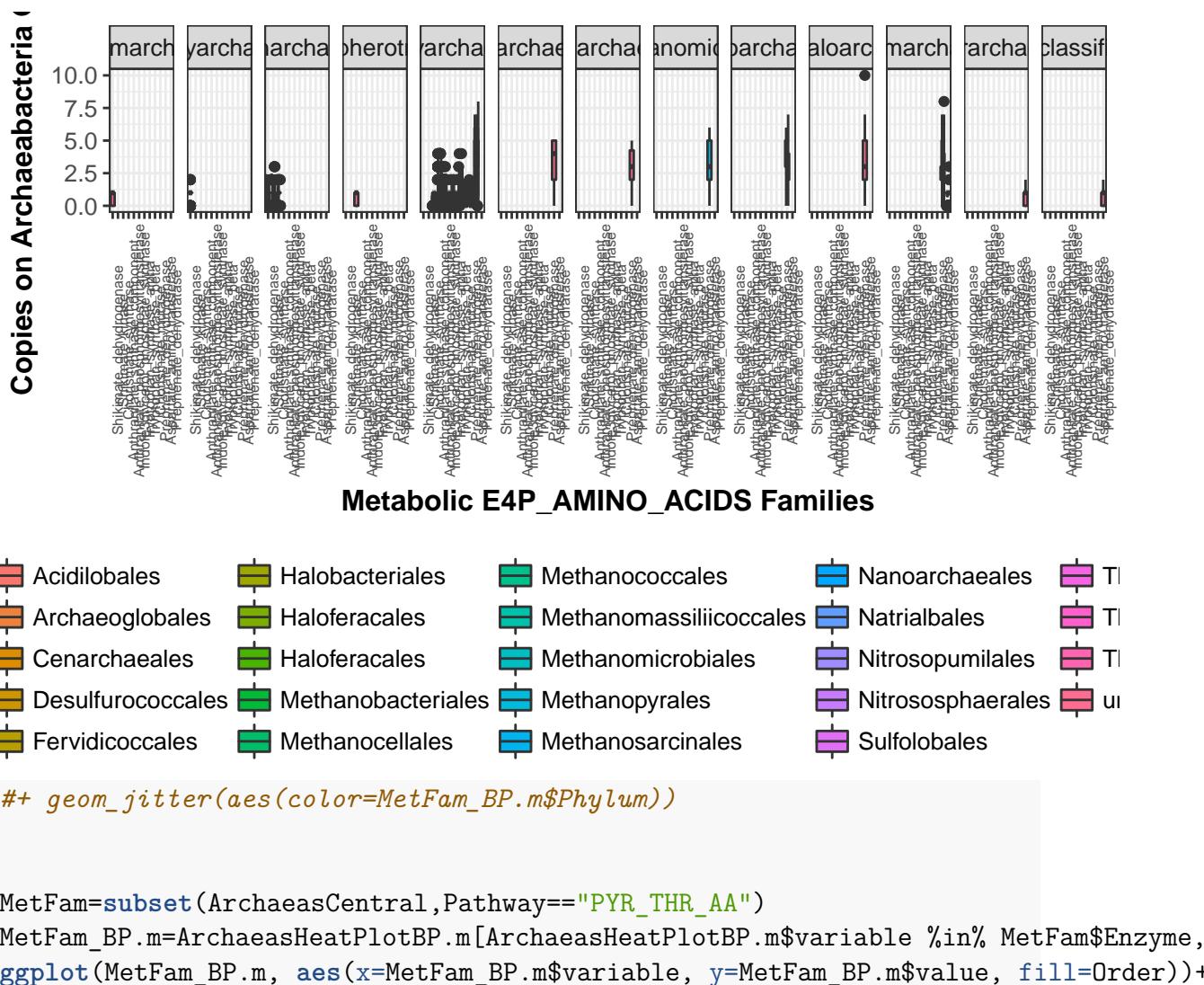
#+ geom_jitter(aes(color=MetFam_BP.m$Phylum))

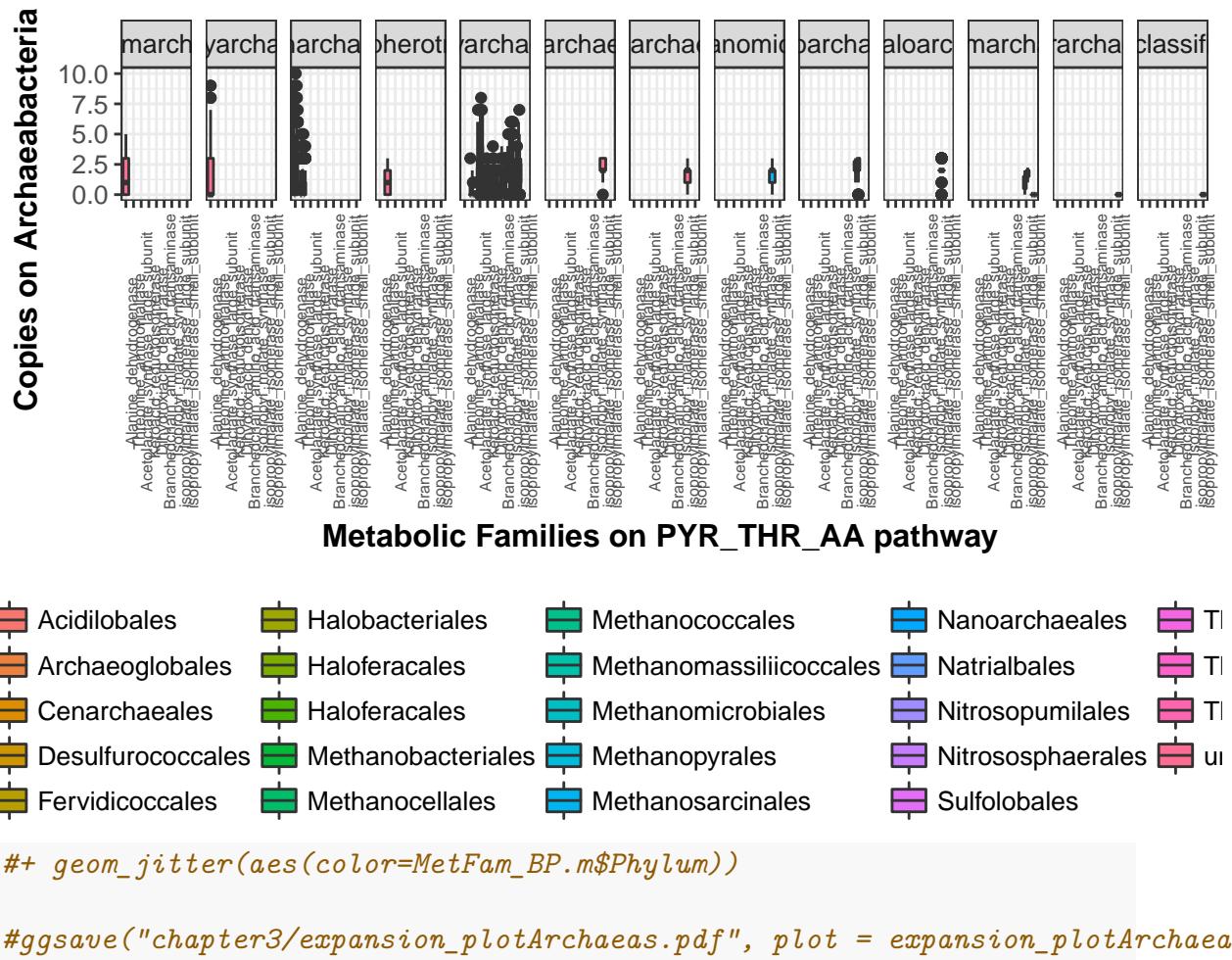
MetFam=subset(ArchaeasCentral,Pathway=="OXALACETATE_AMINOACIDS")
MetFam_BP.m=ArchaeasHeatPlotBP.m[ArchaeasHeatPlotBP.m$variable %in% MetFam$Enzyme,
ggplot(MetFam_BP.m, aes(x=MetFam_BP.m$variable, y=MetFam_BP.m$value, fill=Order))+
```











3.2 Central pathway expansions

Heat plot of central pathways expansions, Needs to be phylogenetically sorted.

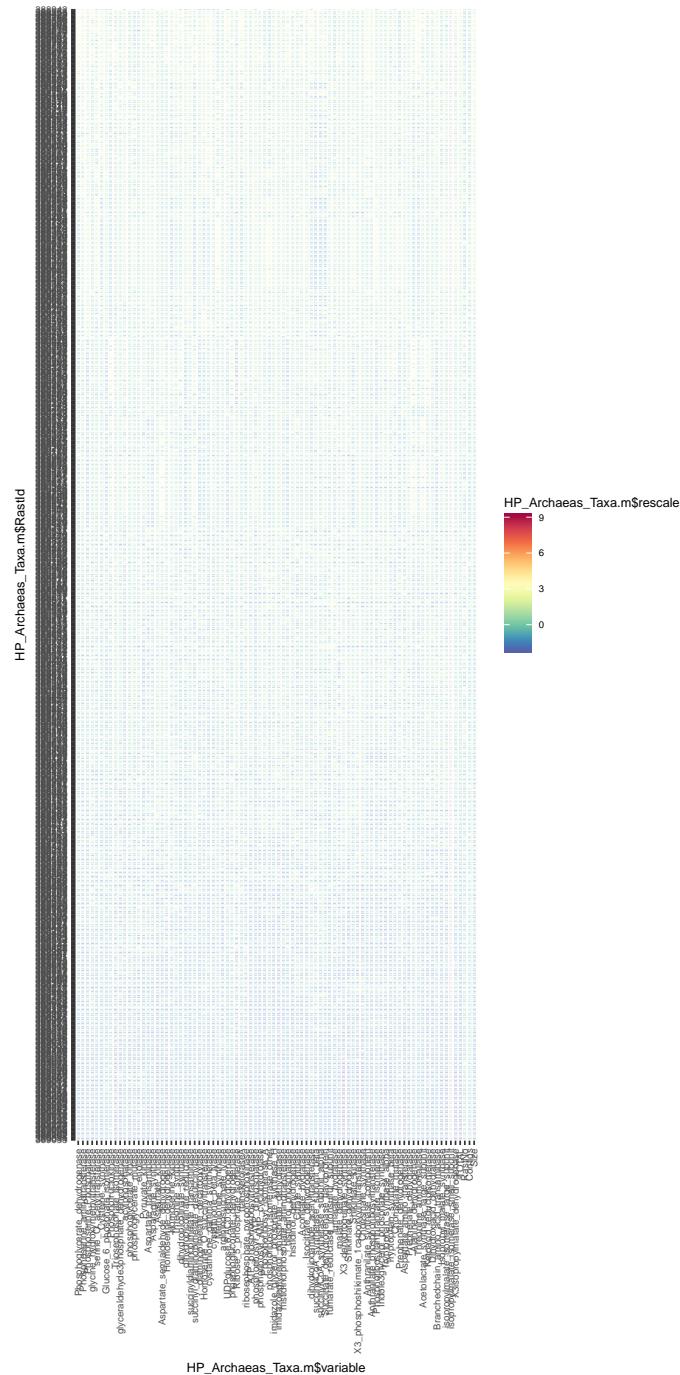


Figure 3.2: Archaea Heatplot

Here is a reference to the HeatPlot: Figure 3.2.

3.3 Genome Size correlations

3.3.1 Correlation between genome size and AntiSMASH products

Genome size vs Total antismash cluster coloured by order

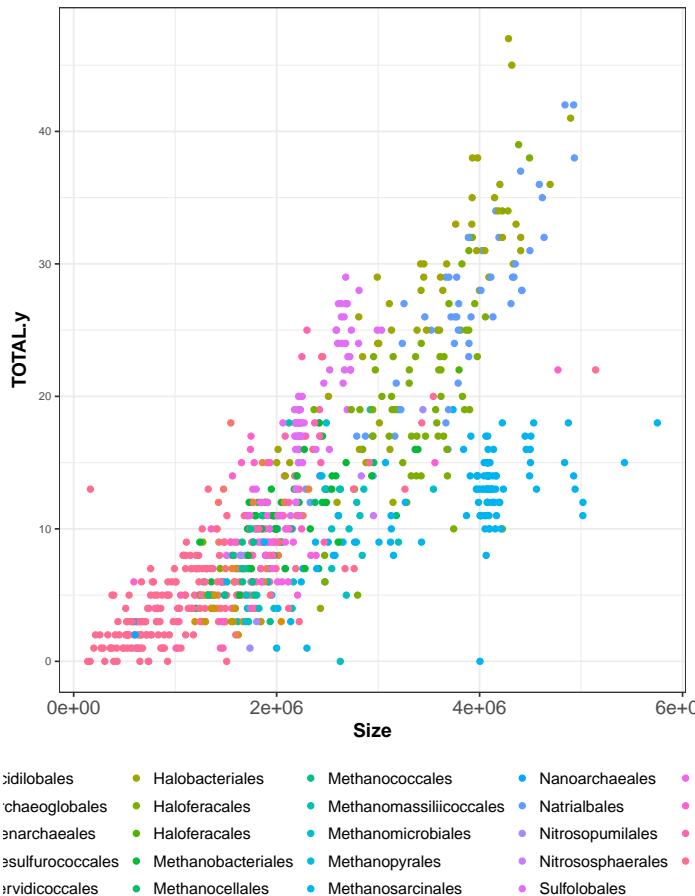


Figure 3.3: Correlation between Archaea genome size and antismash Natural products detection colored by Order

Here is a reference to Genome size vs Total antismash cluster: Figure 3.3.

Genome size vs Total antismash cluster detected splitted by order

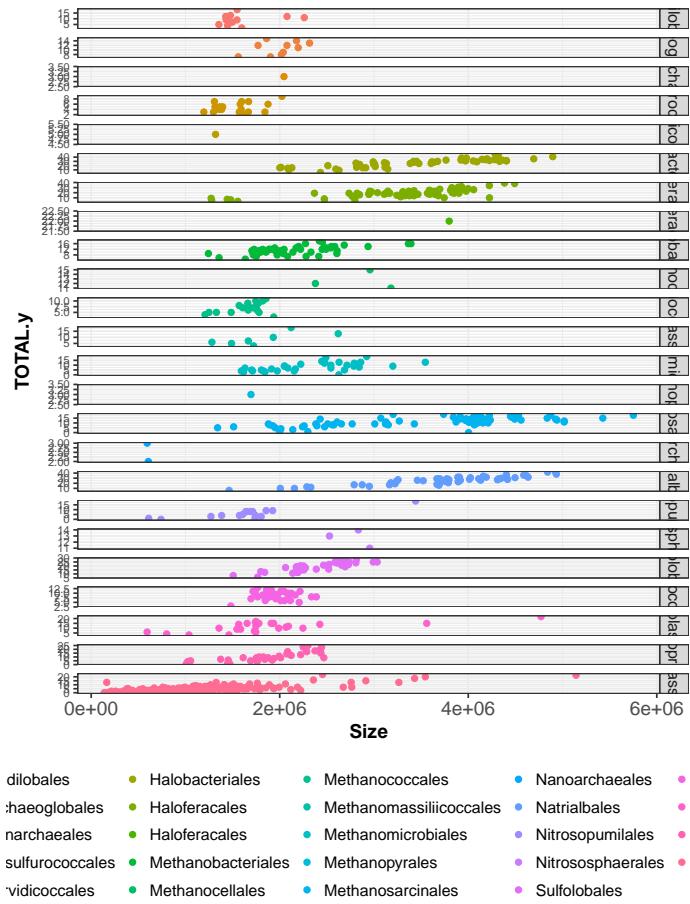


Figure 3.4: Correlation between Archaea genome size and antismash Natural products detection grided by Order

Here is a reference to Correlation between genome size and antismash Natural products detection grided by Order plot: Figure 3.4.

3.3.2 Correlation between genome size and Central pathway expansions

Genome size vs Total central pathway expansion coloured by order

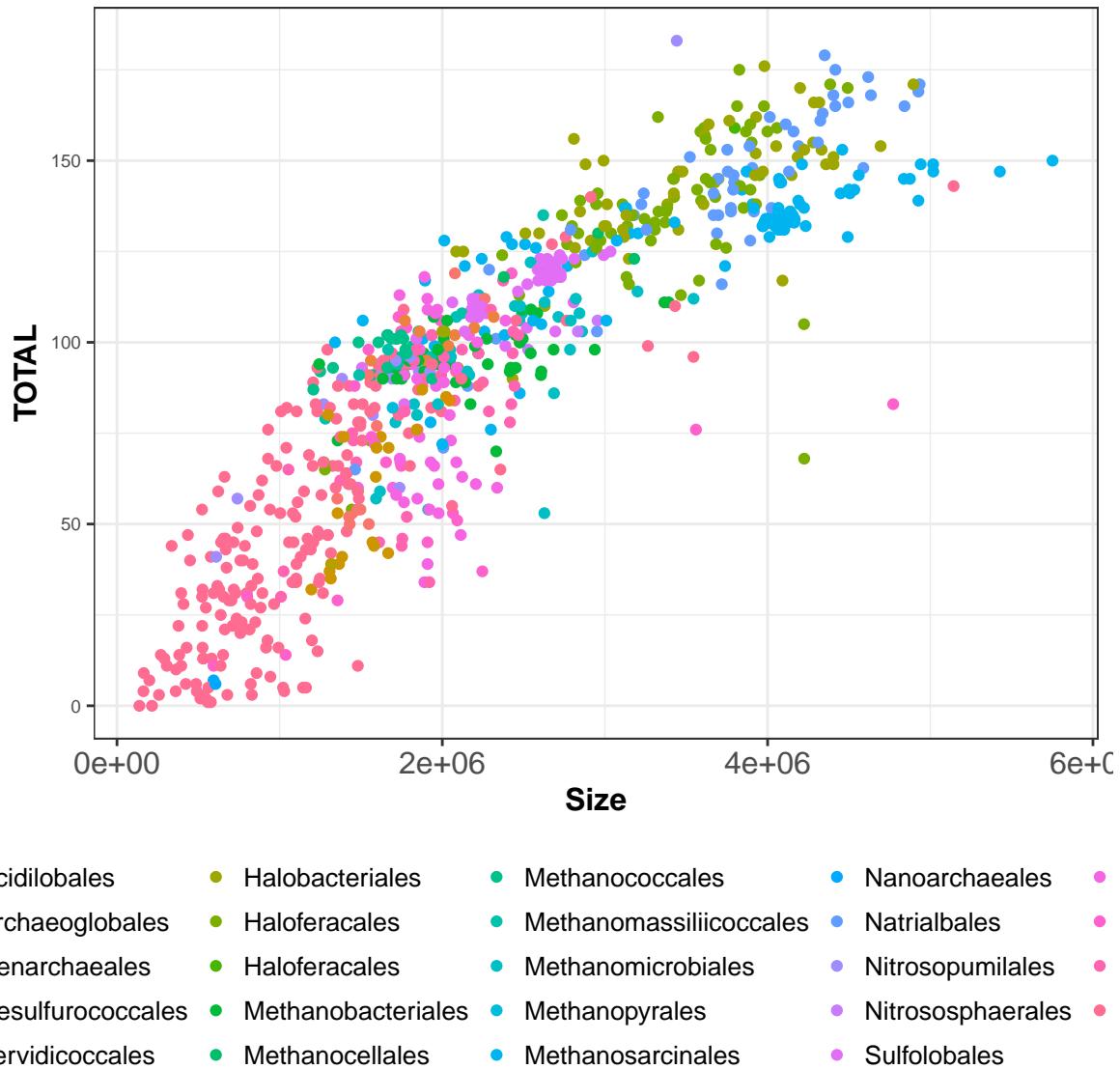


Figure 3.5: Correlation between Archaea genome size and central pathway expansions

Here is a reference to the size vs Total central pathway expansion plot: Figure 3.5.

Genome size vs Total central pathway expansion grided by order

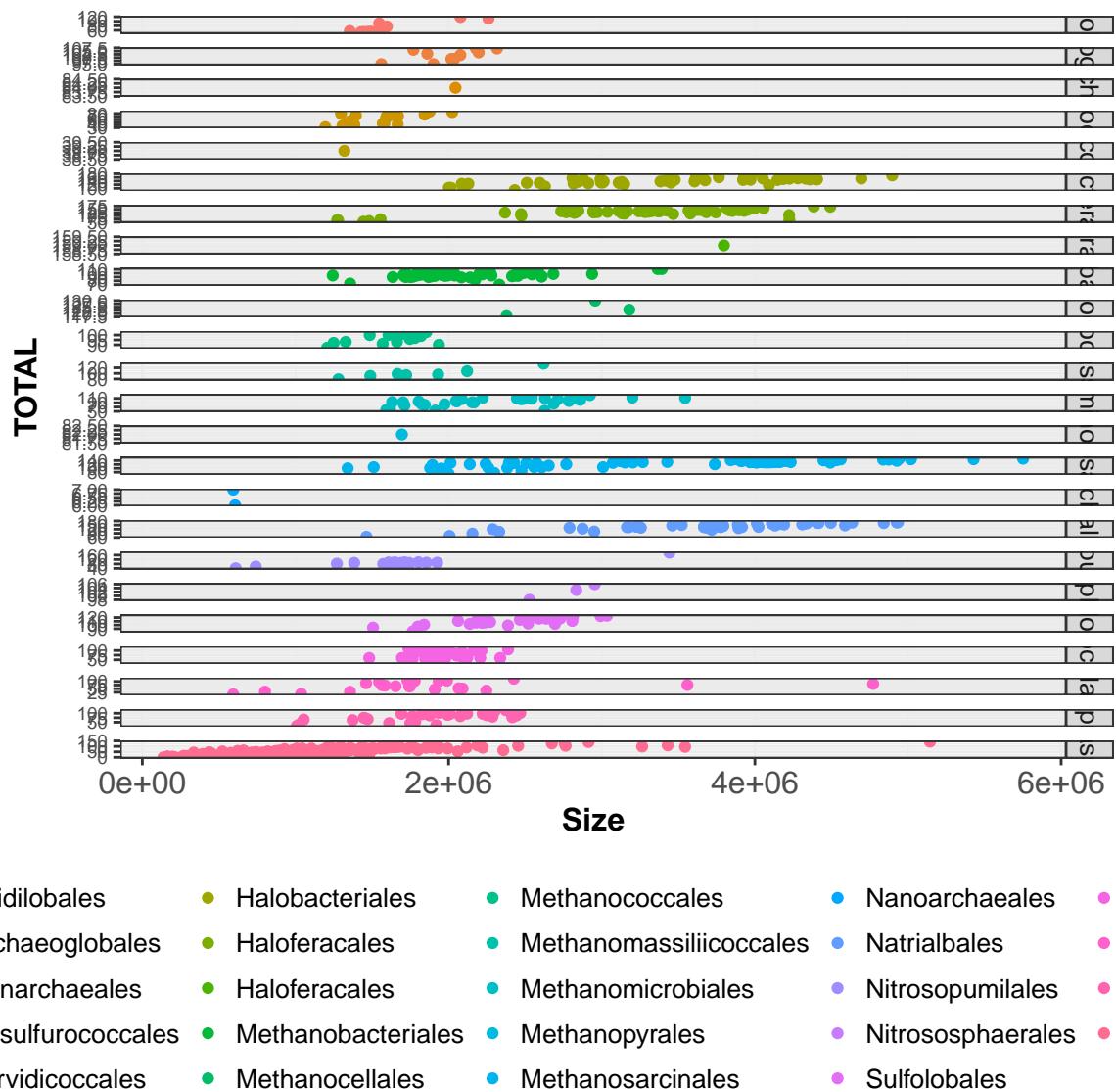


Figure 3.6: Correlation between Archaea genome size and central pathway expansions grided by order

Here is a reference to the Genome size vs Total central pathway expansion grided by order plot: Figure 3.6.

Correlation between genome size and each of the central pathway families. Data are coloured by metabolic family instead of coloured by taxonomical order. This treatment allows to answer how different metabolic families grows when genome size grow. Also I want to add form given by taxonomical order.

Warning: The shape palette can deal with a maximum of 6 discrete values because more than 6 becomes difficult to discriminate; you have
24. Consider specifying shapes manually if you must have them.

Warning: Removed 64823 rows containing missing values (geom_point).

Genome size vs Total central pathway expansion coloured by metabolic Family

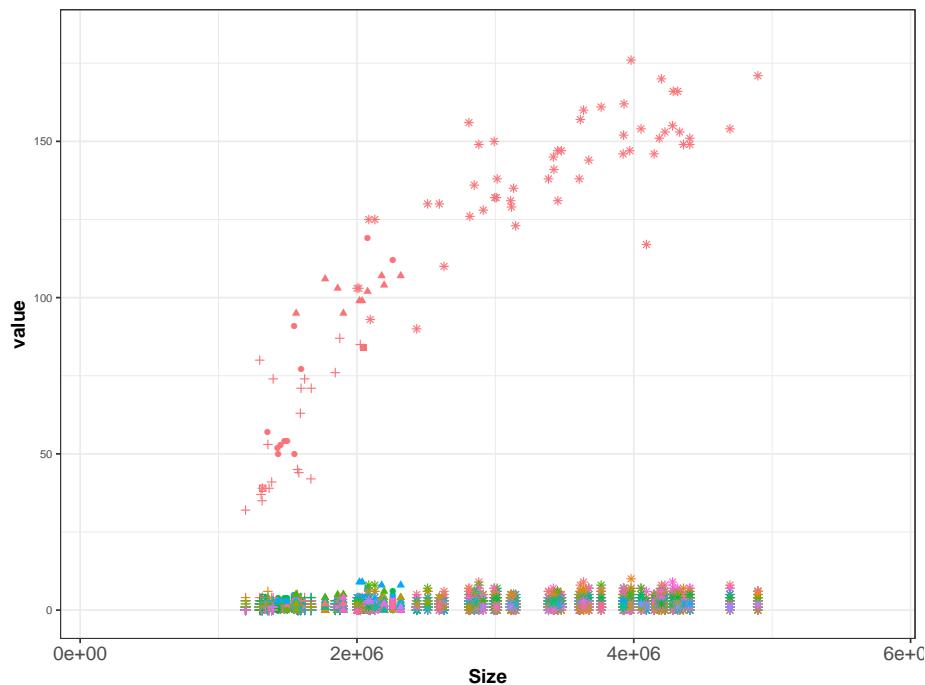


Figure 3.7: Correlation between Archaea's Genome size vs Total central pathway expansion coloured by metabolic Family

Here is a reference to the Genome size vs Total central pathway expansion coloured by metabolic Family plot: Figure 3.7.

Future Work: Genome size vs Total central pathway expansion grided by metabolic Family For clarity I need to also grid and group by Metabolic Pathway

Here is a reference to Genome size vs Total central pathway expansion grided by metabolic Family plot: ??.

3.4 Natural products

3.4.1 Natural products recruitments from EvoMining heat-plot

We can see natural products recruitment after central pathways expansions colored by their kingdom.

Natural products recruited by metabolic family, colored by phylogenetic origin.

Recruitments after central pathways expansions coloured by Kingdom

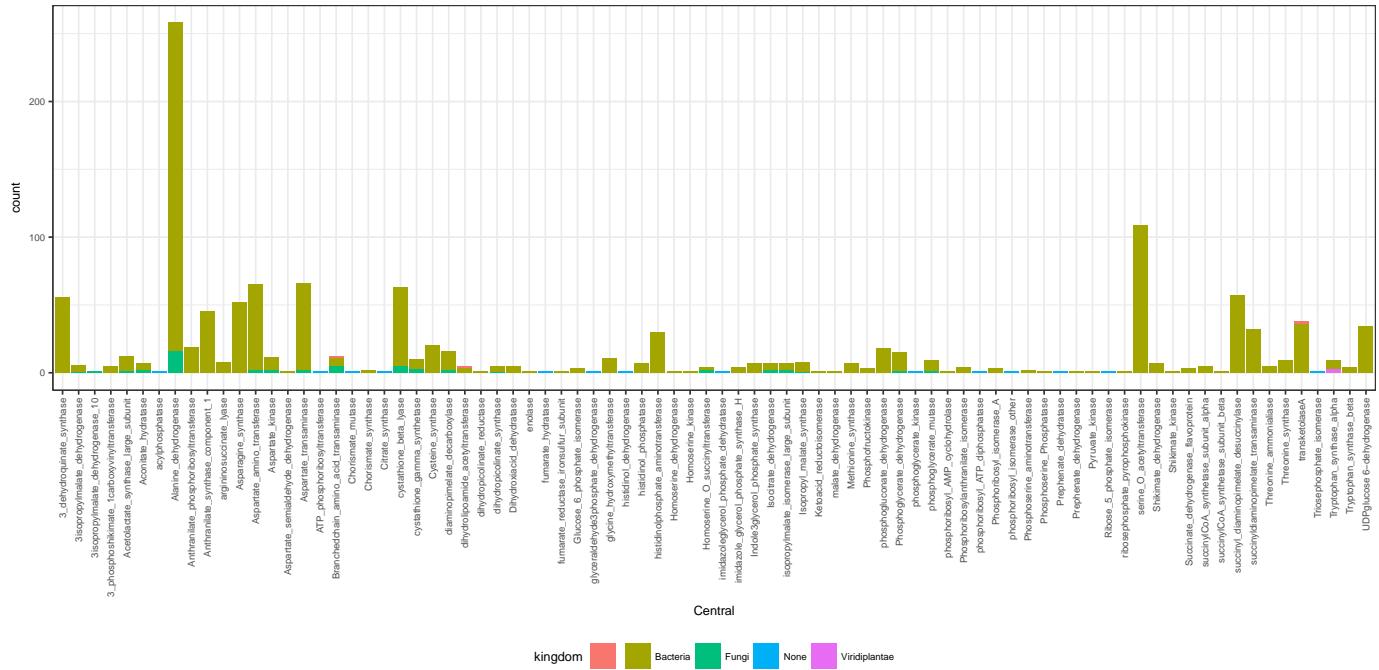


Figure 3.8: Archaeas Recruitmens on central families coloured by kingdom

Here is a reference to Recruitments after central pathways expansions colourd by Kingdom plot: Figure 3.8.

Recruitments after central pathways expansions coloured by taxonomy

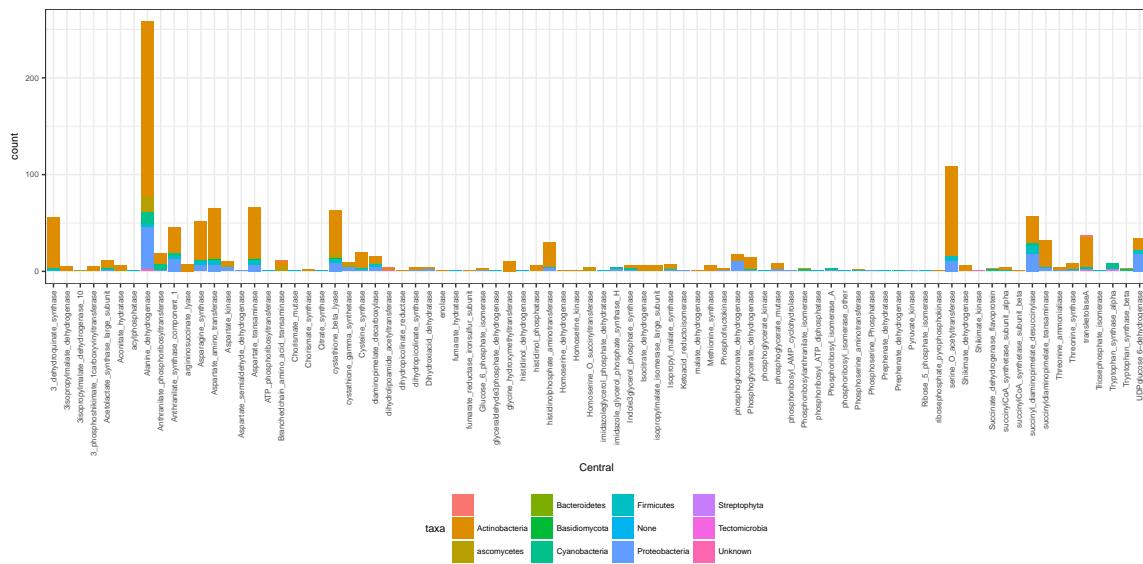


Figure 3.9: Archaeas Recruitmens on central families coloured by taxonomy

Here is a reference to Recruitments after central pathways expansions coloured by taxa plot: Figure 3.9.

3.5 Archaeas AntiSMASH

Taxonomical diversity on Archaeasbacteria Data

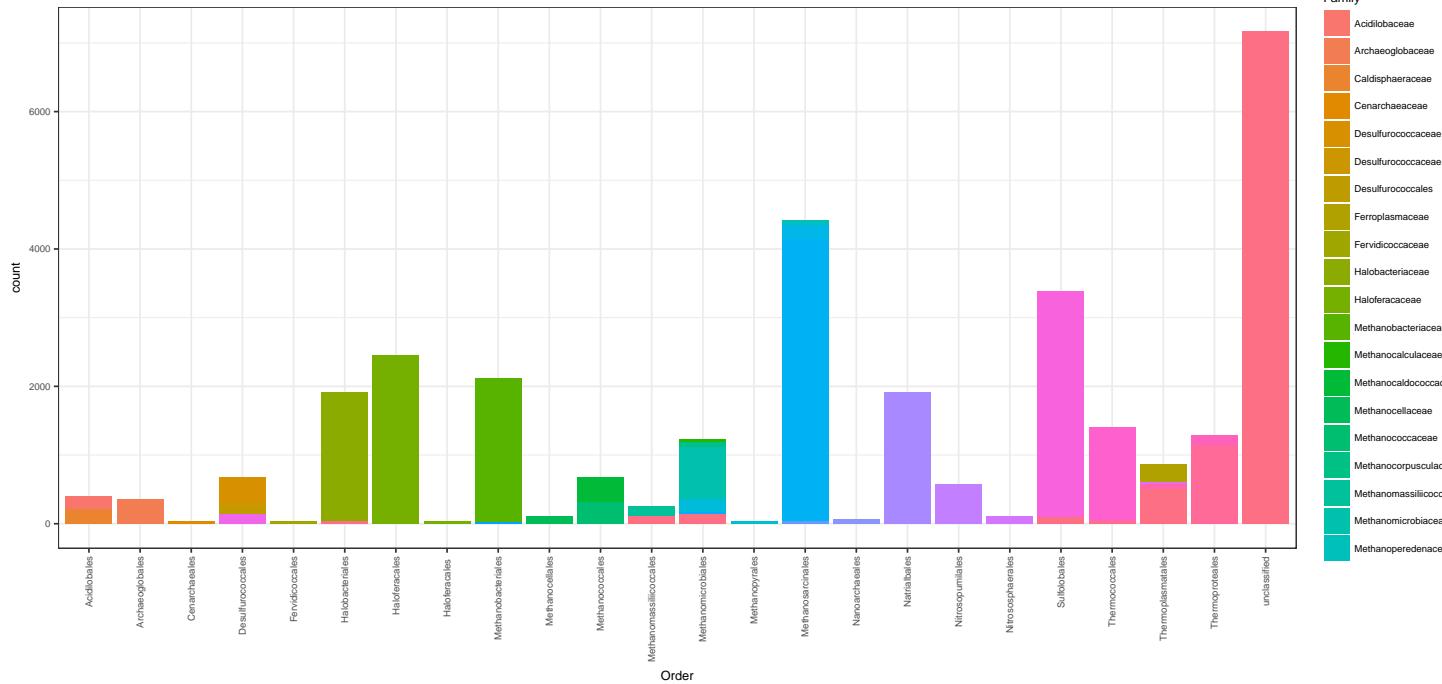


Figure 3.10: Archaea Diversity

Here is a reference to Recruitments after central pathways expansions coloured by taxa plot: Figure 3.10.

Smash diversity

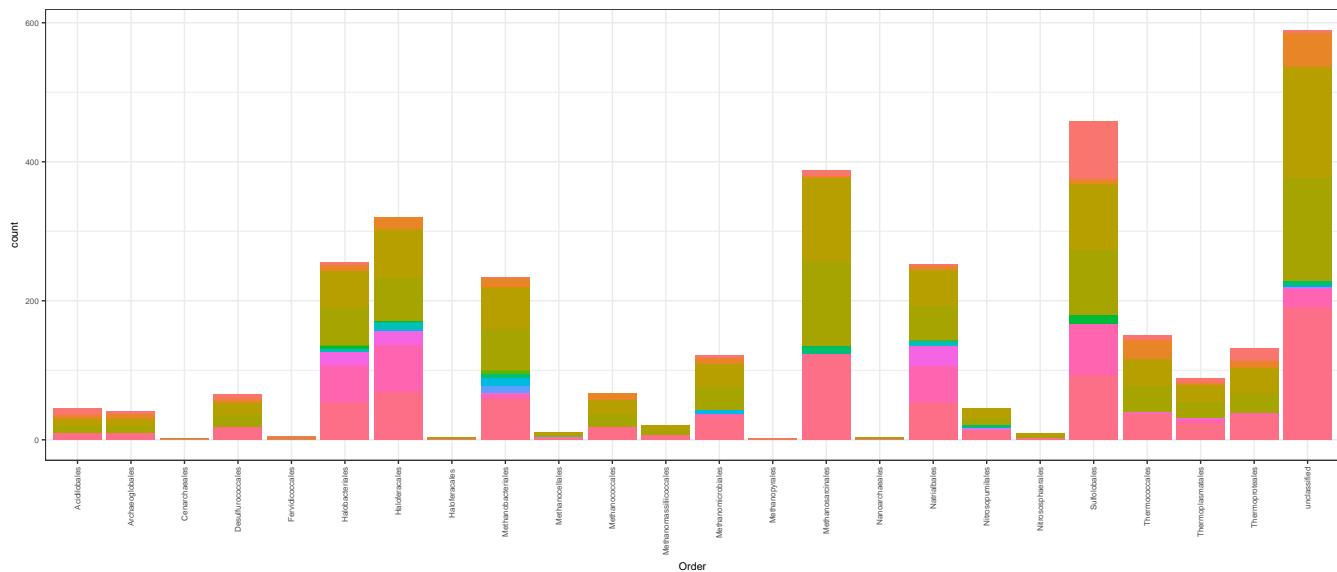


Figure 3.11: Archaeas Smash Taxonomical Diversity

Here is a reference to Recruits after central pathways expansions coloured by taxa plot: Figure 3.11.

3.5.1 AntisMASH vs Central Expansions

Is it a correlation between pangenome grow and central pathways expansions?

Total central pathway expansions by genome vs Total antismash cluster detected coloured by order

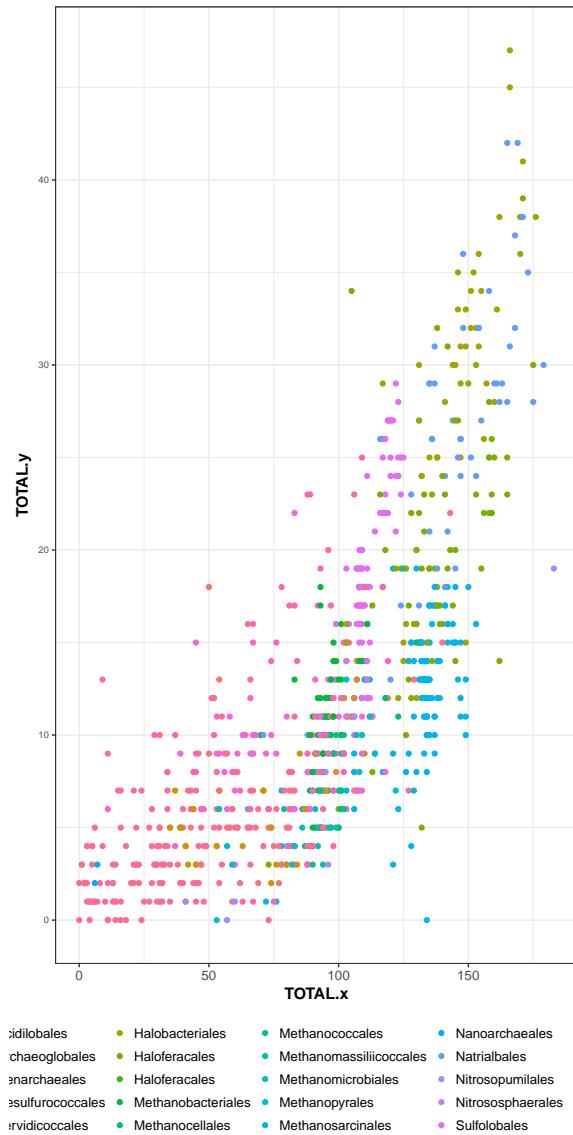


Figure 3.12: Correlation between Archaea's central pathway expansions and antismash Natural products detection

Here is a reference to the expansions vs antismash NP's clusters plot: Figure 3.12.

Total central pathway expansions by genome vs Total antismash cluster detected splitted by order

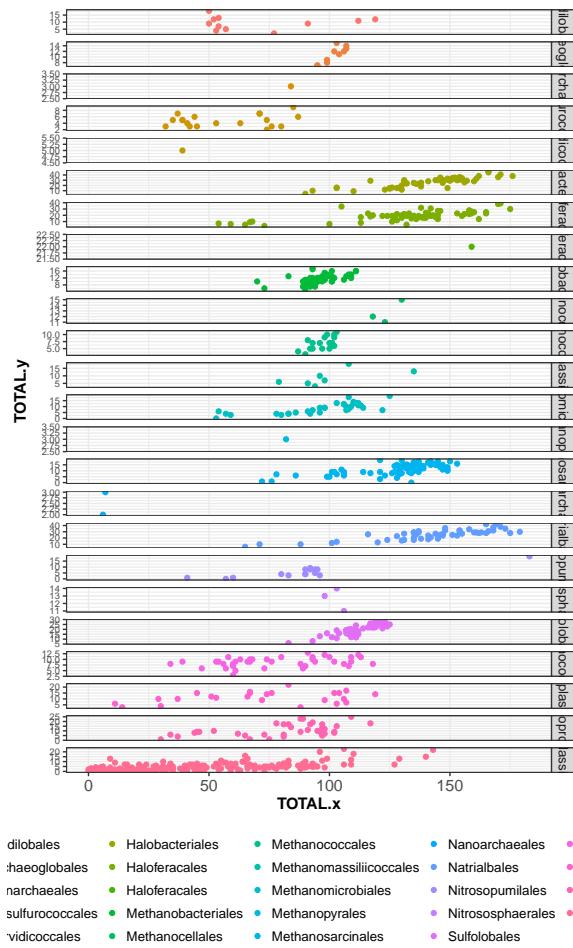


Figure 3.13: Correlation between Archaeas central pathway expansions and antismash NP's clusters splitted by order

Here is a reference to the expansions vs antismash NP's clusters splitted by order plot Figure 3.13.

AntisMAsh vs Expansions by taxonomic Family

Natural products colored by family

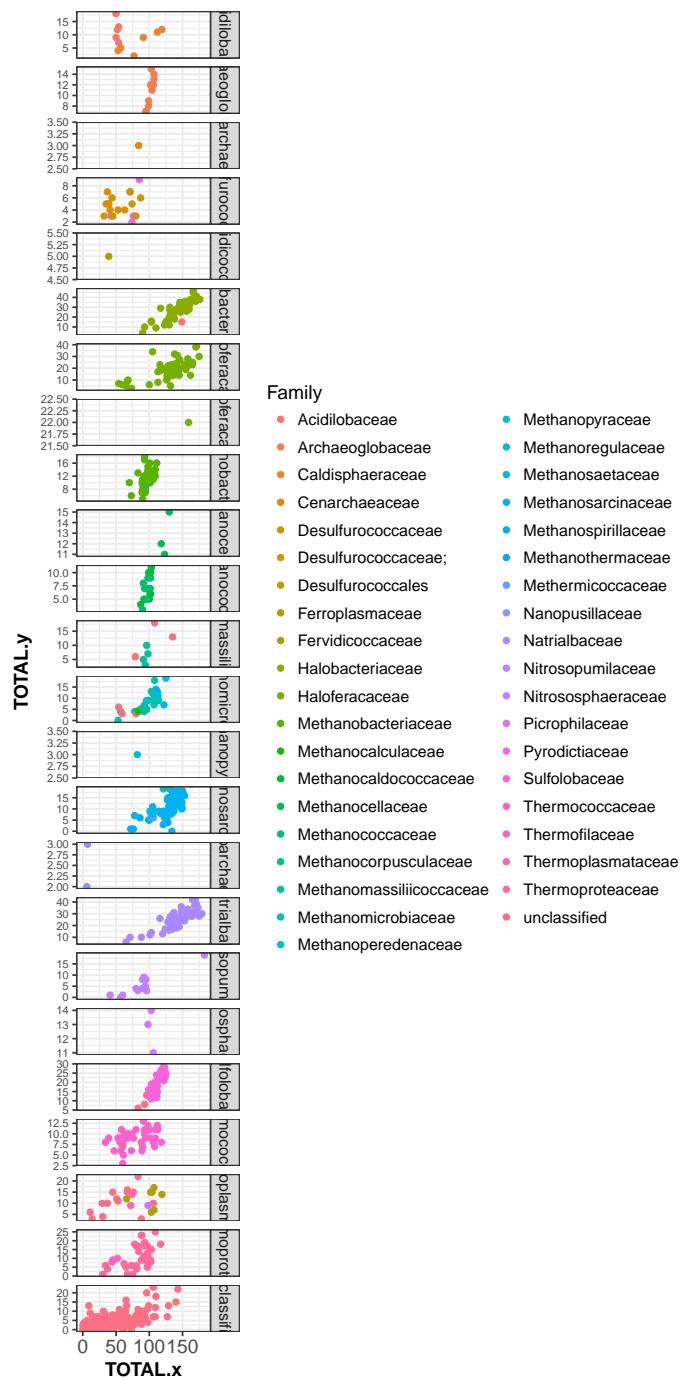


Figure 3.14: Archaeas Natural products by family

Here is a reference to the Natural products colored by family plot Figure 3.14.

3.6 Selected trees from EvoMining

Phosphoribosyl_isomerase_3 family

Figure from EvoMining

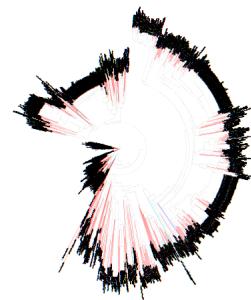


Figure 3.15: Phosphoribosyl isomerase A EvoMiningtree

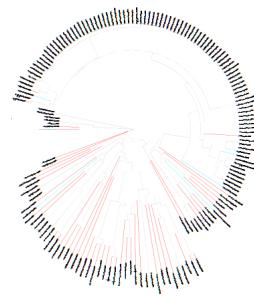


Figure 3.16: Phosphoribosyl isomerase other EvoMiningtree

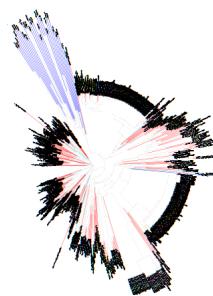


Figure 3.17: Phosphoribosyl anthranilate isomerase EvoMiningtree

3.7

Other possible databases Archaeal signatures *set of protein-encoding genes that function uniquely within the Archaea; most signature proteins have no recognizable bacterial or eukaryal homologs* [117] ## Footnotes and Endnotes

You might want to footnote something.¹ The footnote will be in a smaller font and placed appropriately. Endnotes work in much the same way. More information can be found about both on the CUS site or feel free to reach out to `data@reed.edu`.

3.8 Bibliographies

Of course you will need to cite things, and you will probably accumulate an armful of sources. There are a variety of tools available for creating a bibliography database (stored with the .bib extension). In addition to BibTeX suggested below, you may want to consider using the free and easy-to-use tool called Zotero. The Reed librarians have created Zotero documentation at <http://libguides.reed.edu/citation/zotero>. In addition, a tutorial is available from Middlebury College at <http://sites.middlebury.edu/zoteromiddlebury/>.

R Markdown uses *pandoc* (<http://pandoc.org/>) to build its bibliographies. One nice caveat of this is that you won't have to do a second compile to load in references as standard L^AT_EX requires. To cite references in your thesis (after creating your bibliography database), place the reference name inside square brackets and precede it by the "at" symbol. For example, here's a reference to a book about worrying: [140]. This Molina1994 entry appears in a file called `thesis.bib` in the `bib` folder. This bibliography database file was created by a program called BibTeX. You can call this file something else if you like (look at the YAML header in the main .Rmd file) and, by default, is to placed in the `bib` folder.

For more information about BibTeX and bibliographies, see our CUS site (<http://web.reed.edu/cis/help/latex/index.html>)². There are three pages on this topic: *bibtex* (which talks about using BibTeX, at <http://web.reed.edu/cis/help/latex/bibtex.html>), *bibtexstyles* (about how to find and use the bibliography style that best suits your needs, at <http://web.reed.edu/cis/help/latex/bibtexstyles.html>) and *bibman* (which covers how to make and maintain a bibliography by hand, without BibTeX, at <http://web.reed.edu/cis/help/latex/bibman.html>). The last page will not be useful unless you have only a few sources.

If you look at the YAML header at the top of the main .Rmd file you can see that we can specify the style of the bibliography by referencing the appropriate csl file. You

¹footnote text

²[141]

can download a variety of different style files at <https://www.zotero.org/styles>. Make sure to download the file into the csl folder.

Tips for Bibliographies

- Like with thesis formatting, the sooner you start compiling your bibliography for something as large as thesis, the better. Typing in source after source is mind-numbing enough; do you really want to do it for hours on end in late April? Think of it as procrastination.
- The cite key (a citation’s label) needs to be unique from the other entries.
- When you have more than one author or editor, you need to separate each author’s name by the word “and” e.g. Author = {Noble, Sam and Youngberg, Jessica},.
- Bibliographies made using BibTeX (whether manually or using a manager) accept L^AT_EX markup, so you can italicize and add symbols as necessary.
- To force capitalization in an article title or where all lowercase is generally used, bracket the capital letter in curly braces.
- You can add a Reed Thesis citation³ option. The best way to do this is to use the phdthesis type of citation, and use the optional “type” field to enter “Reed thesis” or “Undergraduate thesis.”

3.9 Anything else?

If you’d like to see examples of other things in this template, please contact the Data @ Reed team (email data@reed.edu) with your suggestions. We love to see people using *R Markdown* for their theses, and are happy to help.

³[142]

Chapter 4

Actinobacteria EvoMining Results

Actinobacteria is an ancient phylum {Referencia de luis}

4.1 Tables

Table 4.1: Correlation of Inheritance Factors for Parents and Child

Factors	Correlation between Parents & Child
GenomeDB	1245
Families	65

4.1.1 Expansions BoxPlot by metabolic family

```
label(path = "chapter4/expansion_plotActinos.pdf", caption = "Expansions Boxplot", label
```

Here is a reference to the expansion boxplot: Figure 4.1.

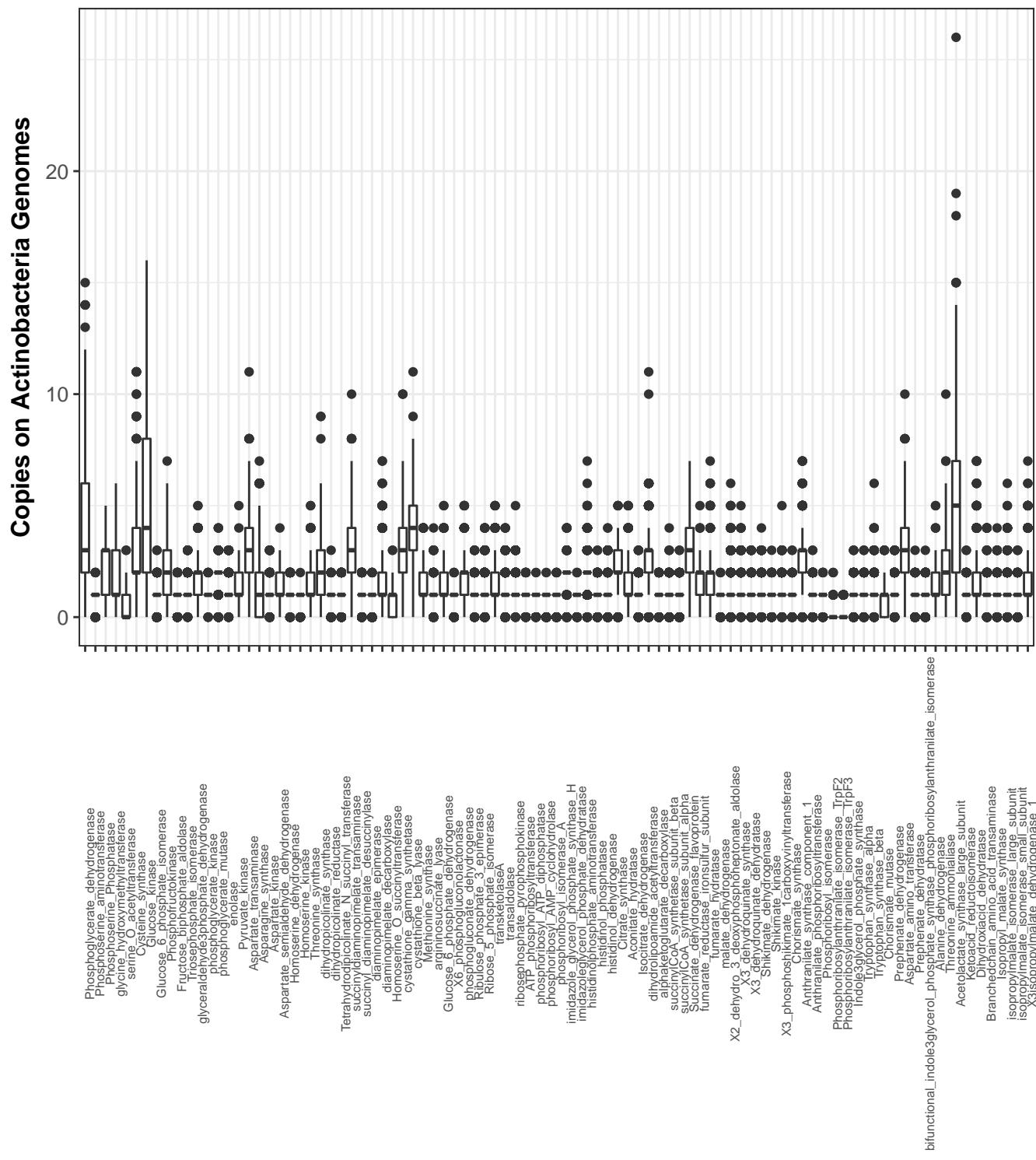
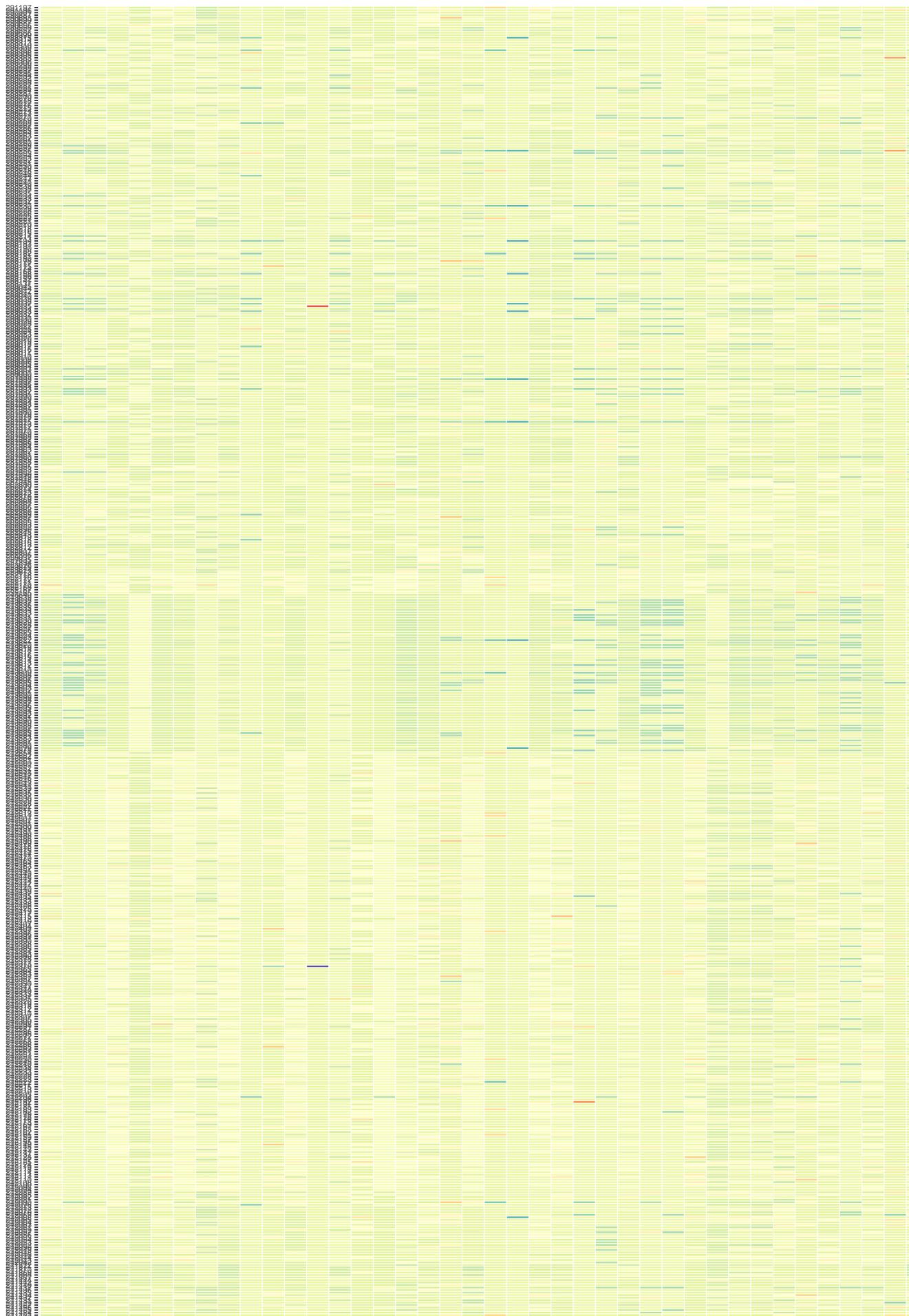


Figure 4.1: Expansions Boxplot

4.2 Central pathway expansions

Heat plot of central pathways expansions, Needs to be phylogenetically sorted.

Here is a reference to the HeatPlot: Figure 4.2.



PPP pahtway expansions restricted to *Streptomycetaceae* family HeatPlot: Figure 4.2.

Here is a reference to the HeatPlot: Figure 4.3.

288310		
288306		
288302		
288308		
288289		
288280		
288278		
288277		
288268		
288267		
288266		
288261		
288254		
288233		
288211		
288218		
288215		
288188		
288178		
288162		
288032		
288019		
288012		
287996		
287981		
287979		
287965		
287955		
287953		
287950		
287948		
282855		
252178		
252176		
252172		
252171		
252170		
252168		
252167		
252165		
242654		
242652		
242564		
242561		
242560		
242557		
242552		
242551		
242548		
242547		
242546		
242545		
242543		
242541		
242539		
242537		
242535		
242532		
242530		
242529		
242528		
242522		
242521		
242515		
242513		
242511		
242507		
242502		
242501		
242500		
242499		
242491		
242490		
242488		
242486		
242480		
242479		
242478		
242476		
242475		
242474		
242471		
242470		
242465		
242464		
242463		
242452		
242451		
242449		
242448		
242445		
242444		
242442		
242441		
242440		
242438		
242437		
242435		
242434		
242433		
242428		
242426		
242425		
242419		
242417		
242415		
242412		
242410		
242407		
242404		
242402		
242397		
242396		
242393		
242391		
242390		
242388		
242386		
242385		
242384		
242383		
242380		
242378		
242377		
242373		
242370		
242365		
242364		
242363		
242357		
242352		
242351		
242350		
242347		
242344		
242340		
242333		
242331		
242325		
242320		
242319		
242318		
242312		
242311		
242310		
242307		
242305		
242300		
242298		
242291		
242287		
242286		
242285		
242272		
242271		
242268		
242266		
242265		
242263		
242261		
242253		
242251		
242250		
242245		
242240		

4.3 Genome Size correlations

4.3.1 Correlation between genome size and AntiSMASH products

Warning: Removed 1 rows containing missing values (geom_point).

Warning: Removed 1 rows containing missing values (geom_point).

Genome size vs Total antismash cluster coloured by order

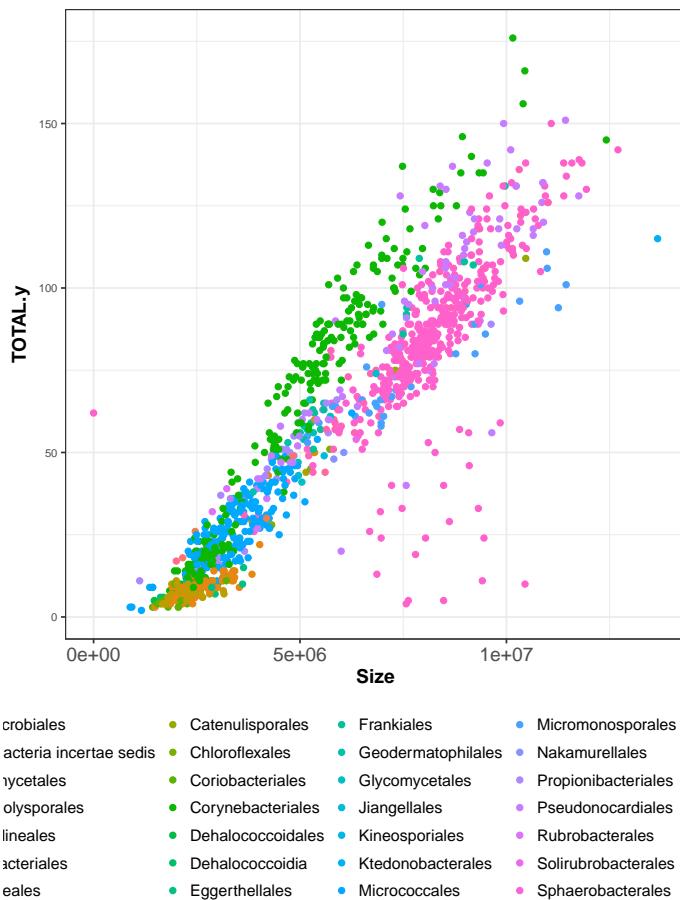


Figure 4.4: Correlation between Actinos genome size and antismash Natural products detection colored by Order

Here is a reference to Genome size vs Total antismash cluster: Figure 4.4.

Genome size vs Total antismash cluster detected splitted by order

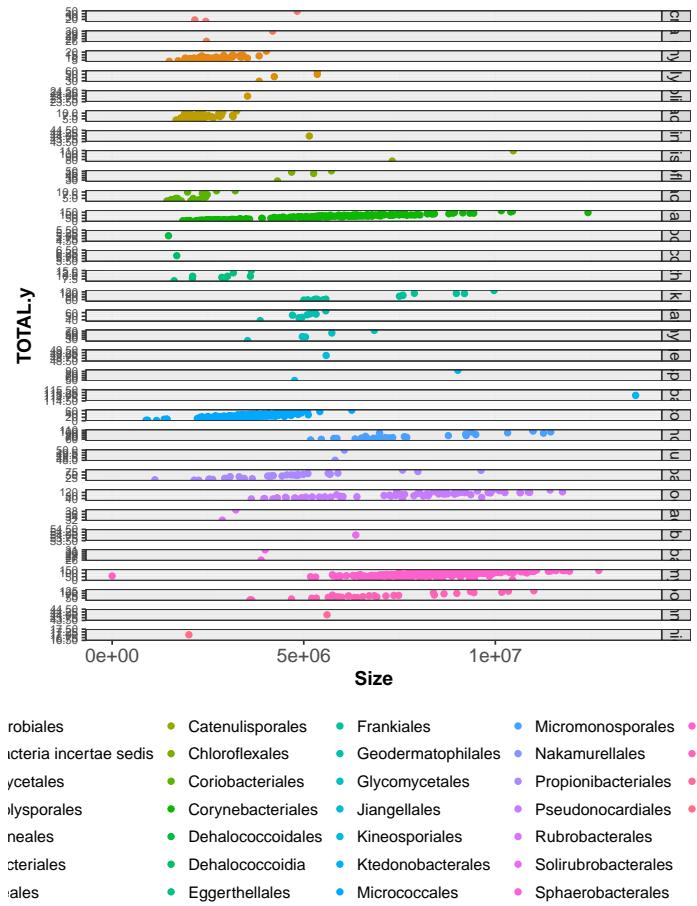


Figure 4.5: Correlation between Actinos genome size and antismash Natural products detection grided by Order

Here is a reference to Correlation between genome size and antismash Natural products detection grided by Order plot: Figure 4.5.

4.3.2 Correlation between genome size and Central pathway expansions

Warning: Removed 1 rows containing missing values (geom_point).

Warning: Removed 1 rows containing missing values (geom_point).

Genome size vs Total central pathway expansion coloured by order

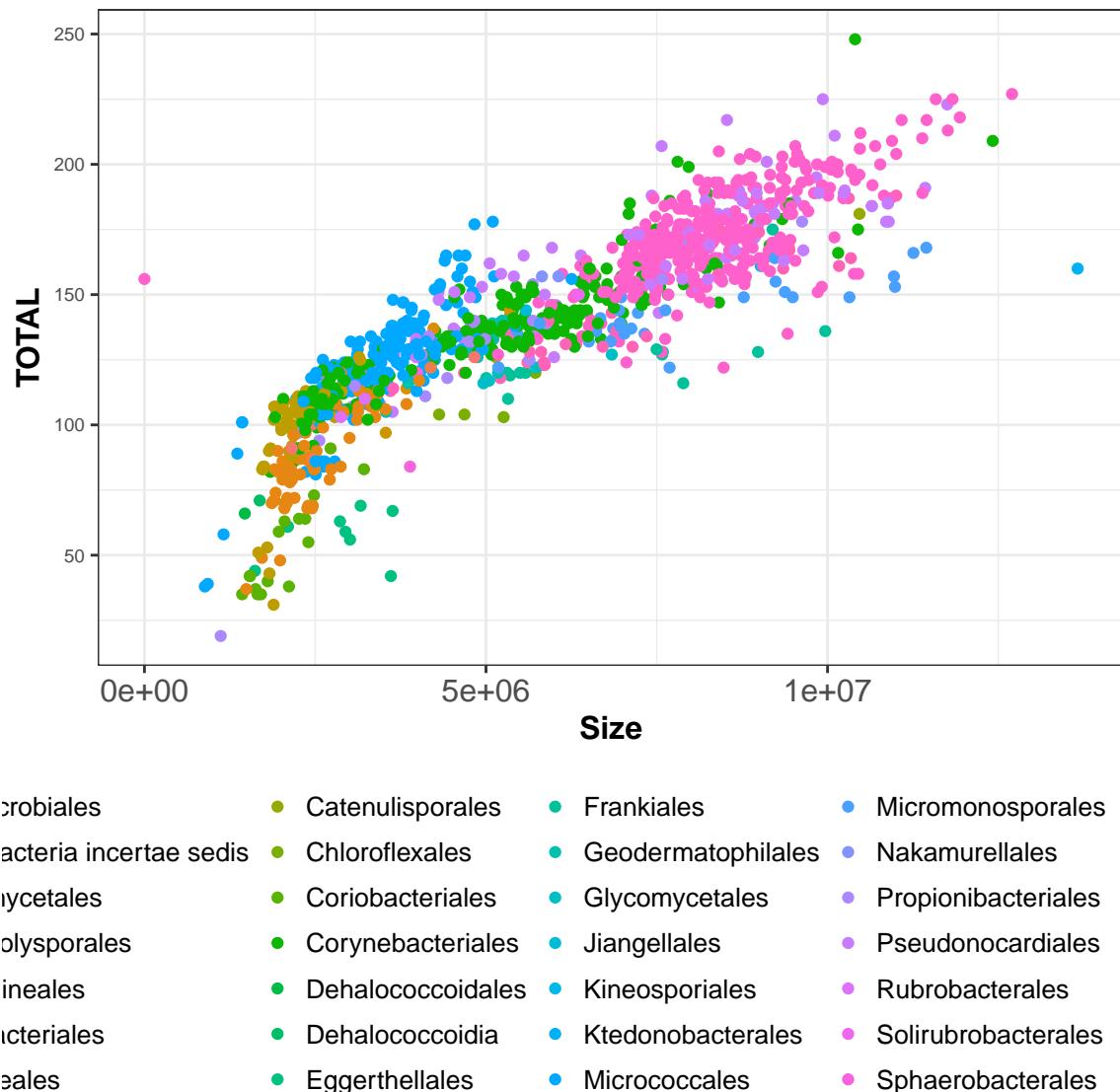


Figure 4.6: Correlation between Actinos genome size and central pathway expansions

Here is a reference to the size vs Total central pathway expansion plot: Figure 4.6.

Genome size vs Total central pathway expansion grided by order

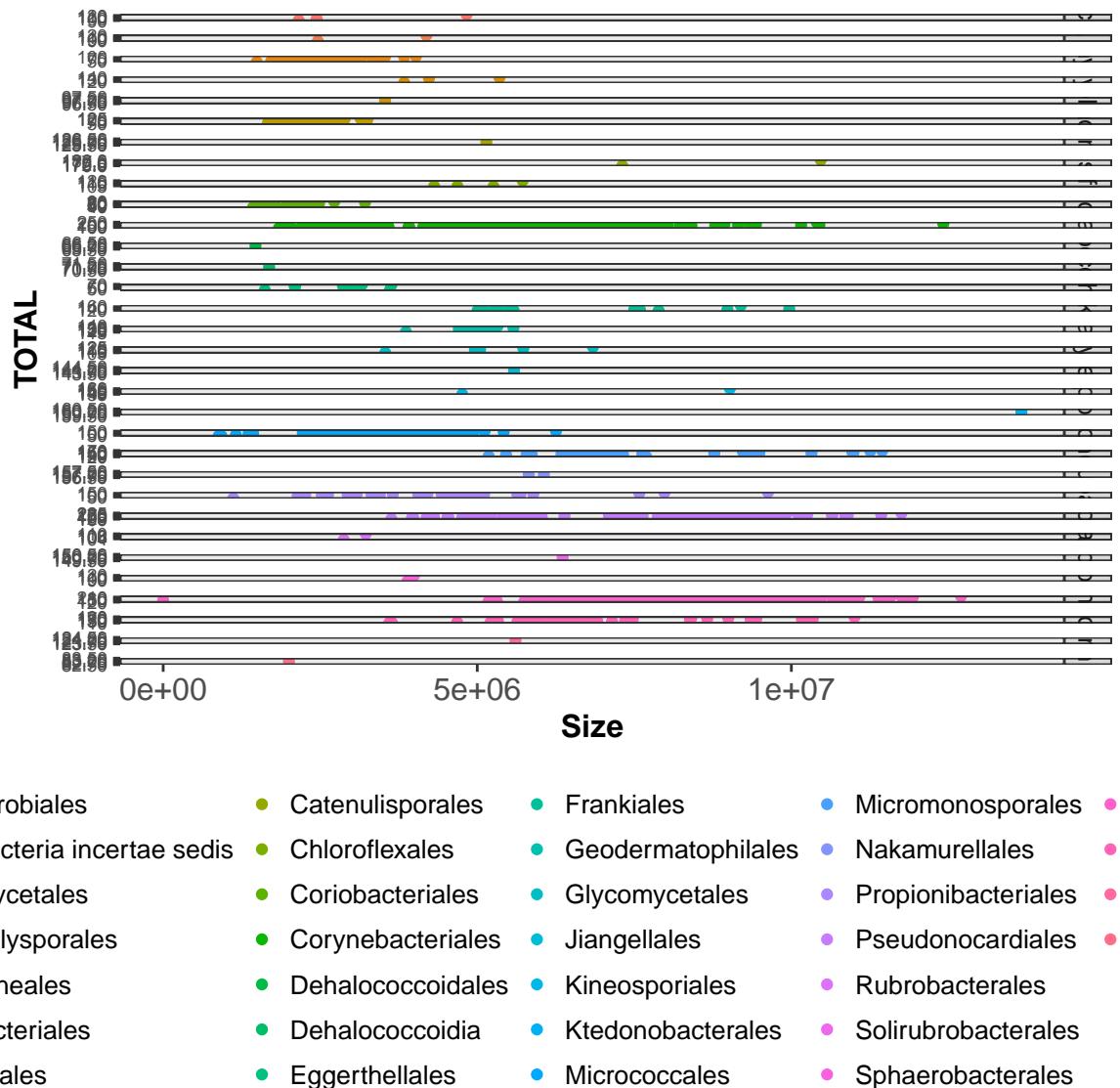


Figure 4.7: Correlation between Actinos genome size and central pathway expansions grided by order

Here is a reference to the Genome size vs Total central pathway expansion grided by order plot: Figure 4.7.

Correlation between genome size and each of the central pathway families. Data are coloured by metabolic family instead of coloured by taxonomical order. This treatment allows to answer how different metabolic families grows when genome size grow. Also I want to add form given by taxonomical order.

Warning: The shape palette can deal with a maximum of 6 discrete values because more than 6 becomes difficult to discriminate; you have 32. Consider specifying shapes manually if you must have them.

Warning: Removed 103306 rows containing missing values (geom_point).

Warning: Removed 94 rows containing missing values (geom_point).

Genome size vs Total central pathway expansion coloured by metabolic Family

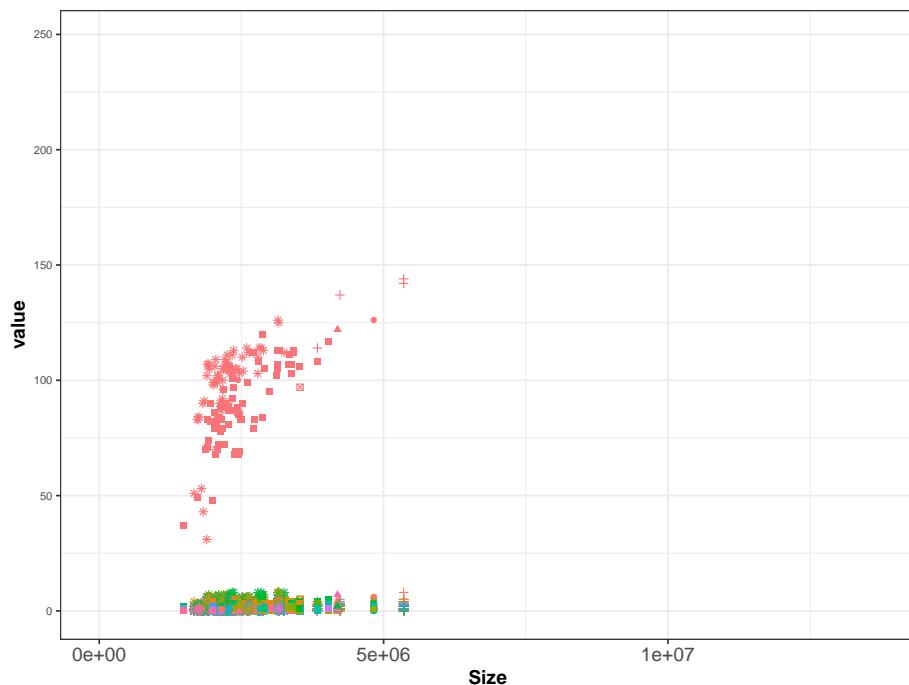


Figure 4.8: Correlation between Actinos Genome size vs Total central pathway expansion coloured by metabolic Family

Here is a reference to the Genome size vs Total central pathway expansion coloured by metabolic Family plot: Figure 4.8.

Future Work: Genome size vs Total central pathway expansion grided by metabolic Family For clarity I need to also grid and group by Metabolic Pathway

Here is a reference to Genome size vs Total central pathway expansion grided by metabolic Family plot: ??.

4.4 Natural products

4.4.1 Natural products recruitments from EvoMining heat-plot

We can see natural products recruitment after central pathways expansions colored by their kingdom.

Natural products recruited by metabolic family, colored by phylogenetic origin.

Recruitments after central pathways expansions coloured by Kingdom

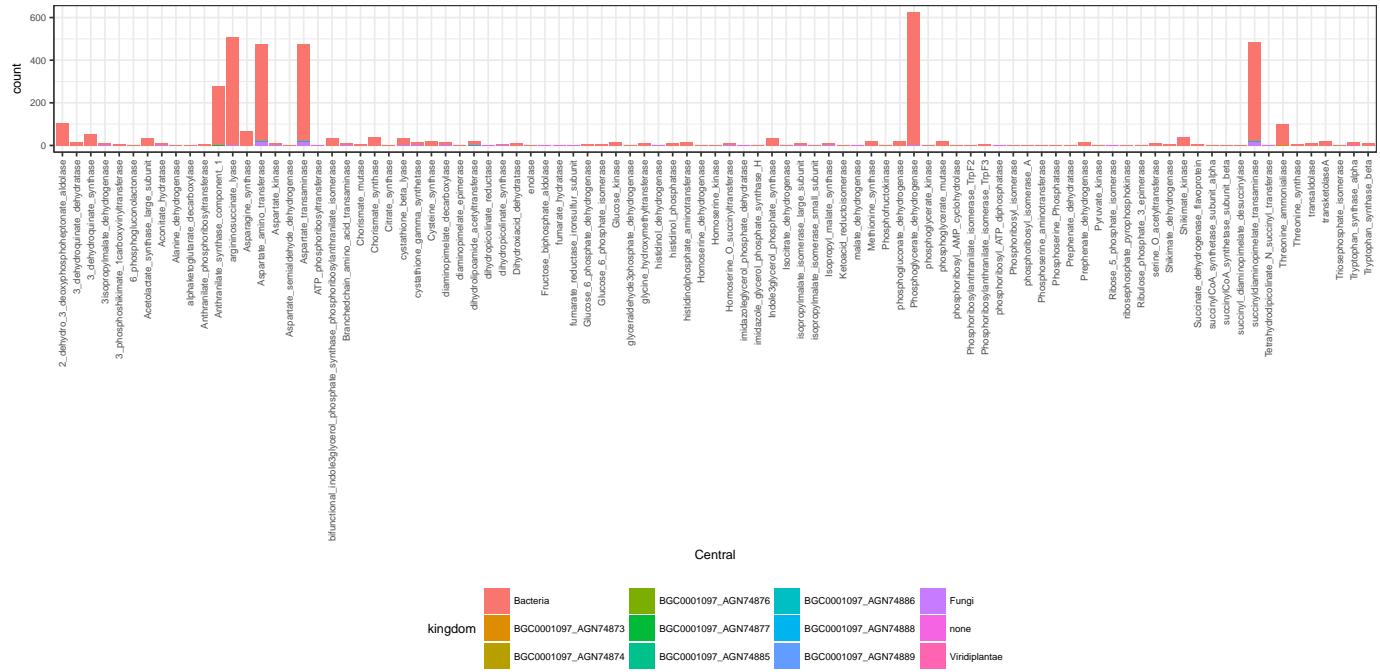


Figure 4.9: Actinos Recruitmens on central families coloured by kingdom

Here is a reference to Recruitments after central pathways expansions coloured by Kingdom plot: Figure 4.9.

Recruitments after central pathways expansions coloured by taxonomy

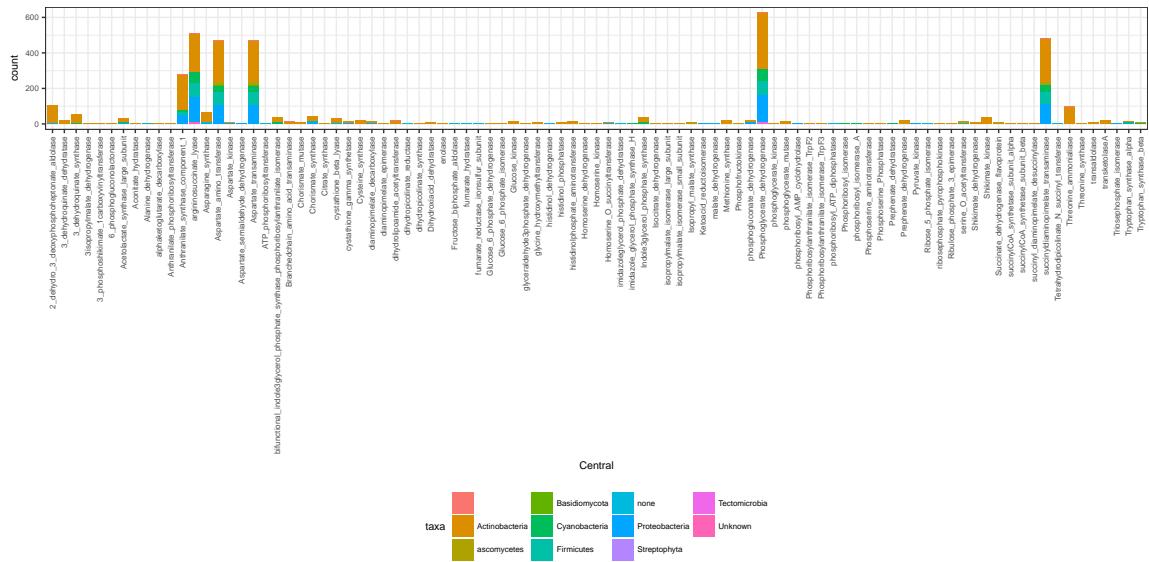


Figure 4.10: Actinos Recruitmens on central families coloured by taxonomy

Here is a reference to Recruitments after central pathways expansions coloured by taxa plot: Figure 4.10.

4.5 Actinos AntiSMASH

Taxonomical diversity on Actinosbacteria Data

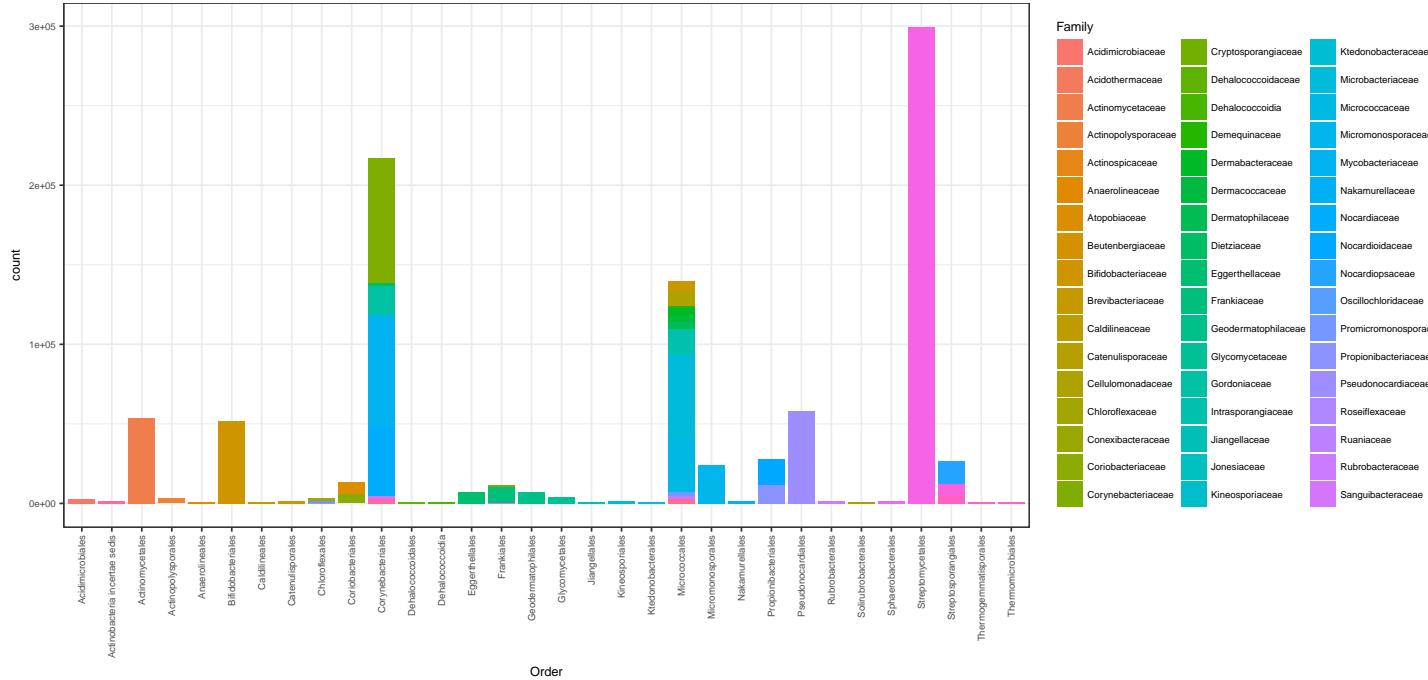


Figure 4.11: Actinos Diversity

Here is a reference to Recruitments after central pathways expansions coloured by taxa plot: Figure 4.11.

Smash diversity

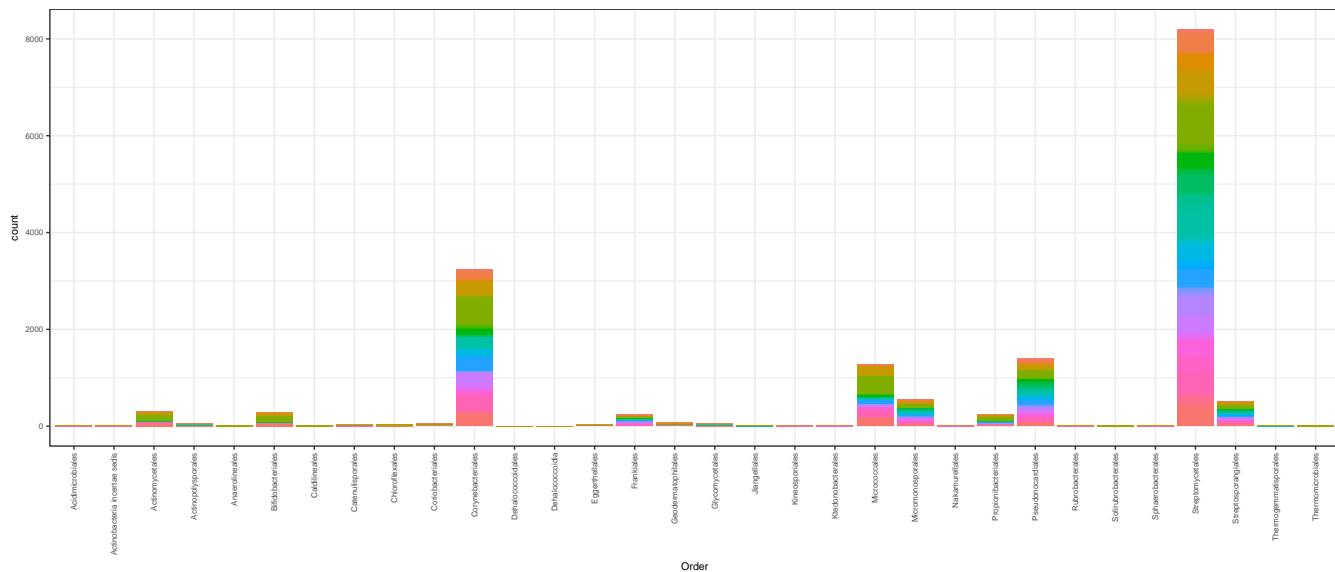


Figure 4.12: Actinos Smash Taxonomical Diversity

Here is a reference to Recruitments after central pathways expansions coloured by taxa plot: Figure 4.12.

4.5.1 AntisMASH vs Central Expansions

Is it a correlation between pangenome grow and central pathways expansions?

Total central pathway expansions by genome vs Total antismash cluster detected coloured by order

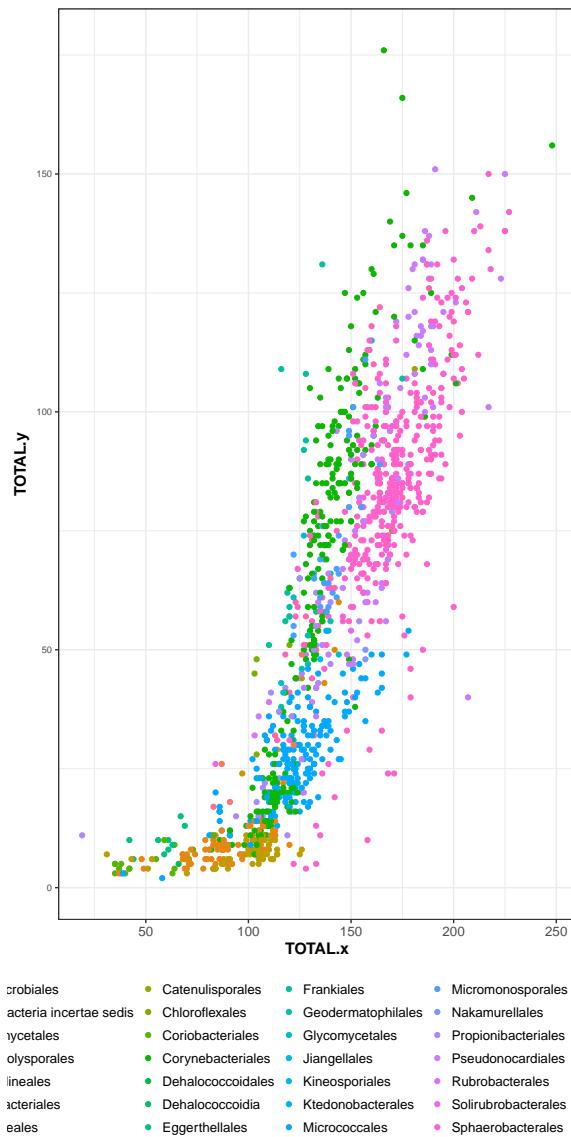


Figure 4.13: Correlation between Actinos central pathway expansions and antismash Natural products detection

Here is a reference to the expansions vs antismash NP's clusters plot: Figure 4.13.

Total central pathway expansions by genome vs Total antismash cluster detected splitted by order

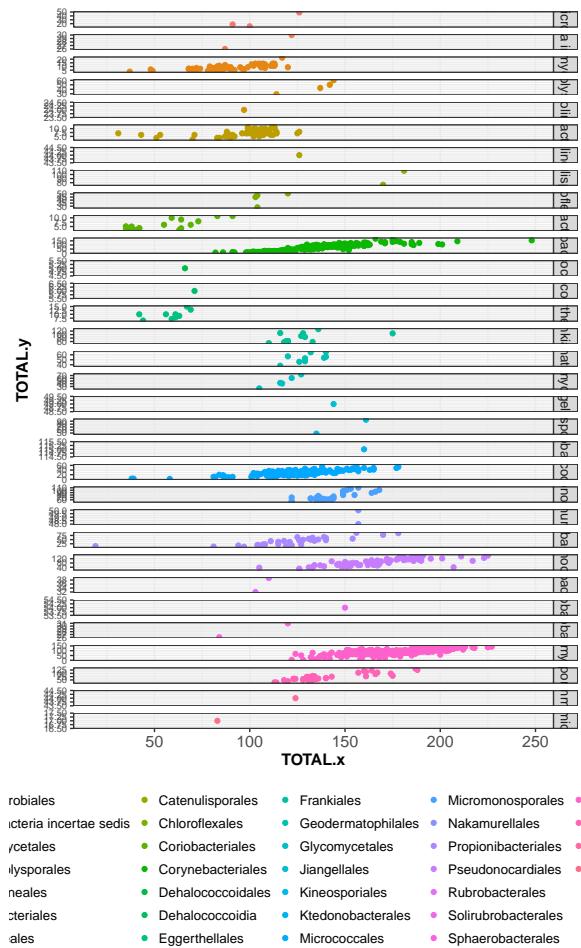


Figure 4.14: Correlation between Actinos central pathway expansions and antismash NP's clusters splitted by order plot

Here is a reference to the expansions vs antismash NP's clusters splitted by order plot Figure 4.14.

AntisMAsh vs Expansions by taxonomic Family

Natural products colured by family



Figure 4.15: Actinos Natural products by family

Here is a reference to the Natural products colured by family plot Figure 4.15.

4.6 Selected trees from EvoMining

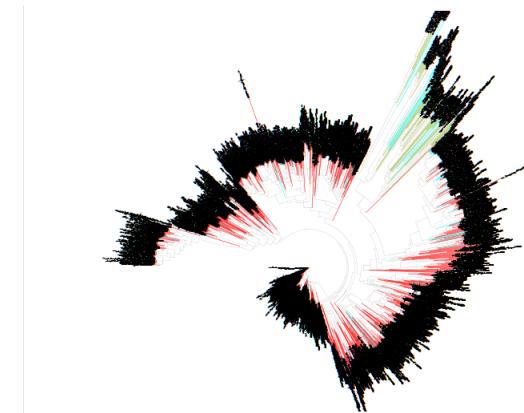


Figure 4.16: Enolase EvoMiningtree

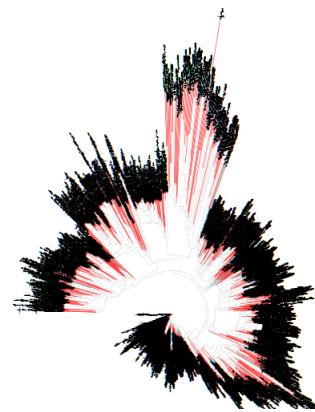


Figure 4.17: Phosphoribosyl isomerase EvoMiningtree

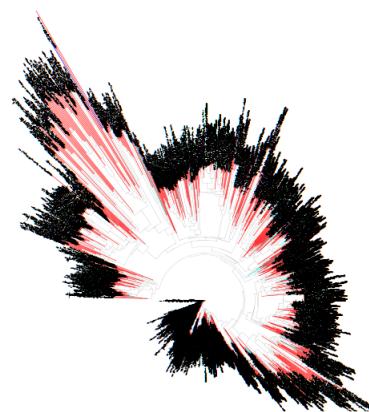


Figure 4.18: Phosphoribosyl isomerase A EvoMiningtree

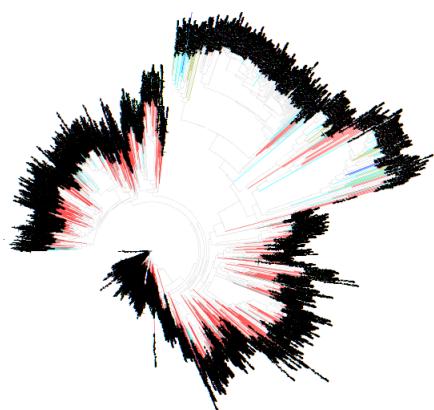


Figure 4.19: phosphoshikimate carboxyvinyltransferase EvoMiningtree

Chapter 5

Cyanobacteria EvoMining Results

Cyanobacteria phylum {Referencia}

Cyanobacteria is a photosynthetic phylum that inhabits a broad range of habitats. The broad adaptive potential is on part driven by gene-family enlargement [128] by the analysis of 58 Cyanobacterial genomes concludes ancestor of cyanobacteria had a genome size of approx. 4.5 Mbp. Cyanobacteria produces natural products as pigments and toxins [129] Example of a PriA cluster toxins[94]

Fossil record situates Cyanobacteria [129] Molecular record and metabolic properties at [132]

5.1 Tables

Table 5.1: Families on Cyanobacteria

Factors	Correlation between Parents & Child
GenomeDB	1245
Families	65

5.1.1 Expansions BoxPlot by metabolic family

```
label(path = "chapter5/expansion_plotCyanos.pdf", caption = "Expansions Boxplot",label =
```

Here is a reference to the expansion boxplot: Figure 5.1.

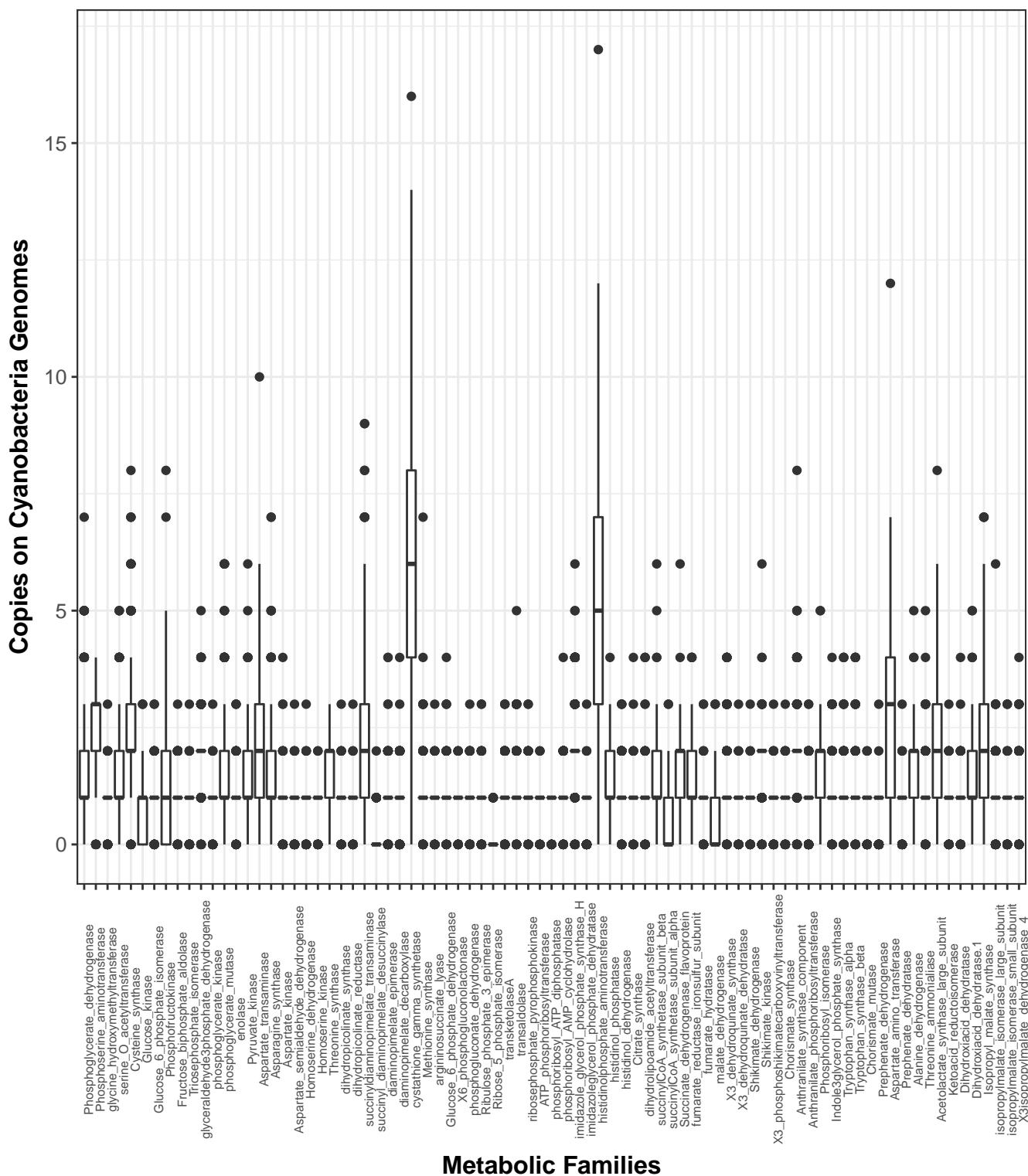


Figure 5.1: Expansions Boxplot

5.2 Central pathway expansions

Heat plot of central pathways expansions, Needs to be phylogenetically sorted.

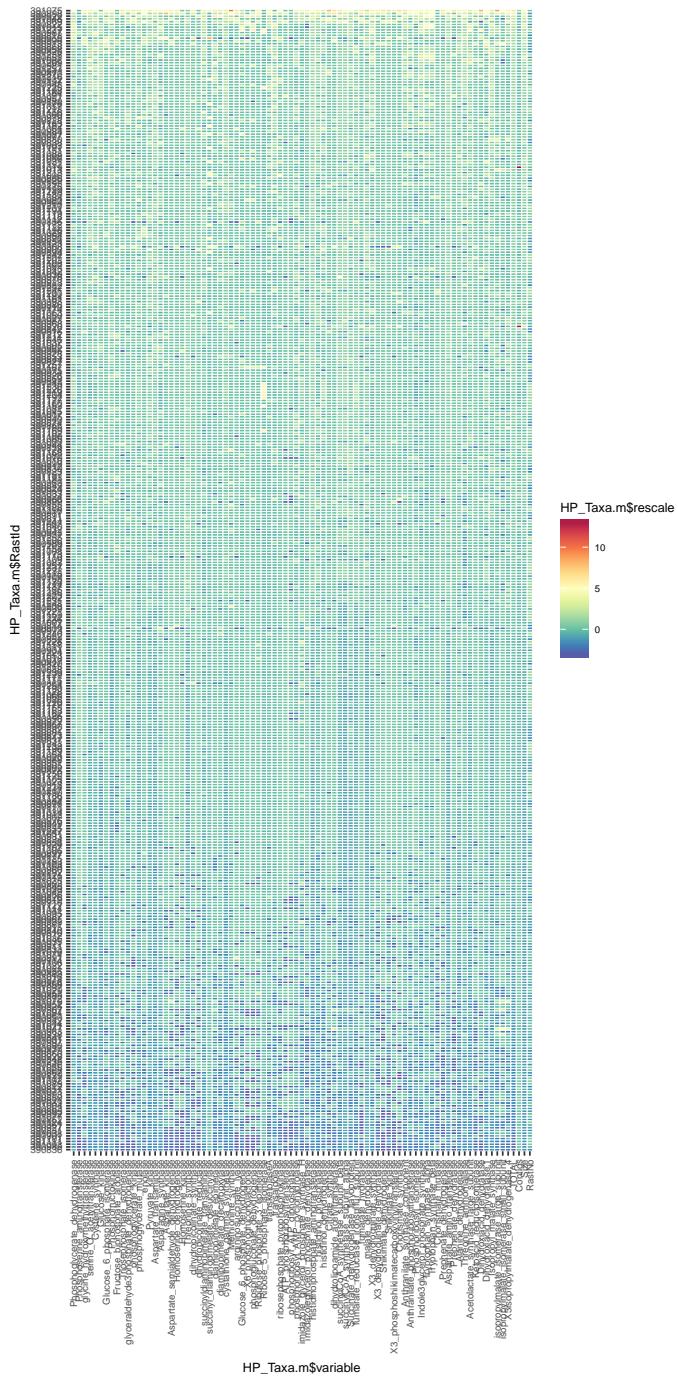


Figure 5.2: Cyanobacterial Heatplot

Here is a reference to the HeatPlot: Figure 5.2.

5.3 Genome Size correlations

5.3.1 Correlation between genome size and AntiSMASH products

Genome size vs Total antismash cluster coloured by order

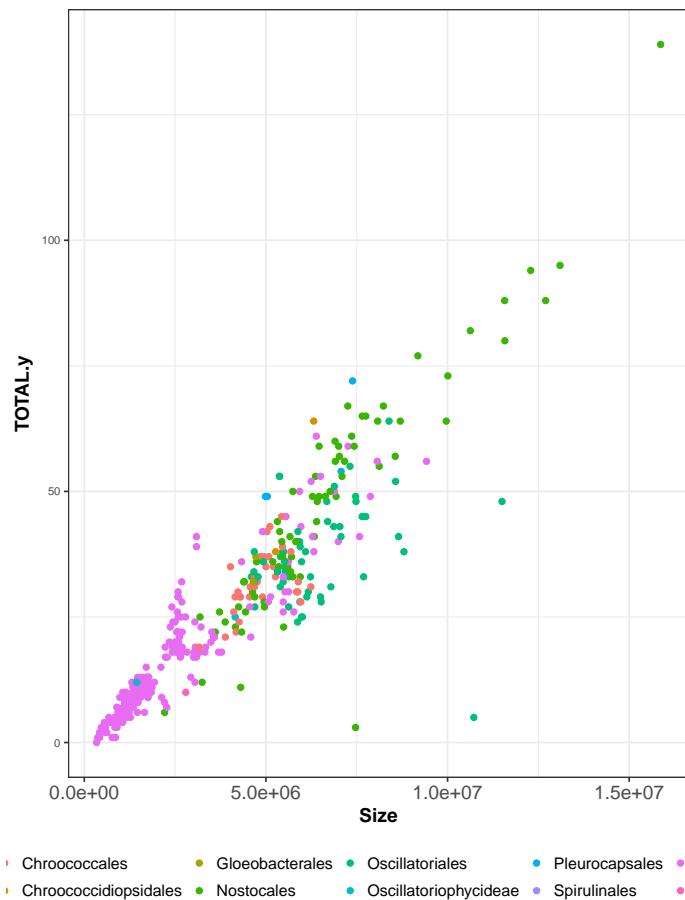


Figure 5.3: Correlation between genome size and antismash Natural products detection colored by Order

Here is a reference to Genome size vs Total antismash cluster: Figure 5.3.

Genome size vs Total antismash cluster detected splitted by order

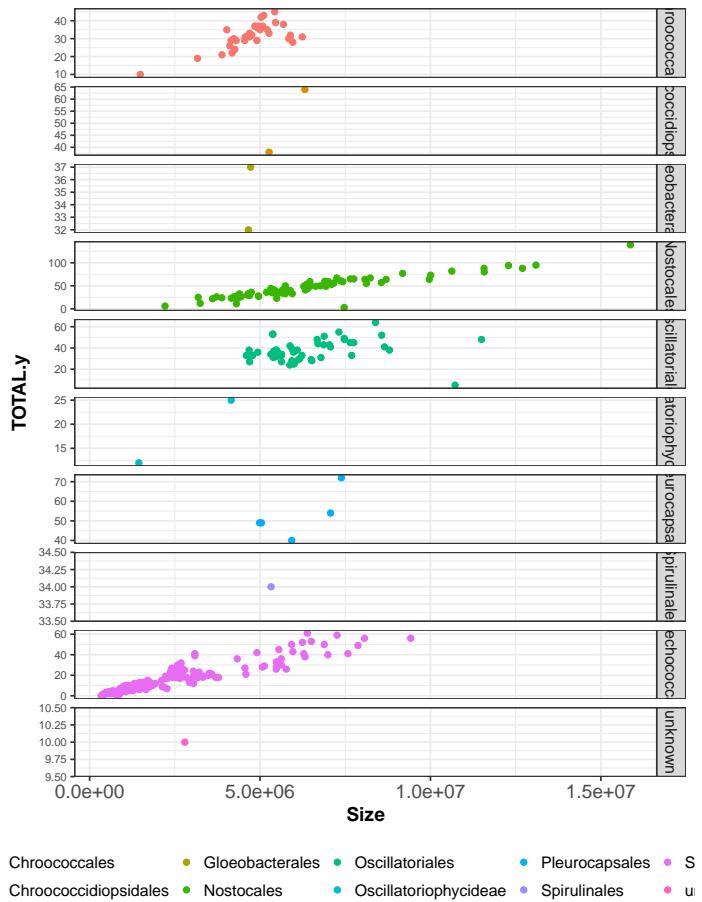


Figure 5.4: Correlation between genome size and antismash Natural products detection grided by Order

Here is a reference to Correlation between genome size and antismash Natural products detection grided by Order plot: Figure 5.4.

5.3.2 Correlation between genome size and Central pathway expansions

Genome size vs Total central pathway expansion coloured by order

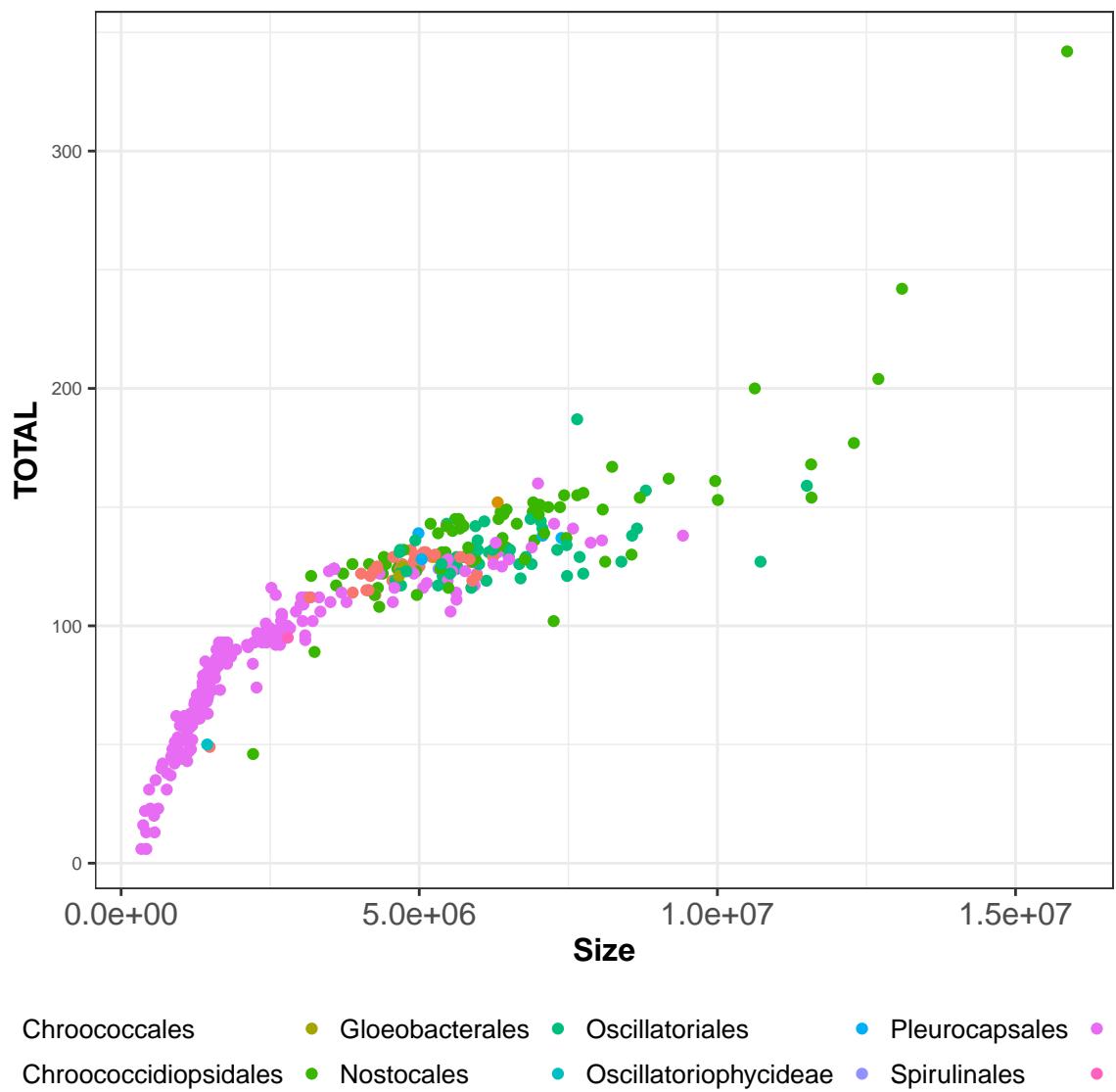


Figure 5.5: Correlation between genome size and central pathway expansions

Here is a reference to the size vs Total central pathway expansion plot: Figure 5.5.

Genome size vs Total central pathway expansion grided by order

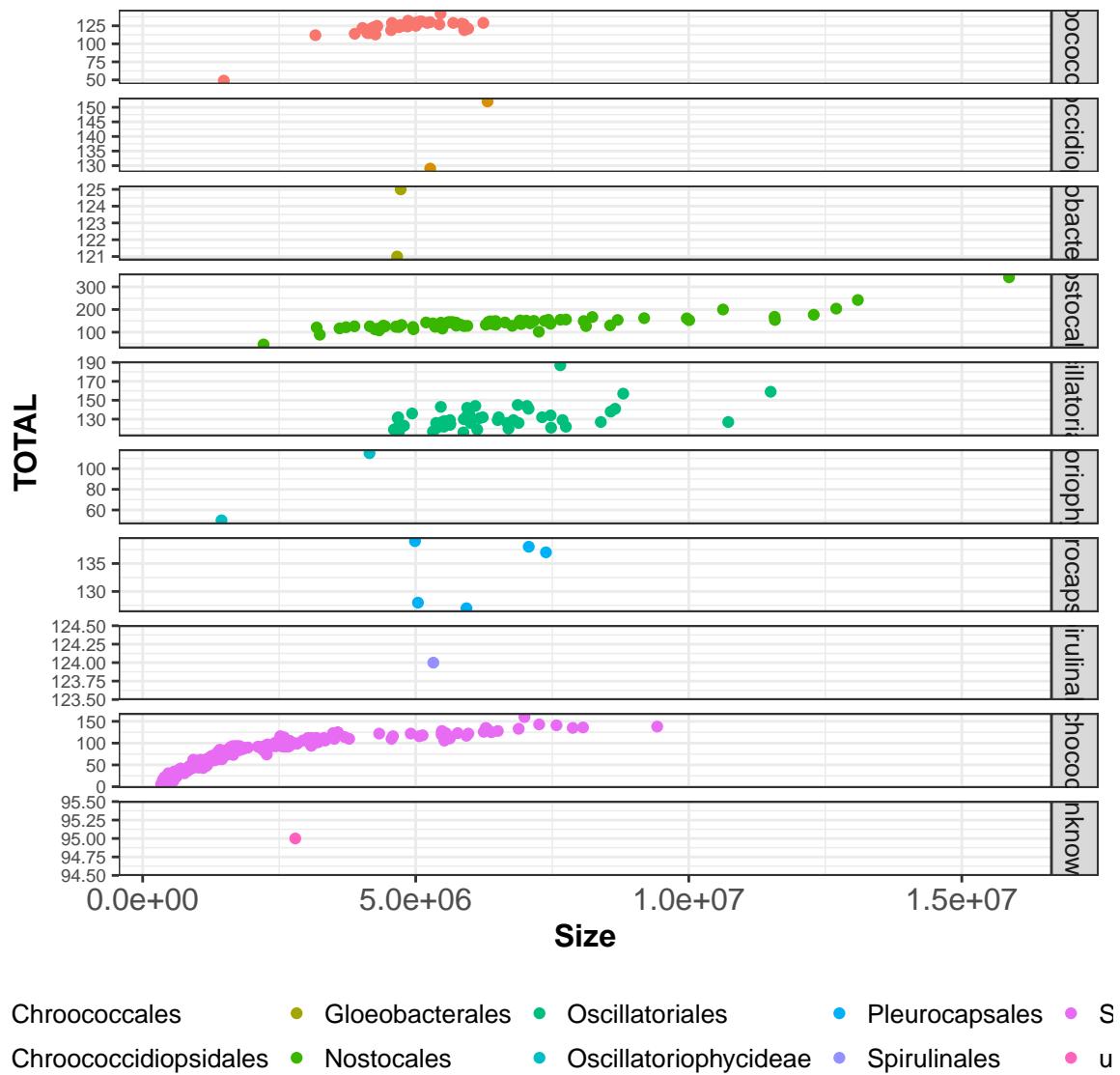


Figure 5.6: Correlation between genome size and central pathway expansions grided by order

Here is a reference to the Genome size vs Total central pathway expansion grided by order plot: Figure 5.6.

Correlation between genome size and each of the central pathway families. Data are coloured by metabolic family instead of coloured by taxonomical order. This treatment allows to answer how different metabolic families grows when genome size grow. Also I want to add form given by taxonomical order.

Warning: The shape palette can deal with a maximum of 6 discrete values because more than 6 becomes difficult to discriminate; you have
 10. Consider specifying shapes manually if you must have them.

Warning: Removed 20418 rows containing missing values (geom_point).

Genome size vs Total central pathway expansion coloured by metabolic Family

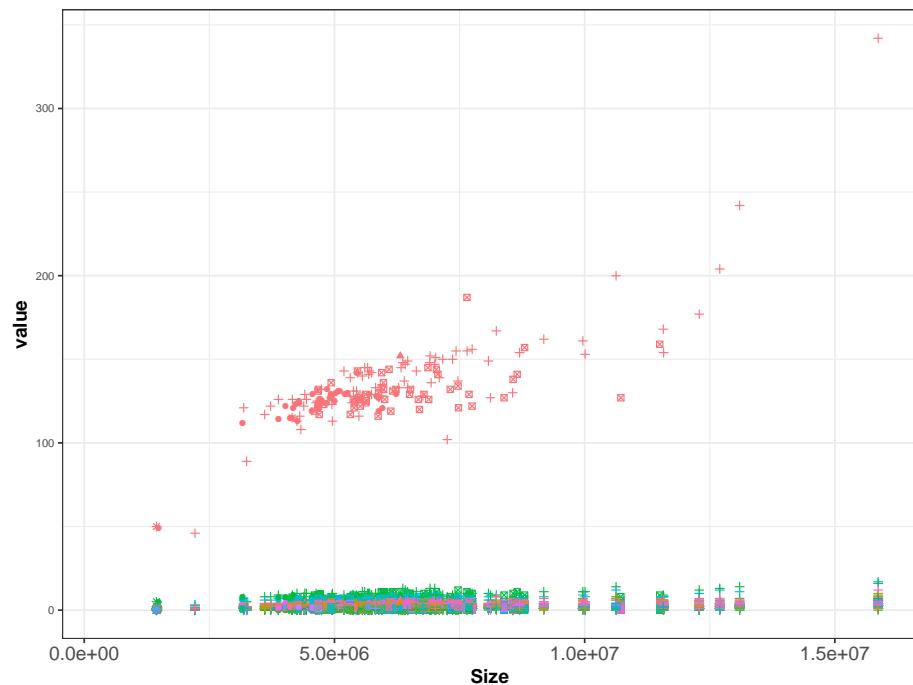


Figure 5.7: Correlation between Genome size vs Total central pathway expansion coloured by metabolic Family

Here is a reference to the Genome size vs Total central pathway expansion coloured by metabolic Family plot: Figure 5.7.

Future Work: Genome size vs Total central pathway expansion grided by metabolic Family For clarity I need to also grid and group by Metabolic Pathway

Here is a reference to Genome size vs Total central pathway expansion grided by metabolic Family plot: ??.

5.4 Natural products

5.4.1 Natural products recruitments from EvoMining heat-plot

We can see natural products recruitment after central pathways expansions colored by their kingdom.

Natural products recruited by metabolic family, colored by phylogenetic origin.

Recruitments after central pathways expansions coloured by Kingdom

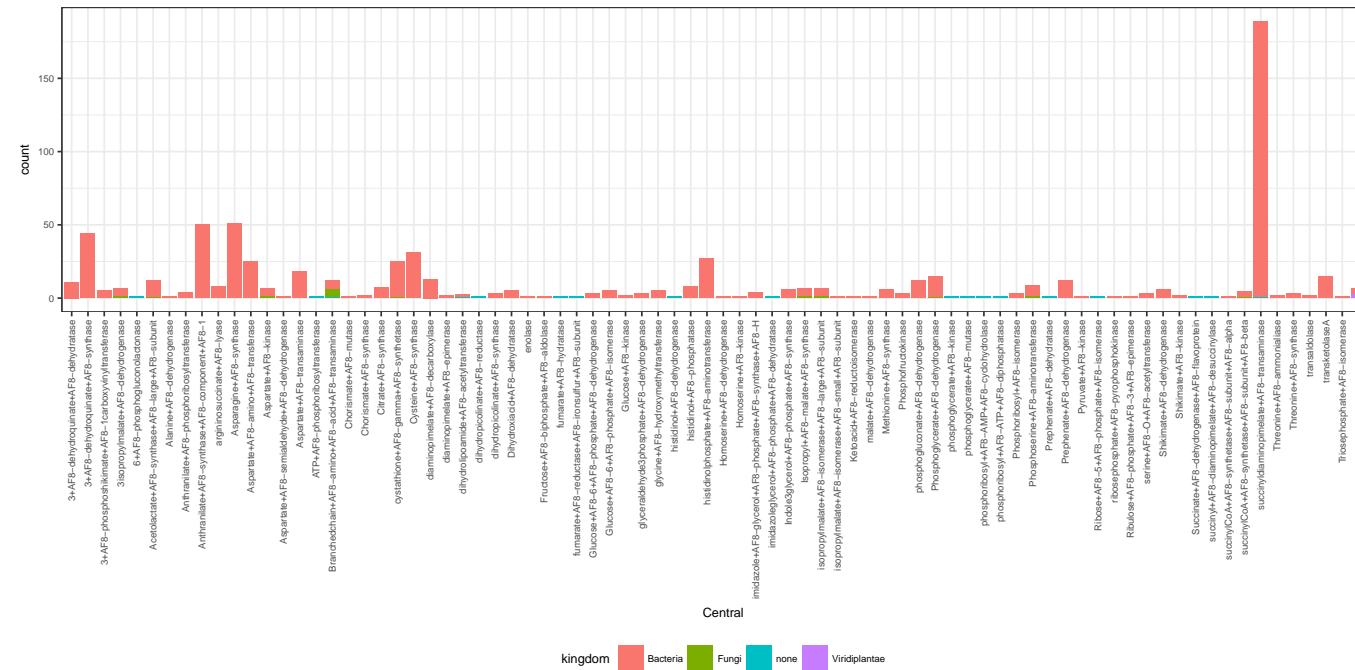


Figure 5.8: Recruitmens on central families coloured by kingdom

Here is a reference to Recruitments after central pathways expansions coloured by Kingdom plot: Figure 5.8.

Recruitments after central pathways expansions colour by taxonomy

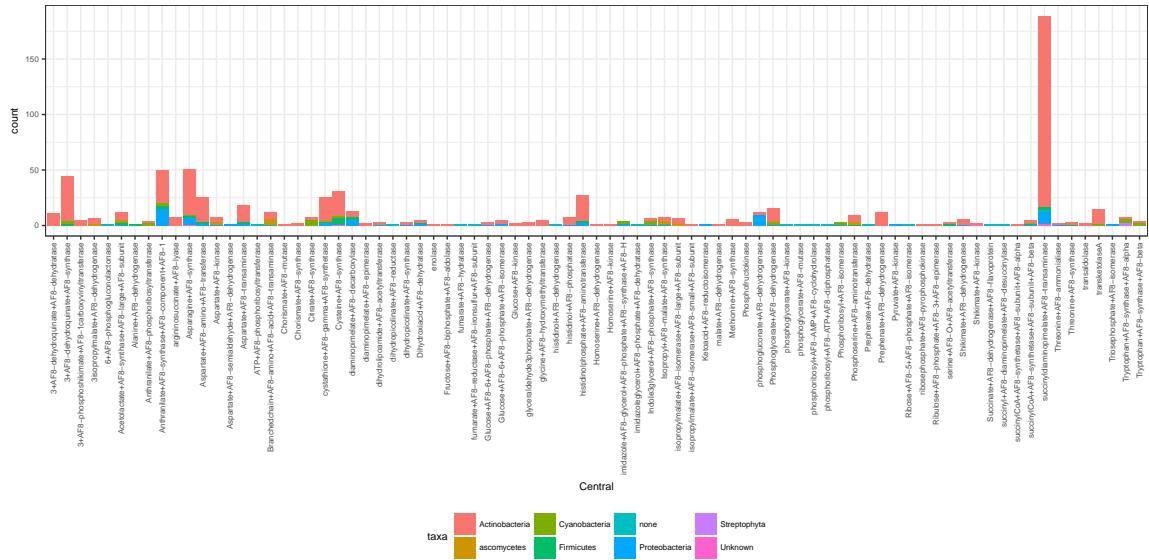


Figure 5.9: Recruitmens on central families coloured by taxonomy

Here is a reference to Recruitments after central pathways expansions colourd by taxa plot: Figure 5.9.

5.5 Cyanobacterias AntiSMASH

Taxonomical diversity on Cyanobacteria Data

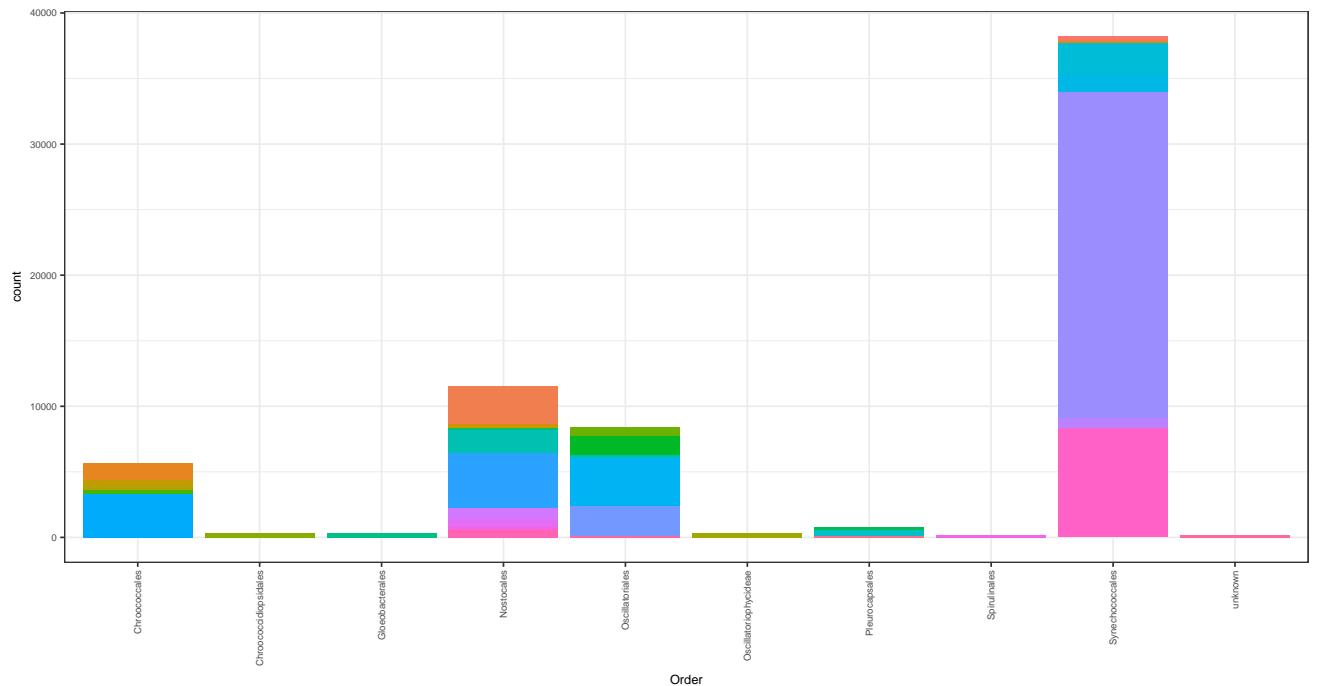


Figure 5.10: Diversity

Here is a reference to Recruitments after central pathways expansions coloured by taxa plot: Figure 5.10.

Smash diversity

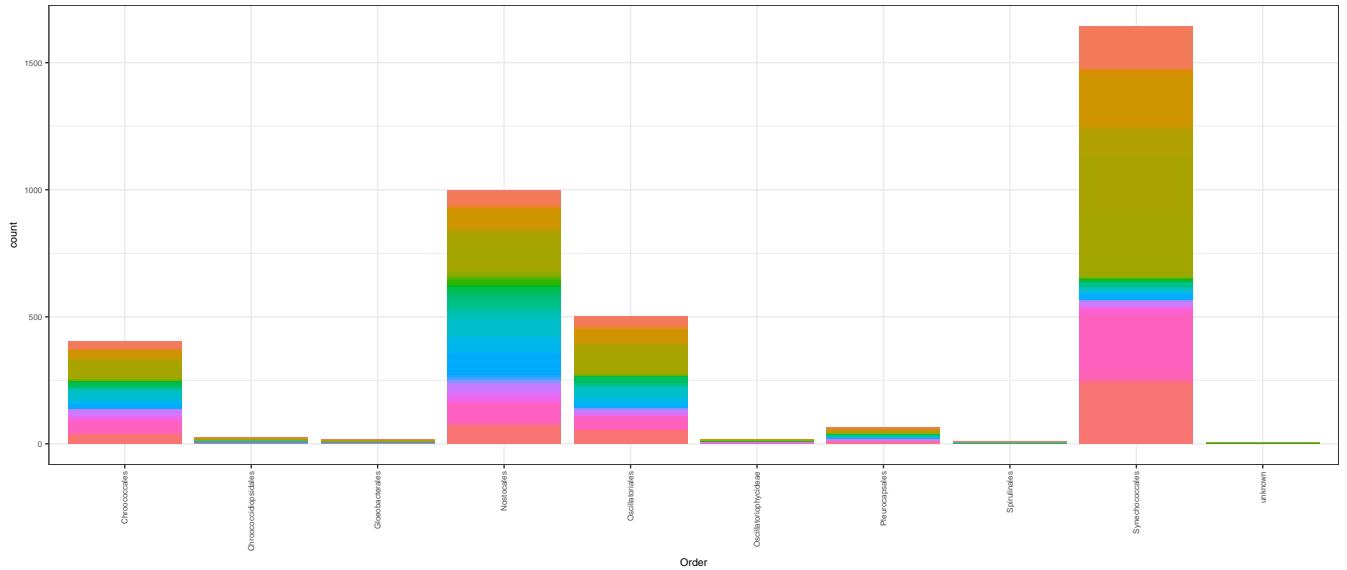


Figure 5.11: Smash

Here is a reference to Recruitments after central pathways expansions coloured by taxa plot: ??.

5.5.1 AntisMASH vs Central Expansions

Is it a correlation between pangenome grow and central pathways expansions?

Total central pathway expansions by genome vs Total antismash cluster detected coloured by order

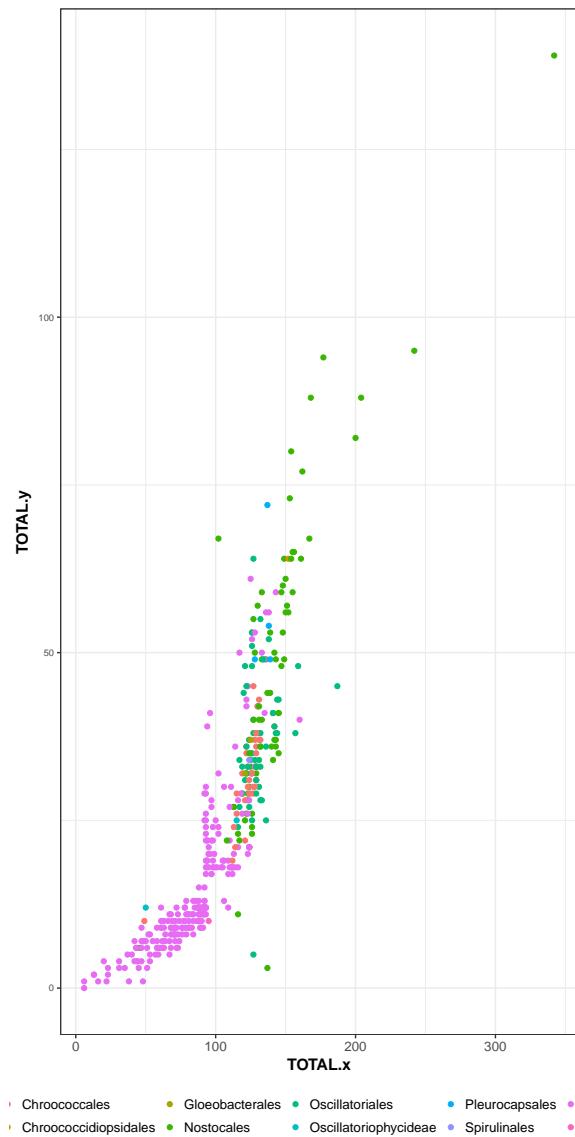


Figure 5.12: Correlation between central pathway expansions and anti-smash Natural products detection

Here is a reference to the expansions vs antismash NP's clusters plot: Figure 5.12.

Total central pathway expansions by genome vs Total antismash cluster detected splitted by order

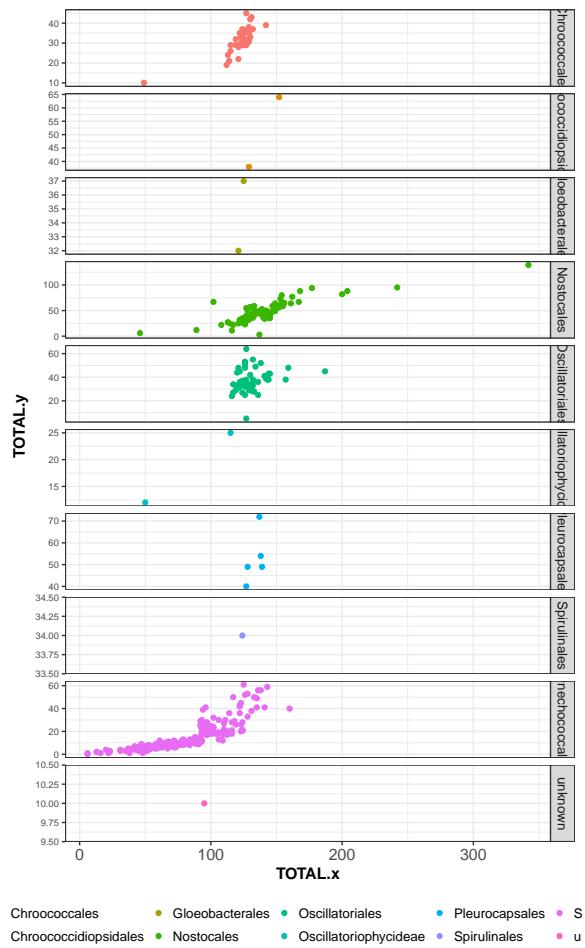


Figure 5.13: Correlation between central pathway expansions and anti-smash Natural products detection

Here is a reference to the expansions vs antismash NP's clusters splitted by order plot ??.

AntisMAsh vs Expansions by taxonomic Family

Natural products colured by family

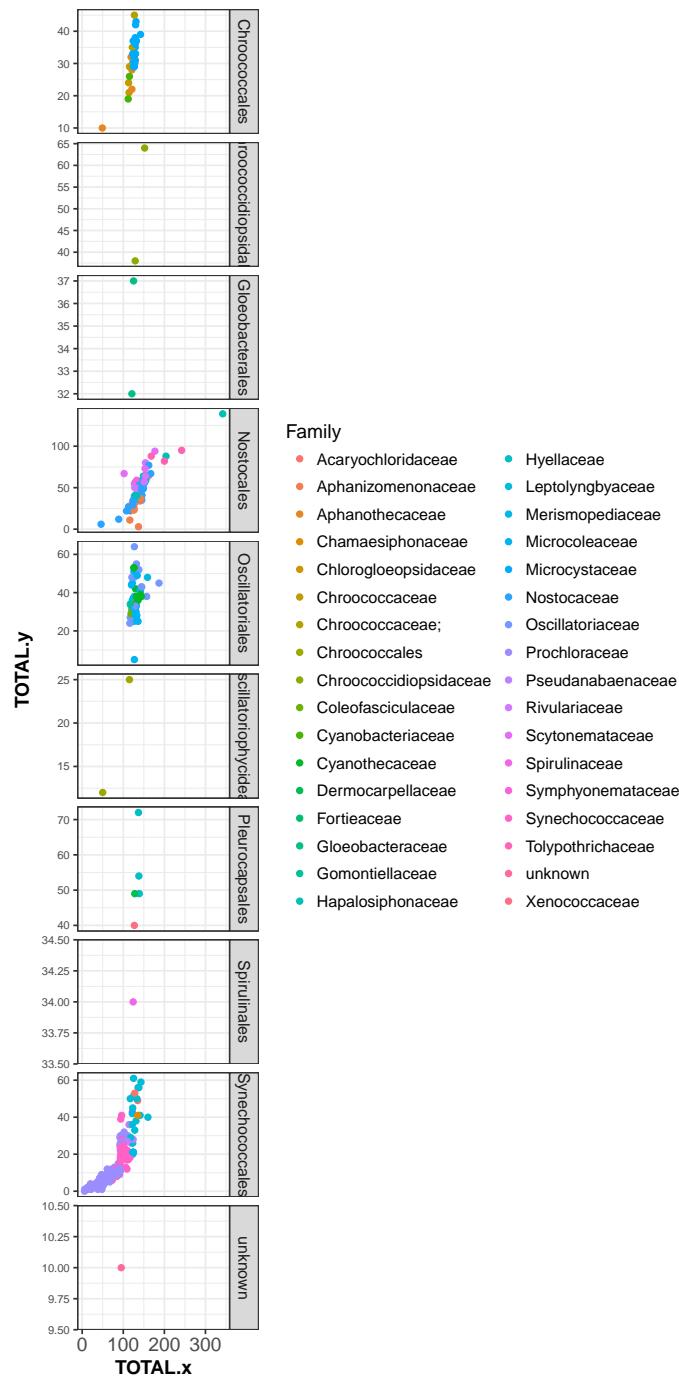


Figure 5.14: Natural products by family

Here is a reference to the Natural products colured by family plot Figure 5.14.

5.6 Selected trees from EvoMining

Phosphoribosyl_isomerase_3 family

Figure from EvoMining

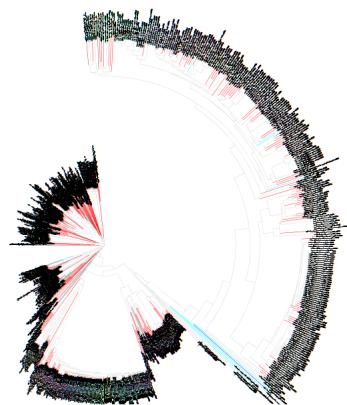


Figure 5.15: Phosphoribosyl isomerase EvoMiningtree

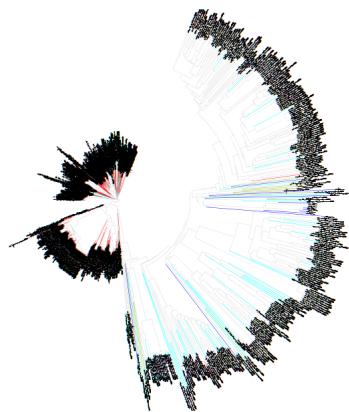


Figure 5.16: Phosphoglycerate dehydrogenase EvoMiningtree

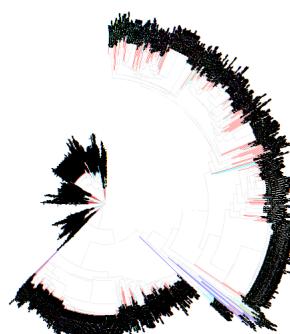


Figure 5.17: Phosphoserine aminotransferase EvoMiningtree

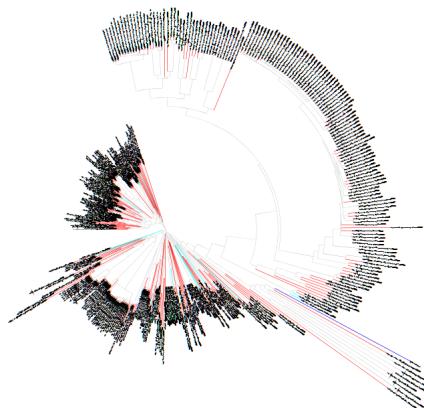


Figure 5.18: Triosephosphate isomerase *EvoMiningtree*

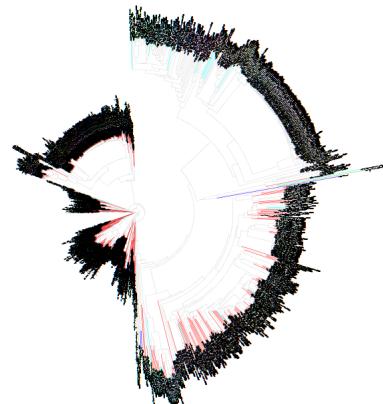


Figure 5.19: glyceraldehyde3phosphate dehydrogenase *EvoMiningtree*

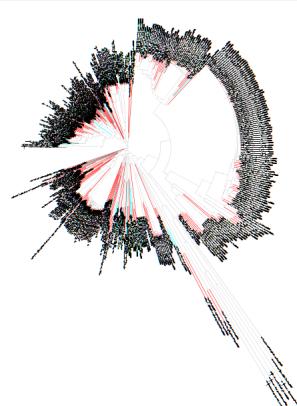


Figure 5.20: phosphoglycerate kinase *EvoMiningtree*

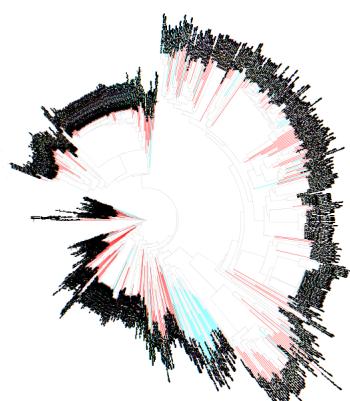


Figure 5.21: phosphoglycerate mutaseEvoMiningtree

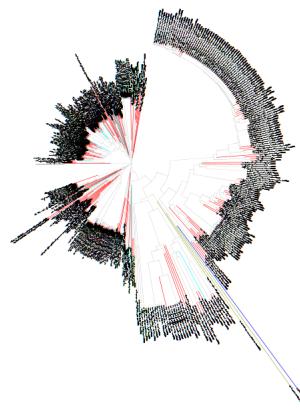


Figure 5.22: enolase EvoMiningtree

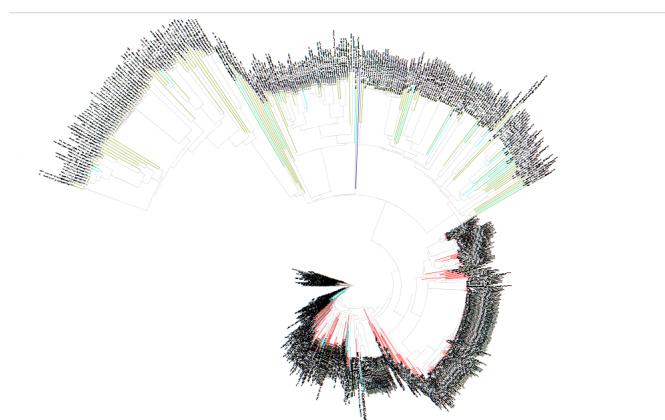


Figure 5.23: Pyruvate kinase EvoMiningtree

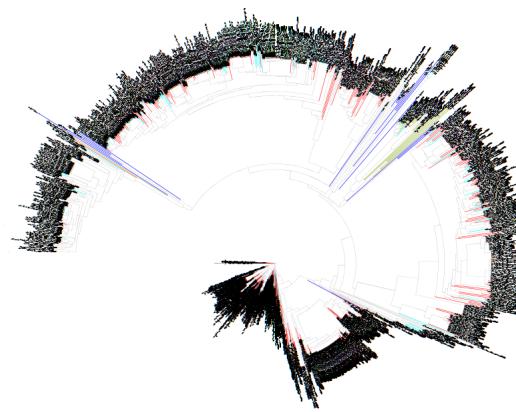


Figure 5.24: Aspartate transaminase EvoMiningtree

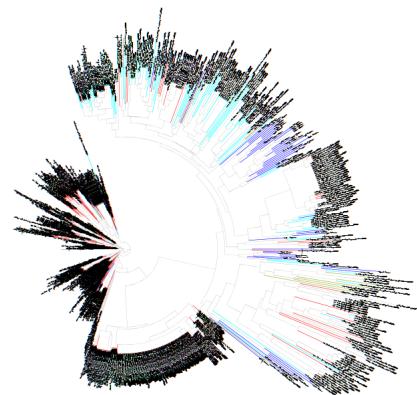


Figure 5.25: Asparagine synthase EvoMiningtree

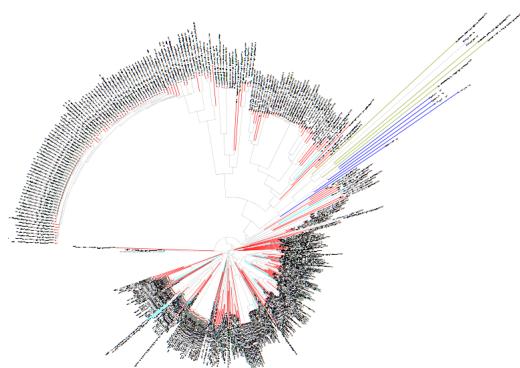


Figure 5.26: Aspartate kinase EvoMiningtree

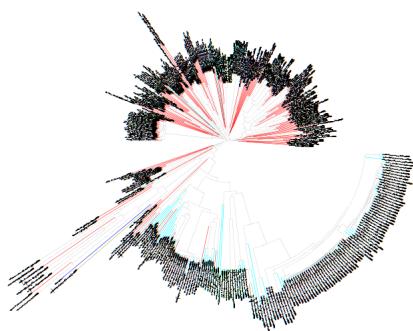


Figure 5.27: Aspartate semialdehyde dehydrogenase EvoMiningtree

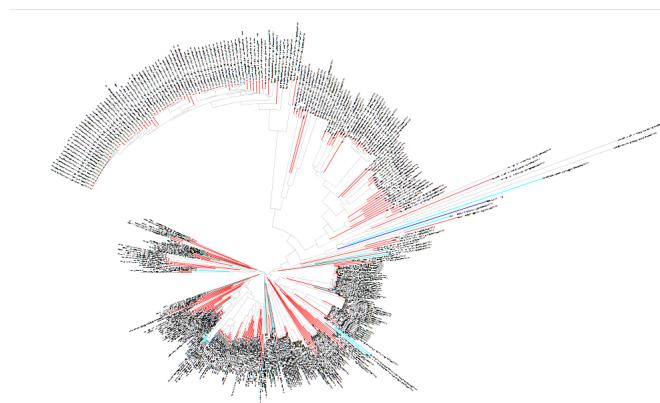


Figure 5.28: Homoserine dehydrogenase EvoMiningtree

Conclusion

Idea de Rosario -ver dell cluster de saxitoxin cuantos pasos se necesitron para llegar ahi.

- A donde se iria el resultado de abrir el GMP
- Otra vez, que Actinos tienen FolE

If we don't want Conclusion to have a chapter number next to it, we can add the `{.unnumbered}` attribute. This has an unintended consequence of the sections being labeled as 3.6 for example though instead of 4.1. The L^AT_EX commands immediately following the Conclusion declaration get things back on track.

More info

And here's some other random info: the first paragraph after a chapter title or section head *shouldn't be* indented, because indents are to tell the reader that you're starting a new paragraph. Since that's obvious after a chapter or section title, proper typesetting doesn't add an indent there.

Appendix A

The First Appendix

This first appendix includes all of the R chunks of code that were hidden throughout the document (using the `include = FALSE` chunk tag) to help with readability and/or setup.

In the main Rmd file:

```
# This chunk ensures that the reedtemplates package is
# installed and loaded. This reedtemplates package includes
# the template files for the thesis and also two functions
# used for labeling and referencing
if(!require(devtools))
  install.packages("devtools", repos = "http://cran.rstudio.com")
if(!require(reedtemplates)){
  library(devtools)
  devtools::install_github("ismayc/reedtemplates")
}
library(reedtemplates)
```

In :

```
# This chunk ensures that the reedtemplates package is
# installed and loaded. This reedtemplates package includes
# the template files for the thesis and also two functions
# used for labeling and referencing
if(!require(devtools))
  install.packages("devtools", repos = "http://cran.rstudio.com")
if(!require(plyr))
  install.packages("plyr", repos = "http://cran.rstudio.com")
```

```
if(!require(dplyr))
  install.packages("dplyr", repos = "http://cran.rstudio.com")
if(!require(ggplot2))
  install.packages("ggplot2", repos = "http://cran.rstudio.com")
if(!require(reedtemplates)){
  library(devtools)
  devtools::install_github("ismayc/reedtemplates")
}
library(reedtemplates)
flights <- read.csv("data/flights.csv")
```

Appendix B

The Second Appendix, Open source code on this document

B.1 R markdown

Thanks to Rmardown Thesis
Apendix one Useful docker commands
-Create a new repository
`docker build . -t evomining`
`docker push nselemevomining`

B.2 Docker

Restart docker and free all ports
`sudo service docker restart`

list containers
`docker ps -a`

ssh or bash into a running docker container
`sudo docker exec -i -t romantic_brahmagupta /bin/bash` `docker exec -it <mycontainer> bash`

Stop all containers
`docker rm $(docker ps -a -q)`

Remove stopped containers
`docker rm $(docker ps -q -f status=exited)`

Remove all images
`docker rmi $(docker images -q)`

uninstall docker from ubuntu (Fresh start)

```
sudo apt-get purge docker-engine
```

```
sudo apt-get autoremove --purge docker-engine
```

```
rm -rf /var/lib/docker # This deletes all images, containers, and volumes
```

Run Evomining container using nselem/newevomining image

```
docker run -i -t -v /home/nelly/GIT/EvoMining:/var/www/html/EvoMining/exchange  
-p 80:80 nselem/newevomining /bin/bash
```

Start evomining inside this container

```
perl startevomining
```

Vizualice a tree

```
http://10.10.100.234/EvoMining/cgi-bin/color_tree.pl?9&&/var/www/html/EvoMining/exchange  
file 9.new must be on folder volume CyanosBBH_MiBIG_DB.faa_CYANOS
```

Find a perl module

```
perl -MList::Util -e'print $_ . " => " . $INC{$_} . "\n" for keys
```

%INC' EvoMining notes

Gblocks only runs inside folder /var/www/html/EvoMining

B.3 Git

```
git add --all  
git commit -m "Some message"  
git push -u origin master  
git clone
```

B.4 Connect GitHub and DockerHub

automated builds The Dockerfile is available to anyone with access to your Docker Hub repository. Your repository is kept up-to-date with code changes automatically.

B.5 Additional resources

- *Markdown Cheatsheet* - <https://github.com/adam-p/markdown-here/wiki/Markdown-Cheatsheet>
- *R Markdown Reference Guide* - <https://www.rstudio.com/wp-content/uploads/2015/03/rmarkdown-reference.pdf>
- Introduction to dplyr - <https://cran.rstudio.com/web/packages/dplyr/vignettes/introduction.html>

- ggplot2 Documentation - <http://docs.ggplot2.org/current/>

References

1. Angel E. Interactive computer graphics : A top-down approach with OpenGL. Boston, MA: Addison Wesley Longman; 2000.
2. Angel E. Batch-file computer graphics : A bottom-up approach with quickTime. Boston, MA: Wesley Addison Longman; 2001.
3. Angel E. Test second book by angel. Boston, MA: Wesley Addison Longman; 2001.
4. Khersonsky O, Tawfik DS. Enzyme promiscuity: A mechanistic and evolutionary perspective. *Annual Review of Biochemistry*. 2010;79: 471–505. doi:10.1146/annurev-biochem-030409-143718
5. Copley SD. Enzymes with extra talents: Moonlighting functions and catalytic promiscuity. *Current Opinion in Chemical Biology*. 2003;7: 265–272. doi:10.1016/S1367-5931(03)00032-2
6. Hult K, Berglund P. Enzyme promiscuity: Mechanism and applications. *Trends in Biotechnology*. 2007;25: 231–238. doi:10.1016/j.tibtech.2007.03.002
7. O'Brien PJ, Herschlag D. Catalytic promiscuity and the evolution of new enzymatic activities. *Chemistry & Biology*. 1999;6: R91–R105. doi:10.1016/S1074-5521(99)80033-7
8. Barona Gómez F, Hodgson DA. Occurrence of a putative ancient like isomerase involved in histidine and tryptophan biosynthesis. *EMBO reports*. 2003;4: 296–300. doi:10.1038/sj.embo.reports.771
9. Risso VA, Gavira JA, Gaucher EA, Sanchez Ruiz JM. Phenotypic comparisons of consensus variants versus laboratory resurrections of precambrian proteins. *Proteins: Structure, Function, and Bioinformatics*. 2014;82: 887–896. doi:10.1002/prot.24575
10. Kumari V, Shah S, Gupta MN. Preparation of Biodiesel by Lipase-Catalyzed Transesterification of High Free Fatty Acid Containing Oil from Madhuca indica. *Energy & Fuels*. 2007;21: 368–372. doi:10.1021/ef0602168
11. Li C, Henry CS, Jankowski MD, Ionita JA, Hatzimanikatis V, Broadbelt LJ.

- Computational discovery of biochemical routes to specialty chemicals. *Chemical Engineering Science*. 2004;59: 5051–5060. doi:10.1016/j.ces.2004.09.021
12. Glasner ME, Gerlt JA, Babbitt PC. Evolution of enzyme superfamilies. *Current Opinion in Chemical Biology*. 2006;10: 492–497. doi:10.1016/j.cbpa.2006.08.012
 13. Baier F, Copp JN, Tokuriki N. Evolution of Enzyme Superfamilies: Comprehensive Exploration of Sequence–Function Relationships. *Biochemistry*. 2016;55: 6375–6388. doi:10.1021/acs.biochem.6b00723
 14. Bloom JD, Romero PA, Lu Z, Arnold FH. Neutral genetic drift can alter promiscuous protein functions, potentially aiding functional evolution. *Biology Direct*. 2007;2: 17. doi:10.1186/1745-6150-2-17
 15. Nath A, Atkins WM. A Quantitative Index of Substrate Promiscuity. *Biochemistry*. 2008;47: 157–166. doi:10.1021/bi701448p
 16. Zou T, Rissó VA, Gavira JA, Sanchez-Ruiz JM, Ozkan SB. Evolution of Conformational Dynamics Determines the Conversion of a Promiscuous Generalist into a Specialist Enzyme. *Molecular Biology and Evolution*. 2015;32: 132–143. doi:10.1093/molbev/msu281
 17. Firn RD, Jones CG. A Darwinian view of metabolism: Molecular properties determine fitness. *Journal of Experimental Botany*. 2009;60: 719–726. doi:10.1093/jxb/erp002
 18. Jia B, Cheong G-W, Zhang S. Multifunctional enzymes in archaea: Promiscuity and moonlight. *Extremophiles*. 2013;17: 193–203. doi:10.1007/s00792-012-0509-1
 19. Aharoni A, Gaidukov L, Khersonsky O, Gould SM, Roodveldt C, Tawfik DS. The 'evolvability' of promiscuous protein functions. *Nature Genetics*. 2005;37: 73–76. doi:10.1038/ng1482
 20. Jensen. Enzyme Recruitment in Evolution of New Function. *Annual Review of Microbiology*. 1976;30: 409–425. doi:10.1146/annurev.mi.30.100176.002205
 21. Pandya C, Farelli JD, Dunaway-Mariano D, Allen KN. Enzyme Promiscuity: Engine of Evolutionary Innovation. *Journal of Biological Chemistry*. 2014;289: 30229–30236. doi:10.1074/jbc.R114.572990
 22. Dean AM, Thornton JW. Mechanistic approaches to the study of evolution. *Nature reviews Genetics*. 2007;8: 675–688. doi:10.1038/nrg2160
 23. Nobeli I, Favia AD, Thornton JM. Protein promiscuity and its implications for biotechnology. *Nature Biotechnology*. 2009;27: 157–167. doi:10.1038/nbt1519
 24. Hopkins AL. Drug discovery: Predicting promiscuity. *Nature*. 2009;462: 167–168. doi:10.1038/462167a
 25. Nath A, Zientek MA, Burke BJ, Jiang Y, Atkins WM. Quantifying and

- Predicting the Promiscuity and Isoform Specificity of Small-Molecule Cytochrome P450 Inhibitors. *Drug Metabolism and Disposition.* 2010;38: 2195–2203. doi:10.1124/dmd.110.034645
26. Eichborn J von, Murgueitio MS, Dunkel M, Koerner S, Bourne PE, Preissner R. PROMISCUOUS: A database for network-based drug-repositioning. *Nucleic Acids Research.* 2011;39: D1060–D1066. doi:10.1093/nar/gkq1037
27. Zhang W, Dourado DFAR, Fernandes PA, Ramos MJ, Mannervik B. Multidimensional epistasis and fitness landscapes in enzyme evolution. *Biochemical Journal.* 2012;445: 39–46. doi:10.1042/BJ20120136
28. Sanchez-Ruiz JM. On promiscuity, changing environments and the possibility of replaying the molecular tape of life. *Biochemical Journal.* 2012;445: e1–e3. doi:10.1042/BJ20120806
29. Martínez-Núñez MA, Rodríguez-Vázquez K, Pérez-Rueda E. The lifestyle of prokaryotic organisms influences the repertoire of promiscuous enzymes. *Proteins: Structure, Function, and Bioinformatics.* 2015;83: 1625–1631. doi:10.1002/prot.24847
30. Patrick WM, Quandt EM, Swartzlander DB, Matsumura I. Multicopy Suppression Underpins Metabolic Evolvability. *Molecular Biology and Evolution.* 2007;24: 2716–2722. doi:10.1093/molbev/msm204
31. Notebaart RA, Szappanos B, Kintses B, Pál F, Györkei Á, Bogos B, et al. Network-level architecture and the evolutionary potential of underground metabolism. *Proceedings of the National Academy of Sciences.* 2014;111: 11762–11767. doi:10.1073/pnas.1406102111
32. Linster CL, Van Schaftingen E, Hanson AD. Metabolite damage and its repair or pre-emption. *Nature Chemical Biology.* 2013;9: 72–80. doi:10.1038/nchembio.1141
33. Khanal A, Yu McLoughlin S, Kershner JP, Copley SD. Differential Effects of a Mutation on the Normal and Promiscuous Activities of Orthologs: Implications for Natural and Directed Evolution. *Molecular Biology and Evolution.* 2015;32: 100–108. doi:10.1093/molbev/msu271
34. Ma H-M, Zhou Q, Tang Y-M, Zhang Z, Chen Y-S, He H-Y, et al. Unconventional Origin and Hybrid System for Construction of Pyrrolopyrrole Moiety in Kosinostatin Biosynthesis. *Chemistry & Biology.* 2013;20: 796–805. doi:10.1016/j.chembiol.2013.04.013
35. Adams NE, Thiaville JJ, Proestos J, Juárez-Vázquez AL, McCoy AJ, Barona-Gómez F, et al. Promiscuous and Adaptable Enzymes Fill “Holes” in the Tetrahydrofolate Pathway in Chlamydia Species. *mBio.* 2014;5. doi:10.1128/mBio.01378-

- 14
36. Soskine M, Tawfik DS. Mutational effects and the evolution of new protein functions. *Nature Reviews Genetics.* 2010;11: 572–582. doi:10.1038/nrg2808
 37. Halachev MR, Loman NJ, Pallen MJ. Calculating Orthologs in Bacteria and Archaea: A Divide and Conquer Approach. *PLOS ONE.* 2011;6: e28388. doi:10.1371/journal.pone.0028388
 38. Kislyuk AO, Haegeman B, Bergman NH, Weitz JS. Genomic fluidity: An integrative view of gene diversity within microbial populations. *BMC Genomics.* 2011;12: 32. doi:10.1186/1471-2164-12-32
 39. Pearson H. Prehistoric proteins: Raising the dead. *Nature News.* 2012;483: 390. doi:10.1038/483390a
 40. Hughes AL. The Evolution of Functionally Novel Proteins after Gene Duplication. *Proceedings of the Royal Society of London B: Biological Sciences.* 1994;256: 119–124. doi:10.1098/rspb.1994.0058
 41. Treangen TJ, Rocha EPC. Horizontal Transfer, Not Duplication, Drives the Expansion of Protein Families in Prokaryotes. *PLOS Genetics.* 2011;7: e1001284. doi:10.1371/journal.pgen.1001284
 42. Overbeek R, Fonstein M, D’Souza M, Pusch GD, Maltsev N. The use of gene clusters to infer functional coupling. *Proceedings of the National Academy of Sciences.* 1999;96: 2896–2901. doi:10.1073/pnas.96.6.2896
 43. Zhao S, Sakai A, Zhang X, Vetting MW, Kumar R, Hillerich B, et al. Prediction and characterization of enzymatic activities guided by sequence similarity and genome neighborhood networks. *eLife.* 2014;3: e03275. doi:10.7554/eLife.03275
 44. Zhao S, Kumar R, Sakai A, Vetting MW, Wood BM, Brown S, et al. Discovery of new enzymes and metabolic pathways by using structure and genome context. *Nature.* 2013;502: 698–702. doi:10.1038/nature12576
 45. Verdel-Aranda K, López-Cortina ST, Hodgson DA, Barona-Gómez F. Molecular annotation of ketol-acid reductoisomerases from *Streptomyces* reveals a novel amino acid biosynthesis interlock mediated by enzyme promiscuity. *Microbial Biotechnology.* 2015;8: 239–252. doi:10.1111/1751-7915.12175
 46. Szklarczyk D, Franceschini A, Wyder S, Forslund K, Heller D, Huerta-Cepas J, et al. STRING v10: Protein–protein interaction networks, integrated over the tree of life. *Nucleic Acids Research.* 2015;43: D447–D452. doi:10.1093/nar/gku1003
 47. Snel B, Lehmann G, Bork P, Huynen MA. STRING: A web-server to retrieve and display the repeatedly occurring neighbourhood of a gene. *Nucleic Acids Research.* 2000;28: 3442–3444. Available: <http://www.ncbi.nlm.nih.gov/pmc/articles/>

PMC110752/

48. Aziz RK, Bartels D, Best AA, DeJongh M, Disz T, Edwards RA, et al. The RAST Server: Rapid Annotations using Subsystems Technology. *BMC Genomics.* 2008;9: 75. doi:10.1186/1471-2164-9-75
49. Overbeek R, Olson R, Pusch GD, Olsen GJ, Davis JJ, Disz T, et al. The SEED and the Rapid Annotation of microbial genomes using Subsystems Technology (RAST). *Nucleic Acids Research.* 2014;42: D206–D214. doi:10.1093/nar/gkt1226
50. Medema MH, Fischbach MA. Computational approaches to natural product discovery. *Nature Chemical Biology.* 2015;11: 639–648. doi:10.1038/nchembio.1884
51. Noda-García L, Camacho-Zarco AR, Medina-Ruiz S, Gaytán P, Carrillo-Tripp M, Fülöp V, et al. Evolution of Substrate Specificity in a Recipient’s Enzyme Following Horizontal Gene Transfer. *Molecular Biology and Evolution.* 2013;30: 2024–2034. doi:10.1093/molbev/mst115
52. Carbonell P, Faulon J-L. Molecular signatures-based prediction of enzyme promiscuity. *Bioinformatics.* 2010;26: 2012–2019. doi:10.1093/bioinformatics/btq317
53. Cheng X-Y, Huang W-J, Hu S-C, Zhang H-L, Wang H, Zhang J-X, et al. A Global Characterization and Identification of Multifunctional Enzymes. *PLoS ONE.* 2012;7. doi:10.1371/journal.pone.0038979
54. Nagao C, Nagano N, Mizuguchi K. Prediction of Detailed Enzyme Functions and Identification of Specificity Determining Residues by Random Forests. *PLOS ONE.* 2014;9: e84623. doi:10.1371/journal.pone.0084623
55. Noda-García L, Juárez-Vázquez AL, Ávila-Arcos MC, Verduzco-Castro EA, Montero-Morán G, Gaytán P, et al. Insights into the evolution of enzyme substrate promiscuity after the discovery of $\beta\alpha_8$ isomerase evolutionary intermediates from a diverse metagenome. *BMC Evolutionary Biology.* 2015;15. doi:10.1186/s12862-015-0378-1
56. Garcia-Seisdedos H, Ibarra-Molero B, Sanchez-Ruiz JM. Probing the Mutational Interplay between Primary and Promiscuous Protein Functions: A Computational-Experimental Approach. *PLOS Computational Biology.* 2012;8: e1002558. doi:10.1371/journal.pcbi.1002558
57. Nesvizhskii AI, Vitek O, Aebersold R. Analysis and validation of proteomic data generated by tandem mass spectrometry. *Nature Methods.* 2007;4: 787–797. doi:10.1038/nmeth1088
58. Campbell I. Biophysical Techniques - Paperback - Iain D. Campbell - Oxford University Press [Internet]. 2012. Available: <https://global.oup.com/ushe/product/biophysical-techniques-9780199642144?cc=mx&lang=en&>
59. Yang JY, Sanchez LM, Rath CM, Liu X, Boudreau PD, Bruns N, et al. Molecular Networking as a Dereplication Strategy. *Journal of Natural Products.* 2013;76:

- 1686–1699. doi:10.1021/np400413s
60. Köcher T, Superti-Furga G. Mass spectrometry-based functional proteomics: From molecular machines to protein networks. *Nature Methods*. 2007;4: 807–815. doi:10.1038/nmeth1093
61. James LC, Tawfik DS. Conformational diversity and protein evolution – a 60-year-old hypothesis revisited. *Trends in Biochemical Sciences*. 2003;28: 361–368. doi:10.1016/S0968-0004(03)00135-X
62. Parisi G, Zea DJ, Monzon AM, Marino-Buslje C. Conformational diversity and the emergence of sequence signatures during evolution. *Current Opinion in Structural Biology*. 2015;32: 58–65. doi:10.1016/j.sbi.2015.02.005
63. Javier Zea D, Miguel Monzon A, Fornasari MS, Marino-Buslje C, Parisi G. Protein Conformational Diversity Correlates with Evolutionary Rate. *Molecular Biology and Evolution*. 2013;30: 1500–1503. doi:10.1093/molbev/mst065
64. Gatti-Lafranconi P, Hollfelder F. Flexibility and Reactivity in Promiscuous Enzymes. *ChemBioChem*. 2013;14: 285–292. doi:10.1002/cbic.201200628
65. Cruz-Morales P, Kopp JF, Martínez-Guerrero C, Yáñez-Guerra LA, Selem-Mojica N, Ramos-Aboites H, et al. Phylogenomic Analysis of Natural Products Biosynthetic Gene Clusters Allows Discovery of Arseno-Organic Metabolites in Model Streptomycetes. *Genome Biology and Evolution*. 2016;8: 1906–1916. doi:10.1093/gbe/evw125
66. Li L, Stoeckert CJ, Roos DS. OrthoMCL: Identification of Ortholog Groups for Eukaryotic Genomes. *Genome Research*. 2003;13: 2178–2189. doi:10.1101/gr.1224503
67. Waterhouse RM, Tegenfeldt F, Li J, Zdobnov EM, Kriventseva EV. OrthoDB: A hierarchical catalog of animal, fungal and bacterial orthologs. *Nucleic Acids Research*. 2013;41: D358–D365. doi:10.1093/nar/gks1116
68. Gao B, Gupta RS. Phylogenetic Framework and Molecular Signatures for the Main Clades of the Phylum Actinobacteria. *Microbiology and Molecular Biology Reviews : MMBR*. 2012;76: 66–112. doi:10.1128/MMBR.05011-11
69. Sen A, Daubin V, Abrouk D, Gifford I, Berry AM, Normand P. Phylogeny of the class Actinobacteria revisited in the light of complete genomes. The orders “Frankiales” and Micrococcales should be split into coherent entities: Proposal of Frankiales ord. nov., Geodermatophilales ord. nov., Acidothermales ord. nov. and Nakamurellales ord. nov. *International Journal of Systematic and Evolutionary Microbiology*. 2014;64: 3821–3832. doi:10.1099/ijss.0.063966-0
70. Zhou Z, Gu J, Li Y-Q, Wang Y. Genome plasticity and systems evolution in Streptomyces. *BMC Bioinformatics*. 2012;13: S8. doi:10.1186/1471-2105-13-S10-

S8

71. Kim J-N, Kim Y, Jeong Y, Roe J-H, Kim B-G, Cho B-K. Comparative Genomics Reveals the Core and Accessory Genomes of Streptomyces Species. *Journal of Microbiology and Biotechnology*. 2015;25: 1599–1605. doi:10.4014/jmb.1504.04008
72. Nam H, Lewis NE, Lerman JA, Lee D-H, Chang RL, Kim D, et al. Network Context and Selection in the Evolution to Enzyme Specificity. *Science*. 2012;337: 1101–1104. doi:10.1126/science.1216861
73. Copley SD. An Evolutionary Biochemist's Perspective on Promiscuity. *Trends in biochemical sciences*. 2015;40: 72–78. doi:10.1016/j.tibs.2014.12.004
74. Divergent Evolution of Enzymatic Function: Mechanistically Diverse Superfamilies and Functionally Distinct Suprafamilies. *Annual Review of Biochemistry*. 2001;70: 209–246. doi:10.1146/annurev.biochem.70.1.209
75. Huang R, Hippauf F, Rohrbeck D, Haustein M, Wenke K, Feike J, et al. Enzyme functional evolution through improved catalysis of ancestrally nonpreferred substrates. *Proceedings of the National Academy of Sciences*. 2012;109: 2966–2971. doi:10.1073/pnas.1019605109
76. Fondi M, Emiliani G, Liò P, Gribaldo S, Fani R. The evolution of histidine biosynthesis in archaea: Insights into the his genes structure and organization in LUCA. *Journal of Molecular Evolution*. 2009;69: 512–526. doi:10.1007/s00239-009-9286-6
77. Merino E, Jensen RA, Yanofsky C. Evolution of bacterial trp operons and their regulation. *Current opinion in microbiology*. 2008;11: 78–86. doi:10.1016/j.mib.2008.02.005
78. Verduzco-Castro EA, Michalska K, Endres M, Juárez-Vazquez AL, Noda-García L, Chang C, et al. Co-occurrence of analogous enzymes determines evolution of a novel $\beta\alpha_8$ -isomerase sub-family after non-conserved mutations in flexible loop. *Biochemical Journal*. 2016;473: 1141–1152. doi:10.1042/BJ20151271
79. Noda-Garcia L. Estudio de la evolución molecular de la función enzimática susando como modelo una enzima con características ancestrales. PhD thesis, Langebio, CINVESTAV. 2012.
80. Petrenko R, Meller J. Molecular Dynamics. eLS. John Wiley & Sons, Ltd; 2001. Available: <http://onlinelibrary.wiley.com/doi/10.1002/9780470015902.a0003048.pub2/abstract>
81. Molecular Modeling of Proteins Andreas Kukol Springer [Internet]. Available: <http://www.springer.com/us/book/9781588298645>
82. Sikosek T, Chan HS. Biophysics of protein evolution and evolutionary protein biophysics. *Journal of The Royal Society Interface*. 2014;11: 20140419.

- doi:10.1098/rsif.2014.0419
83. Zhou R. Replica Exchange Molecular Dynamics Method for Protein Folding Simulation. In: Bai Y, Nussinov R, editors. *Protein Folding Protocols*. Humana Press; 2006. pp. 205–223. Available: <http://dx.doi.org/10.1385/1-59745-189-4%3A205>
 84. Bisswanger H. General Aspects of Enzyme Analysis. *Practical Enzymology*. Wiley-VCH Verlag GmbH & Co. KGaA; 2011. pp. 5–91. Available: <http://onlinelibrary.wiley.com/doi/10.1002/9783527659227.ch2/summary>
 85. Hommel U, Eberhard M, Kirschner K. Phosphoribosyl Anthranilate Isomerase Catalyzes a Reversible Amadori Reaction. *Biochemistry*. 1995;34: 5429–5439. doi:10.1021/bi00016a014
 86. Scheer M, Grote A, Chang A, Schomburg I, Munaretto C, Rother M, et al. BRENDA, the enzyme information system in 2011. *Nucleic Acids Research*. 2011;39: D670–D676. doi:10.1093/nar/gkq1089
 87. Van Der Spoel D, Lindahl E, Hess B, Groenhof G, Mark AE, Berendsen HJC. GROMACS: Fast, flexible, and free. *Journal of Computational Chemistry*. 2005;26: 1701–1718. doi:10.1002/jcc.20291
 88. Odokonyero D, Sakai A, Patskovsky Y, Malashkevich VN, Fedorov AA, Bonanno JB, et al. Loss of quaternary structure is associated with rapid sequence divergence in the OSBS family. *Proceedings of the National Academy of Sciences of the United States of America*. 2014;111: 8535–8540. doi:10.1073/pnas.1318703111
 89. Osbourn A. Gene Clusters for Secondary Metabolic Pathways: An Emerging Theme in Plant Biology. *Plant Physiology*. 2010;154: 531–535. doi:10.1104/pp.110.161315
 90. Makarova KS, Aravind L, Galperin MY, Grishin NV, Tatusov RL, Wolf YI, et al. Comparative Genomics of the Archaea (Euryarchaeota): Evolution of Conserved Protein Families, the Stable Core, and the Variable Shell. *Genome Research*. 1999;9: 608–628. doi:10.1101/gr.9.7.608
 91. Harvey AL, Edrada-Ebel R, Quinn RJ. The re-emergence of natural products for drug discovery in the genomics era. *Nature Reviews Drug Discovery*. 2015;14: 111–129. doi:10.1038/nrd4510
 92. Benedict MN, Gonnerman MC, Metcalf WW, Price ND. Genome-Scale Metabolic Reconstruction and Hypothesis Testing in the Methanogenic Archaeon *Methanosarcina acetivorans* C2A. *Journal of Bacteriology*. 2012;194: 855–865. doi:10.1128/JB.06040-11
 93. Seitz KW, Lazar CS, Hinrichs K-U, Teske AP, Baker BJ. Genomic reconstruction of a novel, deeply branched sediment archaeal phylum with pathways for acetogenesis and sulfur reduction. *The ISME Journal*. 2016;10: 1696–1705.

- doi:10.1038/ismej.2015.233
94. Moustafa A, Loram JE, Hackett JD, Anderson DM, Plumley FG, Bhattacharya D. Origin of Saxitoxin Biosynthetic Genes in Cyanobacteria. *PLOS ONE*. 2009;4: e5758. doi:10.1371/journal.pone.0005758
 95. Medema MH, Osbourn A. Computational genomic identification and functional reconstitution of plant natural product biosynthetic pathways. *Natural Product Reports*. 2016;33: 951–962. doi:10.1039/c6np00035e
 96. Medema MH, Kottmann R, Yilmaz P, Cummings M, Biggins JB, Blin K, et al. Minimum Information about a Biosynthetic Gene cluster. *Nature Chemical Biology*. 2015;11: 625–631. doi:10.1038/nchembio.1890
 97. Iqbal HA, Low-Beinart L, Obiajulu JU, Brady SF. Natural Product Discovery through Improved Functional Metagenomics in Streptomyces. *Journal of the American Chemical Society*. 2016;138: 9341–9344. doi:10.1021/jacs.6b02921
 98. Ulas T, Riemer SA, Zaparty M, Siebers B, Schomburg D. Genome-Scale Reconstruction and Analysis of the Metabolic Network in the Hyperthermophilic Archaeon Sulfolobus Solfataricus. *PLoS ONE*. 2012;7. doi:10.1371/journal.pone.0043401
 99. Charlesworth JC, Burns BP. Untapped Resources: Biotechnological Potential of Peptides and Secondary Metabolites in Archaea. *Archaea*. 2015;2015: e282035. doi:10.1155/2015/282035
 100. Computational Pan-Genomics Consortium. Computational pan-genomics: Status, promises and challenges. *Briefings in Bioinformatics*. 2016; doi:10.1093/bib/bbw089
 101. Chan C, Jayasekera S, Kao B, Páramo M, Grotthuss M von, Ranz JM. Remodelling of a homeobox gene cluster by multiple independent gene reunions in *Drosophila*. *Nature Communications*. 2015;6: 6509. doi:10.1038/ncomms7509
 102. Rinke C, Schwientek P, Sczyrba A, Ivanova NN, Anderson IJ, Cheng J-F, et al. Insights into the phylogeny and coding potential of microbial dark matter. *Nature*. 2013;499: 431–437. doi:10.1038/nature12352
 103. Castelle CJ, Wrighton KC, Thomas BC, Hug LA, Brown CT, Wilkins MJ, et al. Genomic Expansion of Domain Archaea Highlights Roles for Organisms from New Phyla in Anaerobic Carbon Cycling. *Current Biology*. 2015;25: 690–701. doi:10.1016/j.cub.2015.01.014
 104. Spang A, Saw JH, Jørgensen SL, Zaremba-Niedzwiedzka K, Martijn J, Lind AE, et al. Complex archaea that bridge the gap between prokaryotes and eukaryotes. *Nature*. 2015;521: 173–179. doi:10.1038/nature14447
 105. Koonin EV. Archaeal ancestors of eukaryotes: Not so elusive any more. *BMC*

- Biology. 2015;13. doi:10.1186/s12915-015-0194-5
106. Chaudhari NM, Gupta VK, Dutta C. BPGA- an ultra-fast pan-genome analysis pipeline. *Scientific Reports.* 2016;6: 24373. doi:10.1038/srep24373
107. Glass JI, Assad-Garcia N, Alperovich N, Yooseph S, Lewis MR, Maruf M, et al. Essential genes of a minimal bacterium. *Proceedings of the National Academy of Sciences of the United States of America.* 2006;103: 425–430. doi:10.1073/pnas.0510013103
108. Narechania A, Baker RH, Sit R, Kolokotronis S-O, DeSalle R, Planet PJ. Random Addition Concatenation Analysis: A Novel Approach to the Exploration of Phylogenomic Signal Reveals Strong Agreement between Core and Shell Genomic Partitions in the Cyanobacteria. *Genome Biology and Evolution.* 2012;4: 30–43. doi:10.1093/gbe/evr121
109. Stamatakis A. RAxML version 8: A tool for phylogenetic analysis and post-analysis of large phylogenies. *Bioinformatics.* 2014;30: 1312–1313. doi:10.1093/bioinformatics/btu033
110. Powerful tree graphics with ggplot2 [Internet]. Available: http://joey711.github.io/phyloseq/plot_tree-examples.html
111. Zacharia VM, Traxler MF. Exploring new horizons. *eLife.* 2017;6: e23624. doi:10.7554/eLife.23624
112. Woese C. The universal ancestor. *Proceedings of the National Academy of Sciences.* 1998;95: 6854–6859. Available: <http://www.pnas.org/content/95/12/6854>
113. Woese CR, Gupta R. Are archaebacteria merely derived “prokaryotes”? *Nature.* 1981;289: 95–96. doi:10.1038/289095a0
114. Woese CR, Kandler O, Wheelis ML. Towards a natural system of organisms: Proposal for the domains Archaea, Bacteria, and Eucarya. *Proceedings of the National Academy of Sciences of the United States of America.* 1990;87: 4576–4579.
115. Woese CR, Fox GE. Phylogenetic structure of the prokaryotic domain: The primary kingdoms. *Proceedings of the National Academy of Sciences of the United States of America.* 1977;74: 5088–5090. Available: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC432104/>
116. Woese CR. There must be a prokaryote somewhere: Microbiology’s search for itself. *Microbiological Reviews.* 1994;58: 1–9. Available: <http://mmbrr.asm.org/content/58/1/1>
117. Graham DE, Overbeek R, Olsen GJ, Woese CR. An archaeal genomic signature. *Proceedings of the National Academy of Sciences.* 2000;97: 3304–3308.

- doi:10.1073/pnas.97.7.3304
118. Howland JL. *The surprising archaea: Discovering another domain of life.* New York: Oxford University; 2000.
 119. Xu Y, Gogarten JP. *Computational Methods for Understanding Bacterial and Archaeal Genomes.* World Scientific; 2008.
 120. Garrett RA, Klenk H-P. *Archaea: Evolution, Physiology, and Molecular Biology.* John Wiley & Sons; 2008.
 121. Koonin EV, Mushegian AR, Galperin MY, Walker DR. Comparison of archaeal and bacterial genomes: Computer analysis of protein sequences predicts novel functions and suggests a chimeric origin for the archaea. *Molecular Microbiology.* 1997;25: 619–637. doi:10.1046/j.1365-2958.1997.4821861.x
 122. Koonin EV, Wolf YI. Genomics of bacteria and archaea: The emerging dynamic view of the prokaryotic world. *Nucleic Acids Research.* 2008;36: 6688–6719. doi:10.1093/nar/gkn668
 123. Koonin EV. The Turbulent Network Dynamics of Microbial Evolution and the Statistical Tree of Life. *Journal of Molecular Evolution.* 2015;80: 244–250. doi:10.1007/s00239-015-9679-7
 124. Land M, Hauser L, Jun S-R, Nookaew I, Leuze MR, Ahn T-H, et al. Insights from 20 years of bacterial genome sequencing. *Functional & Integrative Genomics.* 2015;15: 141–161. doi:10.1007/s10142-015-0433-4
 125. Nishida H. Evolution of genome base composition and genome size in bacteria. *Frontiers in Microbiology.* 2012;3. doi:10.3389/fmicb.2012.00420
 126. Coyle M, Hu J, Gartner Z. Mysteries in a Minimal Genome. *ACS Central Science.* 2016;2: 274–277. doi:10.1021/acscentsci.6b00110
 127. O'Meara B. CRAN Task View: Phylogenetics, Especially Comparative Methods. 2016; Available: <https://CRAN.R-project.org/view=Phylogenetics>
 128. Larsson J, Nylander JA, Bergman B. Genome fluctuations in cyanobacteria reflect evolutionary, developmental and adaptive traits. *BMC Evolutionary Biology.* 2011;11: 187. doi:10.1186/1471-2148-11-187
 129. Whitton BA. *Ecology of Cyanobacteria II: Their Diversity in Space and Time.* Springer Science & Business Media; 2012.
 130. Cohen GN. The biosynthesis of histidine and its regulation. *Microbial Biochemistry.* Springer Netherlands; 2004. pp. 225–230. Available: http://link.springer.com/chapter/10.1007/978-1-4020-2237-1_29
 131. Plach MG, Reisinger B, Sterner R, Merkl R. Long-Term Persistence of Bi-functionality Contributes to the Robustness of Microbial Life through Exaptation.

- PLOS Genetics. 2016;12: e1005836. doi:10.1371/journal.pgen.1005836
132. Battistuzzi FU, Feijao A, Hedges SB. A genomic timescale of prokaryote evolution: Insights into the origin of methanogenesis, phototrophy, and the colonization of land. *BMC Evolutionary Biology*. 2004;4: 44. doi:10.1186/1471-2148-4-44
133. Lapierre P, Gogarten JP. Estimating the size of the bacterial pan-genome. *Trends in Genetics*. 2009;25: 107–110. doi:10.1016/j.tig.2008.12.004
134. Větrovský T, Baldrian P. The Variability of the 16S rRNA Gene in Bacterial Genomes and Its Consequences for Bacterial Community Analyses. *PLoS ONE*. 2013;8. doi:10.1371/journal.pone.0057923
135. Brettin T, Davis JJ, Disz T, Edwards RA, Gerdes S, Olsen GJ, et al. RASTtk: A modular and extensible implementation of the RAST algorithm for building custom annotation pipelines and annotating batches of genomes. *Scientific Reports*. 2015;5: 8365. doi:10.1038/srep08365
136. chesterismay. Updated R Markdown thesis template [Internet]. Chester's R blog. 2016. Available: <https://chesterismay.wordpress.com/2016/09/01/updated-r-markdown-thesis-template/>
137. Barona-Gómez F, Cruz-Morales P, Noda-García L. What can genome-scale metabolic network reconstructions do for prokaryotic systematics? *Antonie van Leeuwenhoek*. 2012;101: 35–43. doi:10.1007/s10482-011-9655-1
138. Weber T, Blin K, Duddela S, Krug D, Kim HU, Bruccoleri R, et al. antiSMASH 3.0—a comprehensive resource for the genome mining of biosynthetic gene clusters. *Nucleic Acids Research*. 2015;43: W237–W243. doi:10.1093/nar/gkv437
139. Medema MH, Blin K, Cimermancic P, Jager V de, Zakrzewski P, Fischbach MA, et al. antiSMASH: Rapid identification, annotation and analysis of secondary metabolite biosynthesis gene clusters in bacterial and fungal genome sequences. *Nucleic Acids Research*. 2011;39: W339–W346. doi:10.1093/nar/gkr466
140. Molina ST, Borkovec TD. The Penn State worry questionnaire: Psychometric properties and associated characteristics. In: Davey GCL, Tallis F, editors. *Worrying: Perspectives on theory, assessment and treatment*. New York: Wiley; 1994. pp. 265–283.
141. Reed College. LaTeX your document [Internet]. 2007. Available: <http://web.reed.edu/cis/help/LaTeX/index.html>
142. Noble SG. Turning images into simple line-art. Undergraduate thesis, Reed College. 2002.