

生物信息学

天津医科大学
生物医学工程与技术学院

2018-2019 学年上学期 (秋)
2016 级生信班

第五章 基因组功能注释分析

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天津医科大学 (TJMU)
生物医学工程与技术学院

2018 年 12 月



章节内容概览

5.1,5.2 基因组功能注释分析基础

- ① 基础知识：组装版本，坐标系统，常用格式，逻辑运算模式
- ② 准备工作：坐标转换，格式转换，逻辑运算

5.3 基因组功能的高级注释

- ① 高级注释：变异位点注释，富集分析，序列标识

5.3 Galaxy 分析平台

- ① Galaxy 分析平台：简介，使用



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- 1 引言
- 2 基因组组装版本
- 3 基因组坐标系统
- 4 基因组注释常用格式
- 5 基因组坐标的逻辑运算
- 6 总结与答疑
- 7 引言
- 8 变异位点的注释

- 9 基因集富集分析
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- 16 复习思考题

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复习思考题



基因组注释 (genome annotation)

从原始的基因组核酸序列中挖掘有用的生物学信息并阐释其生物学含义，包括基因组结构注释和基因组功能注释两大部分。

基因组结构注释 (structural annotation)

在基因组序列中寻找基因等功能元件并明确其基本结构。

基因组功能注释 (functional annotation)

在结构注释的基础上，将进化保守性 (evolutionary conservation) 和基因本体论 (gene ontology) 等元数据 (meta-data) 与功能元件对应起来，找到其生物学功能。



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基因组注释

- 结构注释 ⇐ 实验手段，单个基因

- 限制性酶切位点分析、开放阅读框分析、启动子分析、CpG 岛识别
- 重复序列分析、基因识别
- mRNA 选择性剪接分析

- 功能注释 ⇐ 组学时代，复杂疾病

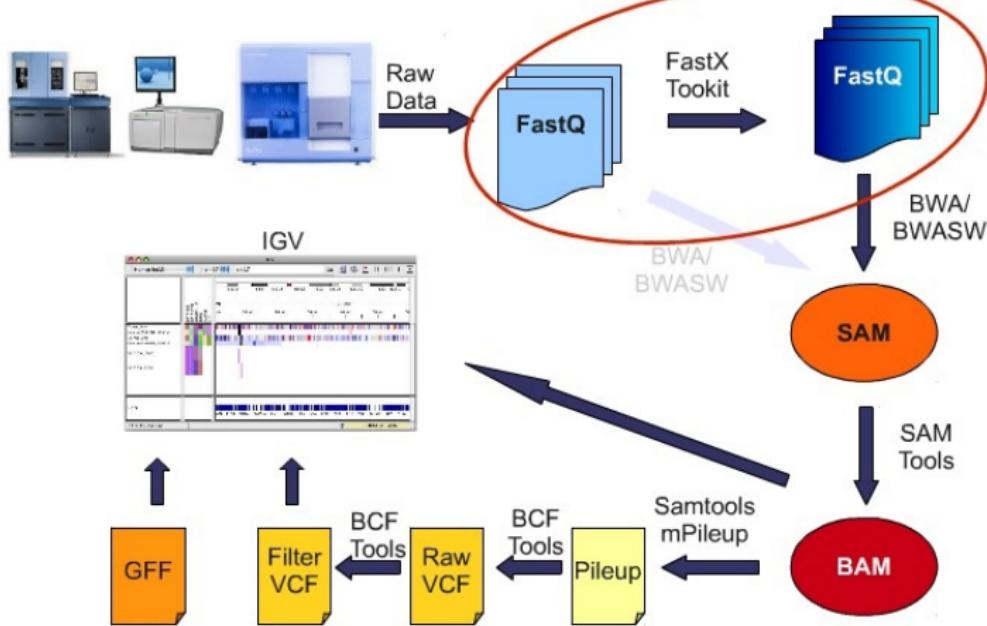
- 变异位点的注释
- 基因集富集分析
- 生物学通路分析
- 相互作用网络分析
- 分子进化分析



- 基因组组装版本
- 基因组坐标系统
- 注释常用格式
- 文本编辑器
- 坐标的逻辑运算



Sequence to Variation Workflow



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- These sequences were mapped to human and mouse genomes sequences ([hg18 and mm9](#), respectively) using BLASTN.
- We used DNA sequences from the human and mouse genome assemblies [hg18 and mm9](#).
- Currently there are 25,000 genes annotated in the human ([hg18](#)) and mouse ([mm9](#)) genome, which comprise less than 3% of the genome (UCSC genome browser; <http://genome.ucsc.edu/>).
- The [GRCh37/hg19](#) and [GRCm38/mm10](#) assemblies at the UCSC genome browser (<http://genome.ucsc.edu/>) were used for mapping the chromosomal defect and gene annotations.
- The genome assemblies from which the sequences obtained were Dec 2011 ([GRCm38/mm10](#)), Feb 2009 ([GRCh37/hg19](#)) and Nov 2004 ([Baylor3.4/rn4](#)) for mouse, human and rat respectively.



基因组序列不是确定的吗？也需要版本升级？

SPECIES	UCSC	DATE	NCBI
Human	hg38	Dec. 2013	GRCh38
	hg19	Feb. 2009	GRCh37
	hg18	Mar. 2006	NCBI Build 36.1
	hg17	May 2004	NCBI Build 35
	hg16	Jul. 2003	NCBI Build 34
Mouse	mm10	Dec. 2011	GRCm38
	mm9	Jul. 2007	NCBI Build 37
	mm8	Feb. 2006	NCBI Build 36
	mm7	Aug. 2005	NCBI Build 35

human: *Homo sapiens*; mouse: *Mus musculus*

hg: human genome; GRC: Genome Reference Consortium



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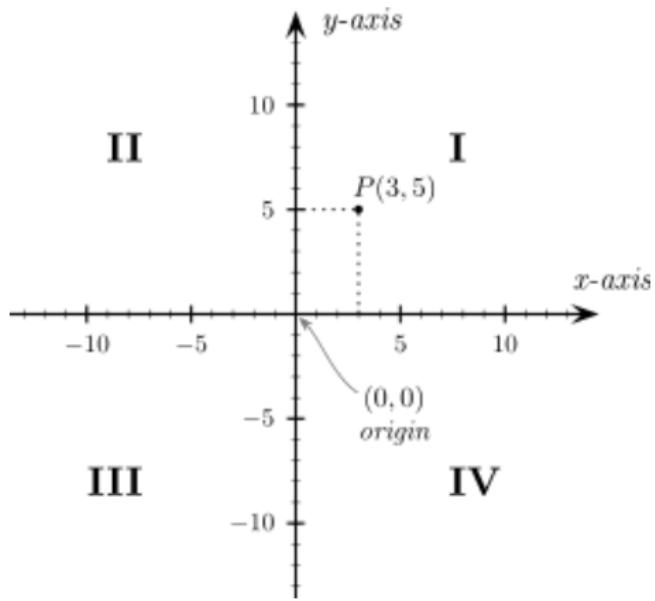
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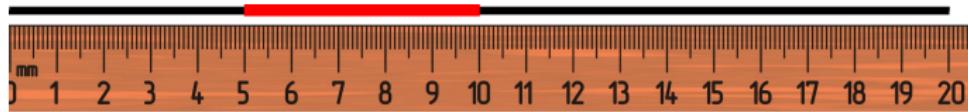
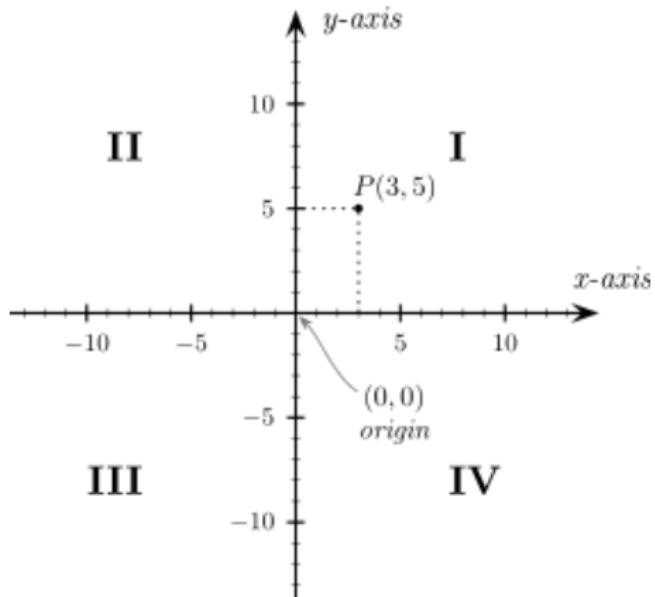
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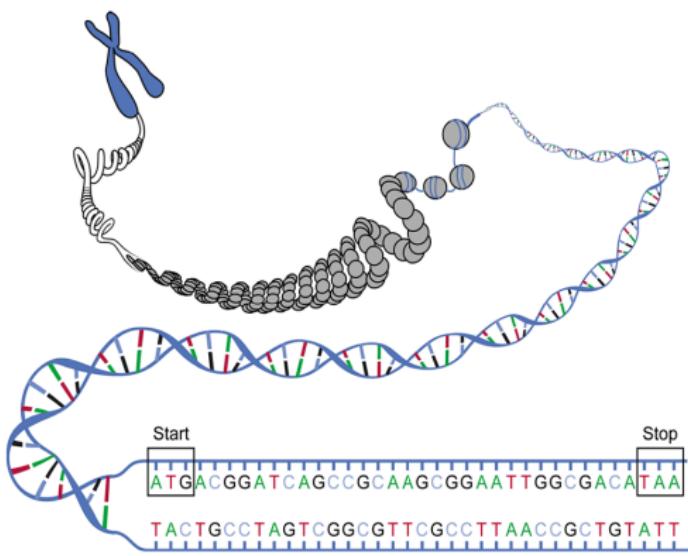
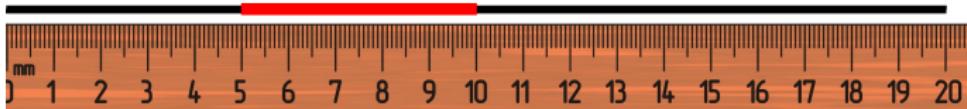
坐标系统 | 坐标轴



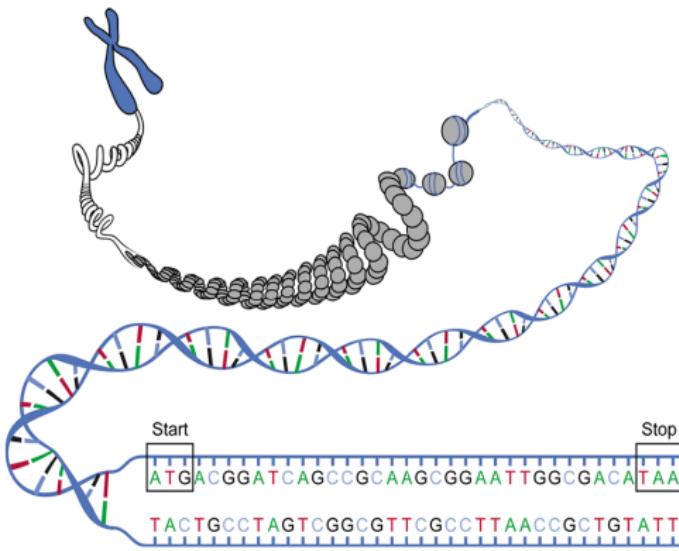
坐标系统 | 坐标轴



坐标系统 | 坐标轴



坐标系统 | 坐标轴



hg19

- SNP, rs1800468: “chr19 41860587”; “chr19:41860587”
- gene, *SAMD11*: “chr1 861121 879961”; “chr1:861121-879961”

坐标系统 | 两大系统

序列

0-based index	0	1	2	3	4	5	6	7
Sequence	A	A	T	T	G	G	C	C
1-based index	1	2	3	4	5	6	7	8

TG 的坐标

- 0-based, half-open : [3,5)
- 1-based, fully-closed : [4,5]

实例

- 0-based : BED、BAM、PSL、dbSNP、Table Browser
- 1-based : GFF、VCF、SAM、Wiggle、DAS、Genome Browser

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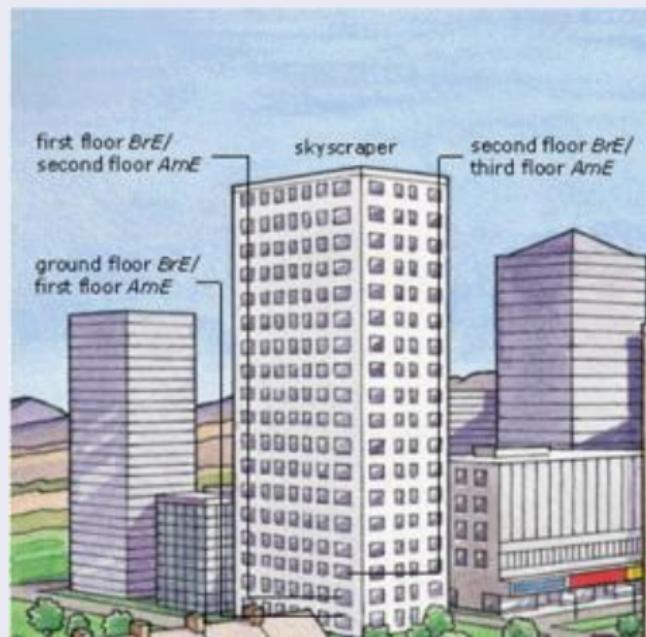
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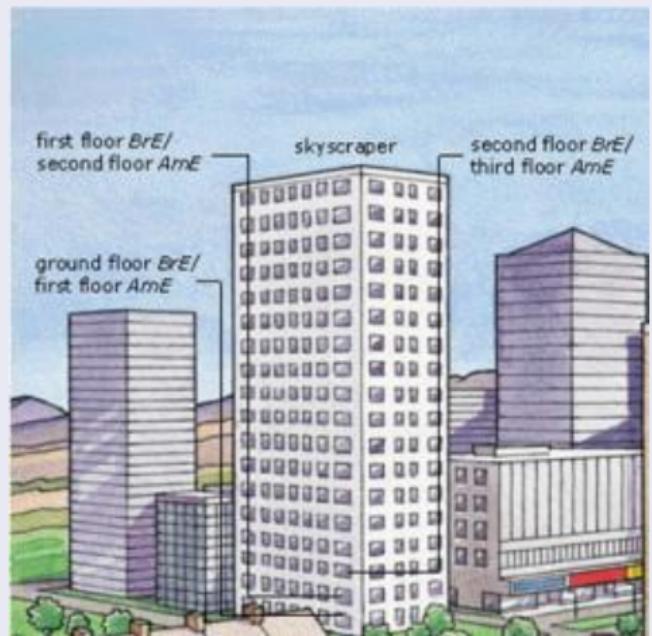
坐标系统 | 类比

first floor

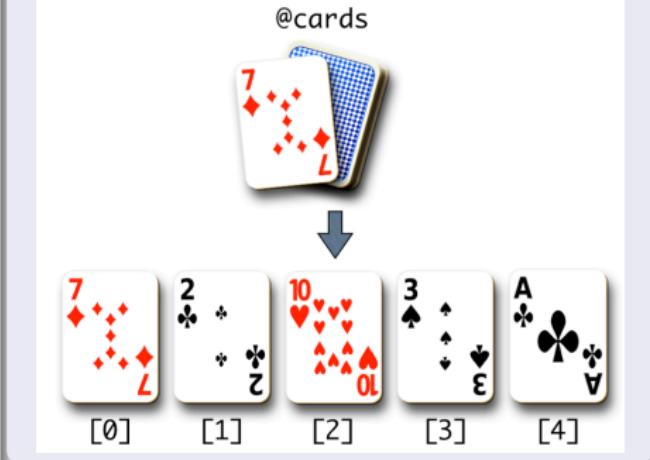


坐标系统 | 类比

first floor



数组



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格式 | 文件格式



EPS



FLA



HTML



GIF



IND



PHP



PPT



PDF



XLS



DOC



MOV



CSS



WAV



JPG



ZIP



MP3

NO.20111025194911037377



格式 | FASTA

```
>gi|183121|gb|M29645.1|HUMGFI Human insulin-like growth factor II mRNA, complete cds  
CAGGGGCCAAGAGTCACCACCGAGCTGTGAGGAGGTGGATTCCAGCCCCAGCCCCAGGGCTCT  
GAATCGCTGCCAGCTCAGCCCCCTGCCAGCCTGCCACAGCCTGAGCCCCAGCAGGCCAGAGAGCCA  
GTCCTGAGGTGAGCTGCTGTGGCTGTGGCCAGGGCACCCCAGCCTCCCAGAACGTGAGGCTGGCAGCCA  
GCCCCAGCCTCAGCCCCAACTGCGAGGCAGAGAGACACCAATGGGAATGCAATGGGAAGTCGATGCTG  
GTGCTTCTCACCTTCTTGGCTTCGCCTCGTGCATTGCTGCTTACCGCCCCAGTGAGACCCCTGTGCG  
GCGGGGAGCTGGGGACACCCCTCCAGTCGCTGTGGGGACCGCGCTCTACTTCAGCAGGCCGCAAG  
CCGTGTGAGCCGTCGCAGCGTGGCATCGTTGAGGAGTGCTGTTCCGCACTGTGACCTGGCCCTCCTG  
GAGACGTACTGTGCTACCCCGCCAAGTCCGAGAGGGACGTGTCACCCCTCCGACCGTGCTTCCGGACA  
ACTTCCCCAGATAACCCGTGGCAAGTTCTCCAATATGACACCTGGAAGCAGTCCACCCAGCGCCTGCG  
CAGGGGCCTGCCTGCCCTCTGCGTGCCGCCGGGTCACGTGCTGCCAAGGAGCTGAGGCCTCAGG  
GAGGCCAAACGTACCGTCCCTGATTGCTCTACCCACCCAAAGACCCCGCCACGGGGCGCCCCCCCAG  
AGATGGCCAGCAATCGGAAGTGAGCAAAACTGCCAAGTCTGCAAGCCGGCGCCACCATCCTGAGCCT  
CCTCCTGACCACGGACGTTCCATCAGGTTCCATCCGAAATCTCTCGGTTCCACGTCCCCCTGGGCTT  
CTCCTGACCCAGTCCCCGTCCCCGCCCTCCCCGAAACAGGCTACTCTCCTGGCCCCCTCCATGGGCTG  
AGGAAGCACAGCAGCATTTCAAACATGTACAAATGATTGGCTTAAACACCTTACACATACCT
```



- 每一行最好不要超过 80 个字符
- 序列中的换行符不会影响序列的连续性
- 使用标准的 IUB/IUPAC 核酸代码和氨基酸代码
- 允许小写字母的存在，但会转换成大写
- 单个 “-” 代表不明长度的空位
- 在氨基酸序列中允许出现 “U” 和 “*”
- 任何数字都应该被去掉或转换成字母
- 不明核酸和氨基酸分别用 “N” 和 “X” 表示



格式 | FASTA | IUB/IUPAC 核酸

Code	Meaning	Code	Meaning
A	Adenine	Y	Pyrimidine (C, T, or U)
C	Cytosine	K	T, U, or G (keto)
G	Guanine	W	T, U, or A (weak)
T	Thymine	B	C, T, U, or G (not A)
U	Uracil	D	A, T, U, or G (not C)
R	Purine (A or G)	H	A, T, U, or C (not G)
S	C or G (strong)	V	A, C, or G (not T, not U)
M	C or A (amino)	N	Any base (A, C, G, T, or U)
X	masked	-	gap of indeterminate length



格式 | FASTA | IUB/IUPAC 氨基酸

1	3	Meaning	1	3	Meaning
A	Ala	Alanine	B	Asx	Aspartic acid or Asparagine
C	Cys	Cysteine	D	Asp	Aspartic acid
E	Glu	Glutamic acid	F	Phe	Phenylalanine
G	Gly	Glycine	H	His	Histidin
I	Ile	Isoleucine	K	Lys	Lysine
L	Leu	Leucine	M	Met	Methionine
N	Asn	Asparagine	P	Pro	Proline
Q	Gln	Glutamine	R	Arg	Arginine
S	Ser	Serine	T	Thr	Threonine
U	Sec	Selenocysteine	V	Val	Valine
W	Trp	Tryptophan	X	Xaa	Any amino acid
Y	Tyr	Tyrosine	Z	Glx	Glutamine or Glutamic acid
*		translation stop	-		gap of indeterminate length
O	Pyl	Pyrrolysine			



格式 | FASTA | FASTA vs. Sequence

FASTA

```
>gi|183121|gb|M29645.1|HUMGFI Human insulin-like growth factor II mRNA, complete cds  
CAGGGGCCGAAGAGTCACCACCGAGCTTGTGAGGAGGTGGATTCCAGCCCCAGCCCCAGGGCTCT  
GAATCGCTGCCAGCTCAGCCCCCTGCCAGCCTGCCACAGCCTGAGCCCCAGCAGGCCAGAGGCCA  
GTCCTGAGGTGAGCTGCTGTGGCCTGTGGCCAGGGCAGCCCCAGCGCTCCAGAACGTGAGGCTGGCAGCCA  
GCCCGAGCCTCAGCCCCAACTTGCAGGGCAGAGAGACACCAATGGGAATGCCAATGGGAAGTCGATGCTG  
GTGCTTCTCACCTTCTTGGCTTCGCCCTGCTGCTGATTGCTGTTACCGCCCCAGTGAGACCCCTGTGCG  
GCGGGGAGCTGGTGGACACCCCTCCAGTTGCTCTGTGGGACCCGGCTTCACTTCAGCAGGCCGCAAG  
CCGTGTGAGCCGTCGAGCGTGGCATCGTTGAGGAGTGCTGTTCCGCAAGCTGTGACCTGGCCCTCTG  
GAGACGTACTGTGCTACCCCGCCAAGTCCAGAGGGACGTGTCGACCCCTCGACCGTGCTCCGGACA  
ACTTCCCCAGATAACCCGTGGCAAGTTCTTCAAATATGACACCTGGAAGCAGTCCACCCAGCGCTGCG  
CAGGGGCTGCCCTGCCCTCTGCGTGCCTGCCGGGTCACTGCTCGCCAAGGAGCTCGAGGCCTTCAGG  
GAGGCCAAACGTCAACCGTCCCCGTATTGCTCTACCCACCCAAAGACCCCGCCACGGGGCGCCCCCAG  
AGATGGCCAGCAATCGGAAGTGAGCAAACACTGCCAAGTCTGCAAGCCGGGCCACCATCCTGAGCCT  
CCTCTGACCCAGCCCCGTGCCCCGCCCTCCCGAAACAGGCTACTCTCCTCGGCCCCCTCATGGCTG  
AGGAAGCACAGCAGCATCTCAAACATGTACAAATGATTGGCTTAAACACCTTACATACCT
```

Sequence

- GTACGACGGAGTGTTATAAGATGGAAATCGGATACCAGATGAAATTGTGGATCAG
- MWTALPLLCAGAWLLSAGATAELTVNAIEKFHFTSWMKQHQKTYSSREYSHRLQVFAN

格式 | BED (Browser Extensible Data)

chr7	127471196	127472363	Pos1	0	+	127471196	127472363	255,0,0
chr7	127472363	127473530	Pos2	0	+	127472363	127473530	255,0,0
chr7	127473530	127474697	Pos3	0	+	127473530	127474697	255,0,0
chr7	127474697	127475864	Pos4	0	+	127474697	127475864	255,0,0
chr7	127475864	127477031	Neg1	0	-	127475864	127477031	0,0,255
chr7	127477031	127478198	Neg2	0	-	127477031	127478198	0,0,255
chr7	127478198	127479365	Neg3	0	-	127478198	127479365	0,0,255
chr7	127479365	127480532	Pos5	0	+	127479365	127480532	255,0,0
chr7	127480532	127481699	Neg4	0	-	127480532	127481699	0,0,255



BED#

BED12 包含全部 12 列

BED6 chrom, start, end, name, score, and strand

BED5 chrom, start, end, name, and score

BED4 chrom, start, end, and name

BED3 chrom, start, and end

例子

chr1	11873	14409	uc001aaa.3	0	+	11873	11873	0
3	354,109,1189,	0,739,1347,						



格式 | BED#

BED#

BED12 包含全部 12 列

BED6 chrom, start, end, name, score, and strand

BED5 chrom, start, end, name, and score

BED4 chrom, start, end, and name

BED3 chrom, start, and end

例子

chr1 11873 14409 uc001aaa.3 0 +



格式 | BED#

BED#

BED12 包含全部 12 列

BED6 chrom, start, end, name, score, and strand

BED5 chrom, start, end, name, and score

BED4 chrom, start, end, and name

BED3 chrom, start, and end

例子

chr1 11873 14409 uc001aaa.3 0



格式 | BED#

BED#

BED12 包含全部 12 列

BED6 chrom, start, end, name, score, and strand

BED5 chrom, start, end, name, and score

BED4 chrom, start, end, and name

BED3 chrom, start, and end

例子

chr1 11873 14409 uc001aaa.3



格式 | BED#

BED#

BED12 包含全部 12 列

BED6 chrom, start, end, name, score, and strand

BED5 chrom, start, end, name, and score

BED4 chrom, start, end, and name

BED3 chrom, start, and end

例子

chr1 11873 14409



格式 | GFF (General Feature Format)

```
##gff-version 3
ctg123 . operon      1300 15000 . + . ID=operon001;Name=superOperon
ctg123 . mRNA        1300 9000  . + . ID=mrna0001;Parent=operon001;Name=sonichedgehog
ctg123 . exon         1300 1500  . + . Parent=mrna0001
ctg123 . exon         1050 1500  . + . Parent=mrna0001
ctg123 . exon         3000 3902  . + . Parent=mrna0001
ctg123 . exon         5000 5500  . + . Parent=mrna0001
ctg123 . exon         7000 9000  . + . Parent=mrna0001
ctg123 . mRNA        10000 15000 . + . ID=mrna0002;Parent=operon001;Name=subsonicsquirrel
ctg123 . exon         10000 12000 . + . Parent=mrna0002
ctg123 . exon         14000 15000 . + . Parent=mrna0002
```



格式 | VCF (Variant Call Format)

```
##fileformat=VCFv4.0
##fileDate=20110705
##reference=1000GenomesPilot-NCBI37
##phasing=partial
##INFO=<ID=NS,Number=1,Type=Integer,Description="Number of Samples With Data">
##INFO=<ID=DP,Number=1,Type=Integer,Description="Total Depth">
##INFO=<ID=AF,Number=.,Type=Float,Description="Allele Frequency">
##INFO=<ID=AA,Number=1,Type=String,Description="Ancestral Allele">
##INFO=<ID=DB,Number=0,Type=Flag,Description="dbSNP membership, build 129">
##INFO=<ID=H2,Number=0,Type=Flag,Description="HapMap2 membership">
##FILTER=<ID=q10,Description="Quality below 10">
##FILTER=<ID=s50,Description="Less than 50% of samples have data">
##FORMAT=<ID=GQ,Number=1,Type=Integer,Description="Genotype Quality">
##FORMAT=<ID=GT,Number=1,Type=String,Description="Genotype">
##FORMAT=<ID=DP,Number=1,Type=Integer,Description="Read Depth">
##FORMAT=<ID=HQ,Number=2,Type=Integer,Description="Haplotype Quality">
```

#CHROM	POS	ID	REF	ALT	QUAL	FILTER	INFO	FORMAT	Sample1	Sample2	Sample3
2	4370	rs6057	G	A	29	.	NS=2;DP=13;AF=0.5;DB;H2	GT:GQ:DP:HQ	0 0:48:1:52,51	1 0:48:8:51,51	1 1:43:5:,,
2	7330	.	T	A	3	q10	NS=5;DP=12;AF=0.017	GT:GQ:DP:HQ	0 0:46:3:58,50	0 1:3:5:65,3	0 0:41:3
2	110696	rs6055	A	G,T	67	PASS	NS=2;DP=10;AF=0.333,0.667;AA=T;DB	GT:GQ:DP:HQ	1 2:21:6:23,27	2 1:2:0:18,2	2/2:35:4
2	130237	.	T	.	47	.	NS=2;DP=16;AA=T	GT:GQ:DP:HQ	0 0:54:7:56,60	0 0:48:4:56,51	0 0:61:2
2	134567	microsat1	GTCT	G,GTACT	50	PASS	NS=2;DP=9;AA=G	GT:GQ:DP	0 1:35:4	0 2:17:2	1 1:40:3



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逻辑运算 | 常见问题

数据

gene1	chr1	10	20	+
gene2	chr1	40	60	+
gene3	chr1	50	100	+
snp1	chr1	15		+
snp2	chr1	55		-
exon3.1	chr1	50	60	+
exon3.2	chr1	90	100	+

问题

- ① 找到 gene1 和 gene2 之间的基因间区域。
- ② snp1 在 gene1 上吗？snp2 在 gene1 上吗（, 在 gene2 上吗）？
- ③ 找到与 gene3 重叠和不重叠的基因？
- ④ 找到 gene3 的内含子区域。

逻辑运算 | 常见问题

数据

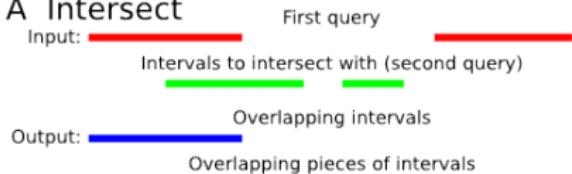
gene1	chr1	10	20	+
gene2	chr1	40	60	+
gene3	chr1	50	100	+
snp1	chr1	15		+
snp2	chr1	55		-
exon3.1	chr1	50	60	+
exon3.2	chr1	90	100	+

问题

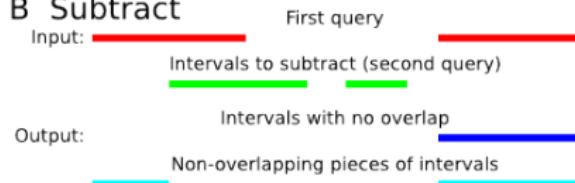
- ① 找到 gene1 和 gene2 之间的基因间区域。
- ② snp1 在 gene1 上吗？snp2 在 gene1 上吗（, 在 gene2 上吗）？
- ③ 找到与 gene3 重叠和不重叠的基因？
- ④ 找到 gene3 的内含子区域。

逻辑运算 | 运算模式

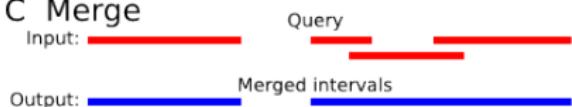
A Intersect



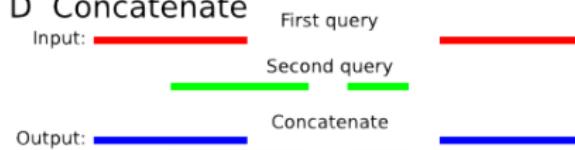
B Subtract



C Merge



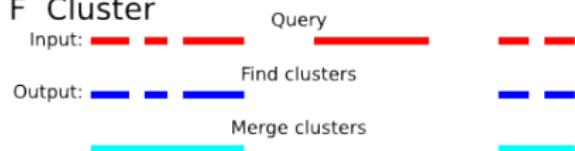
D Concatenate



E Complement



F Cluster



Genome arithmetic

intersect Find overlapping intervals in various ways.

subtract Remove intervals based on overlaps b/w two files.

merge Combine overlapping/nearby intervals into a single interval.

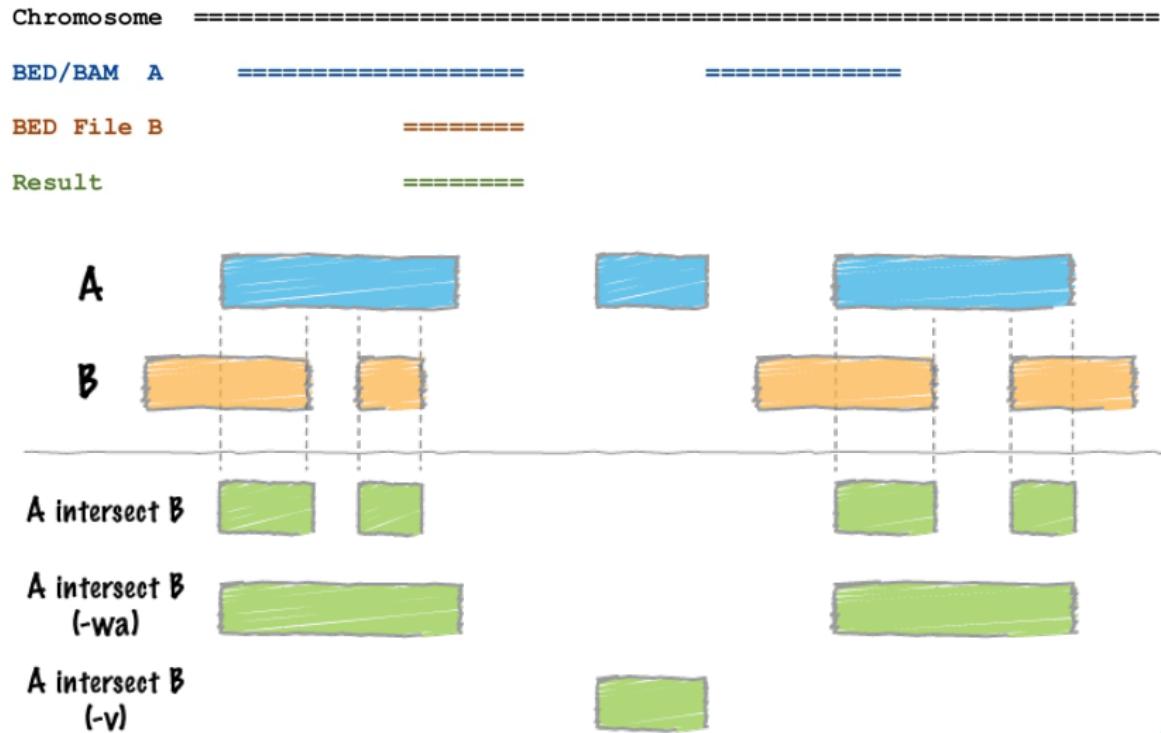
cluster Cluster (but don't merge) overlapping/nearby intervals.

complement Extract intervals **not** represented by an interval file.

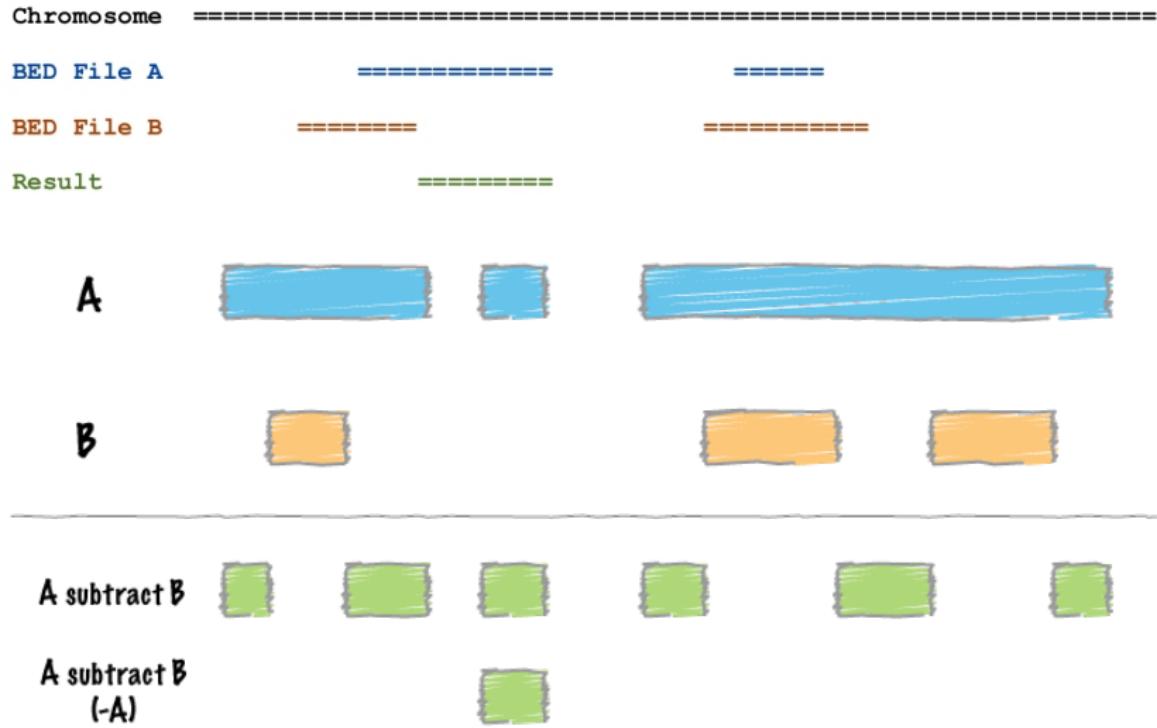
join Join looks at two datasets of intervals, and joins them based on interval overlap. Any interval in the second dataset that overlaps an interval in the first dataset will be appended to the line from the first dataset and output.



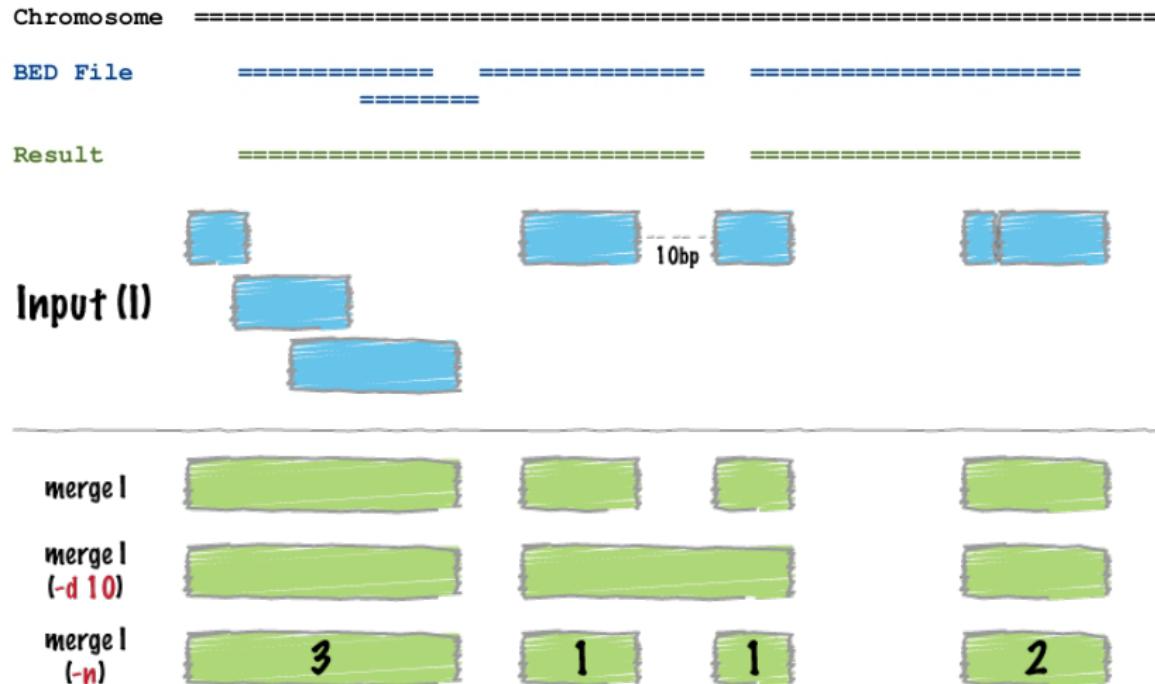
逻辑运算 | intersect



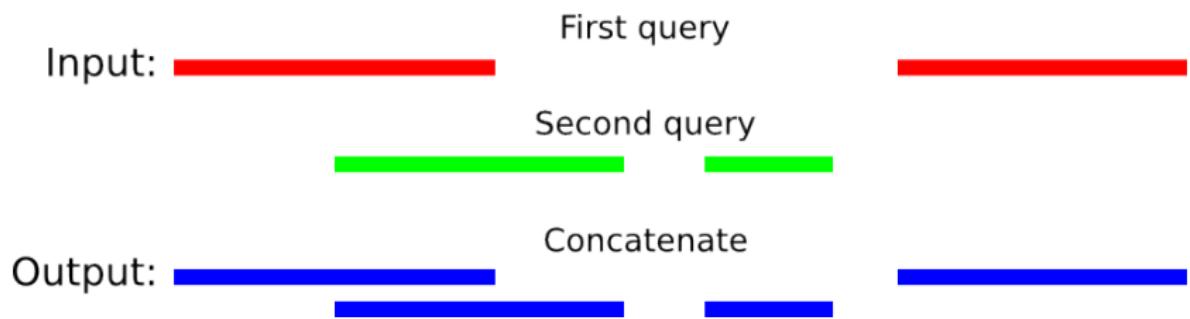
逻辑运算 | subtract



逻辑运算 | merge



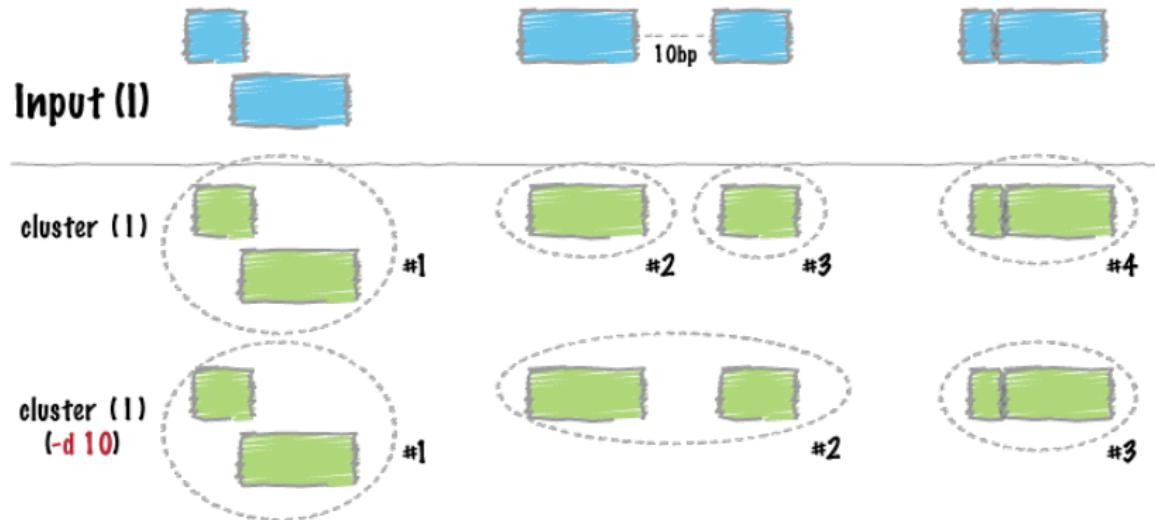
逻辑运算 | concatenate



逻辑运算 | complement



逻辑运算 | cluster



逻辑运算 | join

Query 1:				Query 2:			
chr1	10	100	Query1..1				
chr1	500	1000	Query1..2				
chr1	1100	1250	Query1..3				
				chr1	20	80	Query2..1
				chr1	2000	2204	Query2..2
				chr1	2500	3000	Query2..3

Input

(Return only records that are joined)							
chr1	10	100	Query1..1	chr1	20	80	Query2..1

Output

Return only records that are joined (INNER JOIN)
Return all records of first query (fill null with ".")
Return all records of second query (fill null with ".")
Return all records of both queries (fill nulls with ".")



逻辑运算 | join

Input						
Query 1:						
chr1 10 100 Query1..1						
chr1 500 1000 Query1..2						
chr1 1100 1250 Query1..3						
Query 2:						
chr1 20 80 Query2..1						
chr1 2000 2204 Query2..2						
chr1 2500 3000 Query2..3						
(Return all records of first query)						
chr1 10 100 Query1..1 chr1 20 80 Query2..1						
chr1 500 1000 Query1..2 . . .						
chr1 1100 1250 Query1..3 . . .						
Return only records that are joined (INNER JOIN)						
Return all records of first query (fill null with ".")						
Return all records of second query (fill null with ".")						
Return all records of both queries (fill nulls with ".")						



逻辑运算 | join

Input						
Query 1:						
<code>chr1 10 100 Query1.1</code>						
<code>chr1 500 1000 Query1.2</code>						
<code>chr1 1100 1250 Query1.3</code>						
Query 2:						
<code>chr1 20 80 Query2.1</code>						
<code>chr1 2000 2204 Query2.2</code>						
<code>chr1 2500 3000 Query2.3</code>						
(Return all records of second query)						
<code>chr1 10 100 Query1.1 chr1 20 80 Query2.1</code>						
<code>.</code>						
<code>.</code>						
<code>.</code>						
<code>chr1 chr1 2000 2204 Query2.2</code>						
<code>chr1 chr1 500 3000 Query2.3</code>						
Return only records that are joined (INNER JOIN)						
Return all records of first query (fill null with ".")						
Return all records of second query (fill null with ".")						
Return all records of both queries (fill nulls with ".")						



逻辑运算 | join

Input						
Query 1:						
chr1 10 100 Query1..1						
chr1 500 1000 Query1..2						
chr1 1100 1250 Query1..3						
Query 2:						
chr1 20 80 Query2..1						
chr1 2000 2204 Query2..2						
chr1 2500 3000 Query2..3						
(Return all records of both queries)						
chr1 10 100 Query1..1 chr1 20 80 Query2..1						
chr1 500 1000 Query1..2 chr1 . . .						
chr1 1100 1250 Query1..3 chr1 2000 2200 Query2..2						
. . . . chr1 2500 3000 Query2..3						
Return only records that are joined (INNER JOIN) Return all records of first query (fill null with ".") Return all records of second query (fill null with ".") Return all records of both queries (fill nulls with ".")						



window Find overlapping intervals within a window around an interval.

closest Find the closest, potentially non-overlapping interval.

coverage Compute the coverage over defined intervals.

map Apply a function to a column for each overlapping interval.

shift Adjust the position of intervals.

slop Adjust the size of intervals.

flank Create new intervals from the flanks of existing intervals.

sort Order the intervals in a file.

random Generate random intervals in a genome.

shuffle Randomly redistribute intervals in a genome.

sample Sample random records from file using reservoir sampling.

spacing Report the gap lengths between intervals in a file.

annotate Annotate coverage of features from multiple files.



逻辑运算 | 实例

Dataset 1

chr1	10	49	Feature1.1
chr1	70	119	Feature1.2
chr1	170	209	Feature1.3
chr1	180	229	Feature1.4

Dataset 2

chr1	80	109	Feature2.1
chr1	150	199	Feature2.2
chr1	250	289	Feature2.3
chr1	270	309	Feature2.4



逻辑运算 | 实例

Dataset 1

chr1	10	49	Feature1.1
chr1	70	119	Feature1.2
chr1	170	209	Feature1.3
chr1	180	229	Feature1.4

Dataset 2

chr1	80	109	Feature2.1
chr1	150	199	Feature2.2
chr1	250	289	Feature2.3
chr1	270	309	Feature2.4

intersect

chr1	80	109	Feature3.1
chr1	170	199	Feature3.2
chr1	180	199	Feature3.3



逻辑运算 | 实例

Dataset 1

chr1	10	49	Feature1.1
chr1	70	119	Feature1.2
chr1	170	209	Feature1.3
chr1	180	229	Feature1.4

Dataset 2

chr1	80	109	Feature2.1
chr1	150	199	Feature2.2
chr1	250	289	Feature2.3
chr1	270	309	Feature2.4

subtract (1-2)

chr1	10	49	Feature4.1
chr1	70	80	Feature4.2
chr1	109	119	Feature4.3
chr1	199	209	Feature4.4
chr1	199	229	Feature4.5

subtract (2-1)

chr1	150	170	Feature5.1
chr1	250	289	Feature5.2
chr1	270	309	Feature5.3



逻辑运算 | 实例

Dataset 1

chr1	10	49	Feature1.1
chr1	70	119	Feature1.2
chr1	170	209	Feature1.3
chr1	180	229	Feature1.4

Dataset 2

chr1	80	109	Feature2.1
chr1	150	199	Feature2.2
chr1	250	289	Feature2.3
chr1	270	309	Feature2.4

join

chr1	70	119	Feature1.2	chr1	80	109	Feature2.1
chr1	170	209	Feature1.3	chr1	150	199	Feature2.2
chr1	180	229	Feature1.4	chr1	150	199	Feature2.2



实际问题

- ① Find genes that overlap LINEs.
- ② Remove introns from gene features. Exons will (should) be reported.
- ③ Merge overlapping repetitive elements into a single entry.
- ④ Report all intervals in the human genome that are not covered by repetitive elements.

解决策略

- ① intersect
- ② subtract
- ③ merge
- ④ complement

实际问题

- ① Find genes that overlap LINEs.
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- ③ Merge overlapping repetitive elements into a single entry.
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解决策略

- ① intersect
- ② subtract
- ③ merge
- ④ complement

- Interval Operations in Galaxy
- Galaxy 中的 “Operate on Genomic Intervals” 工具集
- bedtools: a powerful toolset for genome arithmetic
- BEDOPS: the fast, highly scalable and easily-parallelizable genome analysis toolkit



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知识点——基因组注释基础

- 基因组组装版本——对应关系
- 两种坐标系统——0-based 和 1-based
- 四种常用格式——FASTA, BED, GFF, VCF
- 坐标逻辑运算——常见模式及其适用范围
- 逻辑运算的工具



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前期准备工作

- 组装版本
- 坐标系统
- 常用格式
- 逻辑运算

后续功能注释

- 变异位点的注释
- 基因集富集分析
- 制作序列标识
- ...



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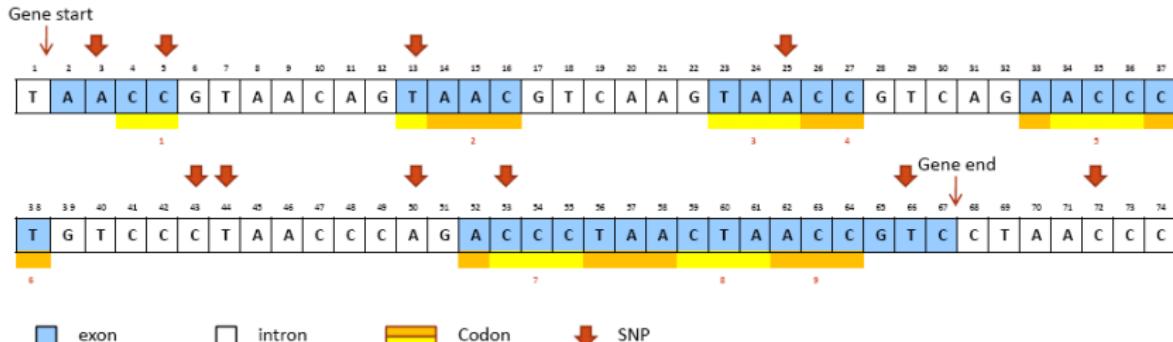


变异位点的注释 | SNP

ID	Chromosome	Position	Reference	Mutation	TotalHit
SNP00000001	15	20833654	C	A	38
SNP00000002	15	23501058	C	A	31
SNP00000003	15	45564496	C	A	20
SNP00000004	15	45564498	A	T	20
SNP00000005	15	45564501	G	T	20
SNP00000006	15	45564504	C	A	20
SNP00000007	15	45564505	C	T	20
SNP00000008	15	45564506	T	C	20
SNP00000009	15	45564508	A	T	20
SNP00000010	15	50212324	G	C	21
SNP00000011	15	50212325	A	T	21
SNP00000012	15	50212326	A	C	21
SNP00000013	15	50212328	G	A	21
SNP00000014	15	50212329	A	G	21
SNP00000015	15	50212330	G	A	21
SNP00000016	15	50212342	G	T	21
SNP00000017	15	52098626	A	G	20
SNP00000018	15	52098627	G	A	20



变异位点的注释 | SNP 注释



Pos	Alt SNP	Ref SNP	Alt SNP Codon	Ref SNP Codon	Alt SNP AA	Ref SNP AA	Anno Type
3	G	A	--	--	--	--	5'UTR
5	A	C	CAT	CCT	His	Pro	Non_Synonymous
13	G	T	CCG	CCT	Pro	Pro	Synonymous
25	C	A	TAC	TAA	Tyr	Stop	Stop Loss
43	A	C	--	--	--	--	Splice Site
44	G	T	--	--	--	--	Intronic
50	C	A	--	--	--	--	Essential Splice Site
53	A	C	ACC	CCC	Thr	Pro	Non_Synonymous
66	C	T	--	--	--	--	3'UTR
72	A	C	--	--	--	--	Downstram



- SNVs 的注释：SeattleSeq Annotation、VEP (Variant Effect Predictor) 、SnpEff、ANNOVAR、Variant Tools
- 非同义多态性的功能注释：SIFT、PolyPhen-2、SNPs3D
- indels 的功能注释：PROVEAN



变异位点的注释 | 结果解析 | SeattleSeq Annotation

File:
 /data/jboss-as-
 7.1.1.Final/gvsBatchOutput/SeattleSeqAnnotation137.1individual.294000040650.txt

Title:
 1individual

Counts:
 HapMapFreqType HapMapFreqMinor
 polyPhenType polyPhenScore

Count missense SNPs = 8
 Count stop SNPs = 0
 Count SNPs in splice sites = 0
 Count SNPs in coding synonymous = 8
 Count SNPs in coding (not mod 3) = 0
 Count SNPs in a UTR = 0
 Count SNPs near a gene = 0
 Count SNPs in introns = 0
 Count intergenic SNPs = 0

number SNPs in microRNAs = 0

number accessions coding-synonymous NCBI = 19
 number accessions missense NCBI = 15
 number accessions stop NCBI = 0
 number accessions splice-site NCBI = 0
 number SNPs in dbSNP = 16
 number SNPs not in dbSNP = 0
 number SNPs total = 16

Add or Remove Columns:	Sort by Column Value:	Sort Direction:
<input checked="" type="checkbox"/> Sample Alleles <input checked="" type="checkbox"/> Alleles in dbSNP <input checked="" type="checkbox"/> GVS Function <input checked="" type="checkbox"/> dbSNP Function <input checked="" type="checkbox"/> Chimp Allele <input checked="" type="checkbox"/> Copy Number Variations <input checked="" type="checkbox"/> HapMap Rare-Allele Frequencies <input checked="" type="checkbox"/> dbSNP Validation <input checked="" type="checkbox"/> RepeatMasker <input checked="" type="checkbox"/> Tandem Repeats <input checked="" type="checkbox"/> microRNAs <input checked="" type="checkbox"/> Grantham Score <input checked="" type="checkbox"/> cDNA Position <input checked="" type="checkbox"/> PolyPhen Prediction <input checked="" type="checkbox"/> Clinical Association <input checked="" type="checkbox"/> Distance to Nearest Splice Site <input checked="" type="checkbox"/> NHLBI ESP Allele Counts	<input checked="" type="radio"/> Original Order <input type="radio"/> dbSNP Function <input type="radio"/> GVS Function <input type="radio"/> Conservation Score phastCons <input type="radio"/> Conservation Score GERP <input type="radio"/> In dbSNP	<input checked="" type="radio"/> Forward <input type="radio"/> Reverse
Filter: <input type="checkbox"/> Only missense, nonsense, splice, frameshift (GVS) <input type="checkbox"/> Only synonymous SNPs or coding (not frameshift) indels (GVS) <input type="checkbox"/> Only intron (GVS) <input type="checkbox"/> Only variations not in dbSNP <input type="checkbox"/> Only variations with clinical association		
Table <input style="float: right;" type="button" value="reset"/>		

16 SNP locations 36 accession lines page 1 of 1

inDBSNPOrNot	chromosome	position	referenceBase	sampleGenotype	sampleAlleles	allelesDBSNP	accession	functionGVS	functionDBSNP	rsID	aminoAcids	proteinPosition
dbSNP_130	10	1126383	A	R	A/G	A/G	NM_014023.3	coding-synonymous	synonymous-codon	73578536	none	121/495
dbSNP_86	10	3150973	C	Y	C/T	C/T	NM_001242339.1	coding-synonymous	synonymous-codon	1132173	none	309/777
dbSNP_86	10	3150973	C	Y	C/T	C/T	NM_002627.4	coding-synonymous	synonymous-codon	1132173	none	317/785

变异位点的注释 | 结果解析 | SeattleSeq Annotation

inDBSNPOrNot	chromosome	position	referenceBase	sampleGenotype	sampleAlleles	allelesDBSNP
dbSNP_130	10	1126383	A	R	A/G	A/G
dbSNP_86	10	3150973	C	Y	C/T	C/T
dbSNP_86	10	3150973	C	Y	C/T	C/T
accession	functionGVS	functionDBSNP	rsID	aminoAcids	proteinPosition	
NM_014023.3	coding-synonymous	synonymous-codon	73578536	none	121/495	
NM_001242339.1	coding-synonymous	synonymous-codon	1132173	none	309/777	
NM_002627.4	coding-synonymous	synonymous-codon	1132173	none	317/785	



变异位点的注释 | 结果解析 | SIFT

Transcript ID	Protein ID	Substitution	Region	dbSNP ID	SNP Type	Prediction	SIFT Score
ENST00000294724	ENSP00000294724	R1487G	EXON CDS	rs12118058:G	Nonsynonymous	TOLERATED	0.46
ENST00000294724	ENSP00000294724	E1405G	EXON CDS	rs28730708:G	Nonsynonymous	DAMAGING	0.01
ENST00000294724	ENSP00000294724	R1487R	EXON CDS	rs12118058:G	Synonymous	TOLERATED	0.64
ENST00000330029	ENSP00000332887	E49A	EXON CDS	novel	Nonsynonymous	DAMAGING	0.02
ENST00000371564	ENSP00000360619	T612N	EXON CDS	rs6067785:T	Nonsynonymous	DAMAGING	0
ENST00000283943	ENSP00000283943	Q1910*	EXON CDS	rs1803846:A	Nonsynonymous	N/A	N/A
ENST00000341772	ENSP00000345229	P433L	EXON CDS	rs17853365:A	Nonsynonymous	DAMAGING	0.02



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富集分析 | 基因集

Table 7 The minimum gene set selected in PRI dataset (gene scores rank from high to low)

Probe ID	Gene symbol	Gene name	Chromosomal regions
219868_s_at	ANKFY1	Ankyrin repeat and FYVE domain containing1	17p13.3
213613_s_at	NADK	NAD kinase	1p36.33-p36.21
208002_s_at	ACOT7	Acyl-coa thioesterase 7	1p36
222133_s_at	PHF20L1	PHD finger protein 20-like 1	8q24.22
203858_s_at	COX10	COX10 homolog, cytochrome c oxidase assembly protein, heme A: farnesyltransferase (yeast)	17p12
204051_s_at	SFRP4	Secreted frizzled-related protein 4	7p14.1
207567_at	SLC13A2	Solute carrier family 13 (sodium-dependent dicarboxylate transporter), member 2	17p13.2
225803_at	FBXO32	F-box protein 32	8q24.13
205527_s_at	GEMIN4	Gem (nuclear organelle) associated protein 4	17p13
207017_at	RAB27B	RAB27B, member RAS oncogene family	18q21.2
206746_at	BFSP1	Beaded filament structural protein 1, filensin	20p12.1
217099_s_at	GEMIN4	Gem (nuclear organelle) associated protein 4	17p13
233638_s_at	POMGNT1	Protein O-linked mannose beta1,2-N-acetylglucosaminyltransferase	1p34.1
217381_s_at	TRGV5	T cell receptor gamma variable 5	7p14



数据库

GO Gene Ontology

KEGG Kyoto Encyclopedia of Genes and Genomes

分析工具

DAVID Database for Annotation, Visualization and Integrated Discovery

Metascape A Gene Annotation & Analysis Resource

Enrichr interactive and collaborative HTML5 gene list enrichment analysis tool



数据库

[GO](#) Gene Ontology

[KEGG](#) Kyoto Encyclopedia of Genes and Genomes

分析工具

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[Enrichr](#) interactive and collaborative HTML5 gene list enrichment analysis tool



三个方面

- biological process, BP, 生物学过程
- molecular function, MF, 分子功能
- cellular component, CC, 细胞组份

两大关系

- is_a: for simple, hierarchical connections between terms
- part_of: for describing how the components of a living system fit together



三个方面

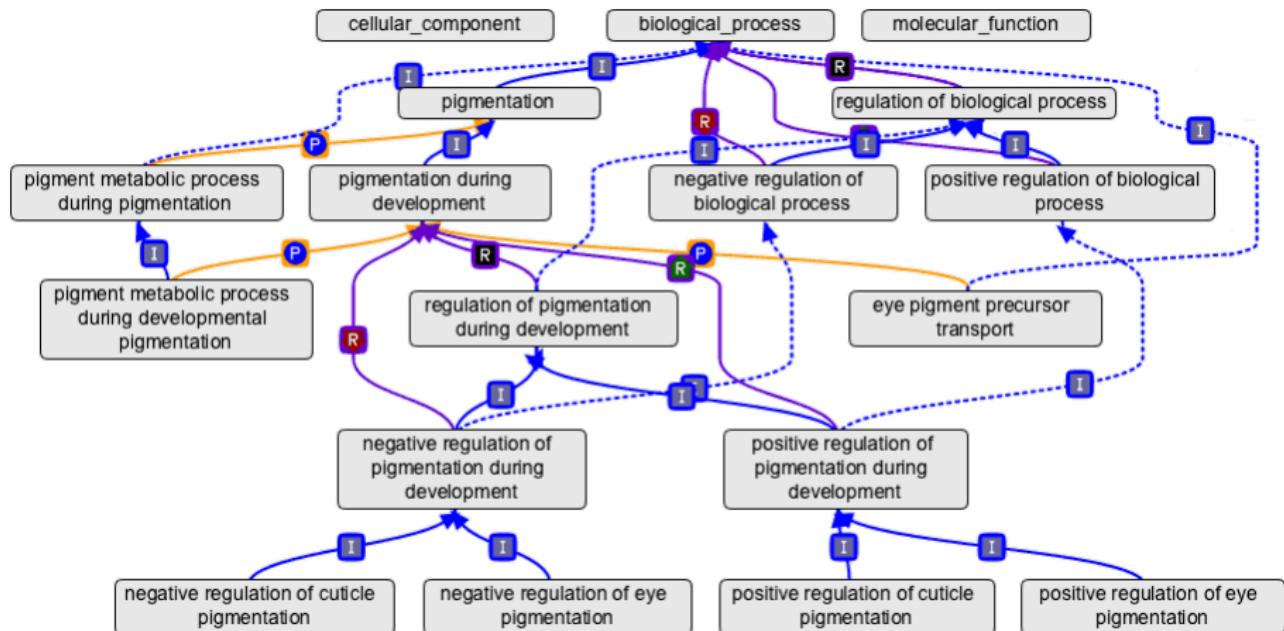
- biological process, BP, 生物学过程
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两大关系

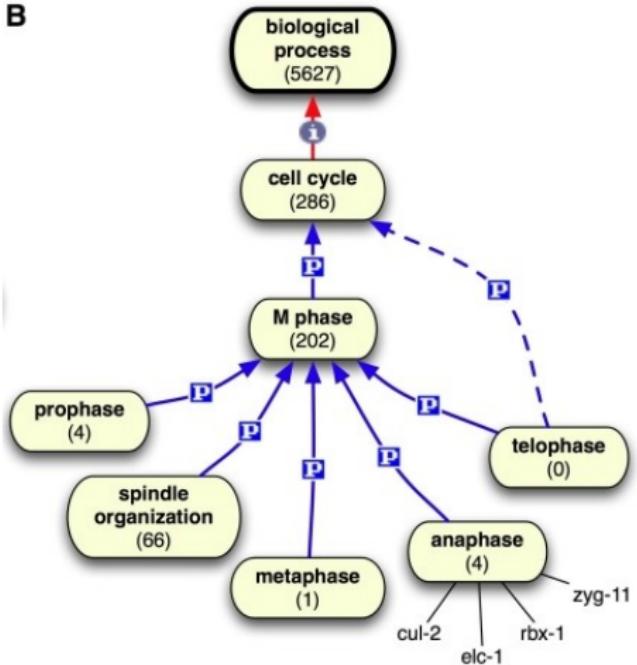
- is_a: for simple, hierarchical connections between terms
- part_of: for describing how the components of a living system fit together



富集分析 | GO



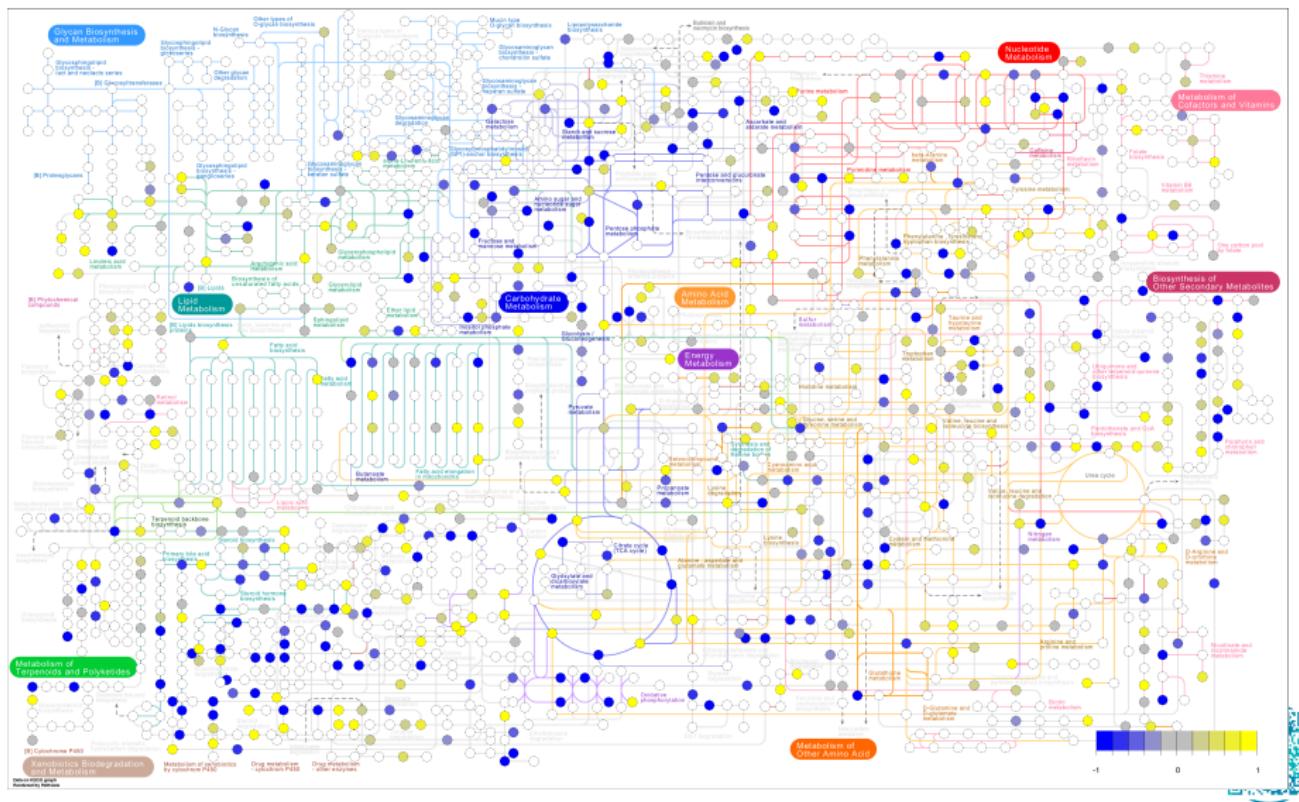
B



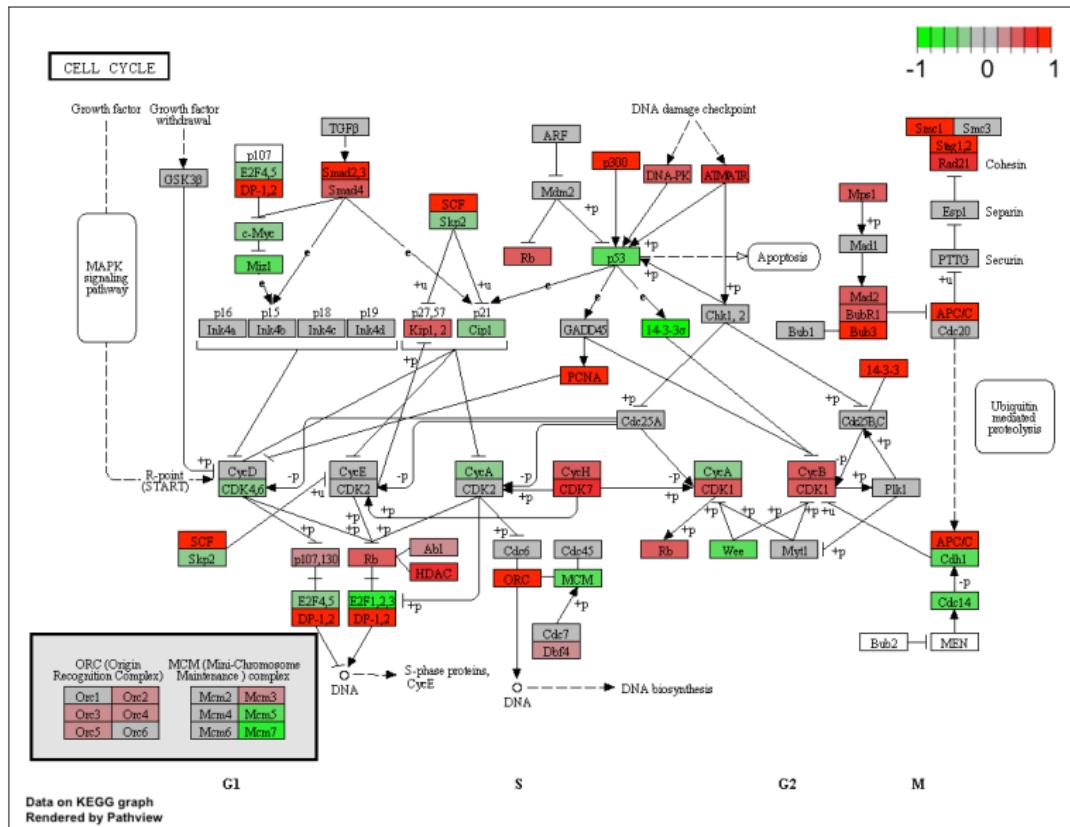
Relationships	Nodes
→ part_of	ontology term
→ is_a	root node
→ develops_from	
- - - → inferred	
— — — annotation	



富集分析 | KEGG



富集分析 | KEGG



- Gene Name Batch Viewer
- Gene ID Conversion Tool
- Gene Functional Classification Tool
- Functional Annotation Tool
 - Functional Annotation Clustering
 - **Functional Annotation Chart** : 富集分析
 - Functional Annotation Table



富集分析 | DAVID | 结果解析

Functional Annotation Chart

[Help and Manual](#)**Current Gene List: demolist1****Current Background: Homo sapiens****155 DAVID IDs****Options**[Rerun Using Options](#)[Create Sublist](#)**105 chart records** [Download File](#) [<<](#) [<](#) [1](#), [2](#), [3](#), [4](#), [5](#), [6](#) [>](#) [>>](#)

Category	Term	RT	Genes	Count	%	P-Value	Benjamini
GOTERM_CC_FAT	extracellular_region	RT		40	25.8	6.9E-6	1.5E-3
GOTERM_CC_FAT	extracellular_region_part	RT		24	15.5	3.8E-5	4.0E-3
GOTERM_MF_FAT	oxygen_binding	RT		6	3.9	3.8E-5	1.4E-2
GOTERM_CC_FAT	extracellular_space	RT		19	12.3	9.4E-5	6.5E-3
GOTERM_MF_FAT	heme_binding	RT		8	5.2	1.0E-4	1.9E-2
GOTERM_BP_FAT	defense_response	RT		18	11.6	1.3E-4	1.7E-1
GOTERM_BP_FAT	response_to_bacterium	RT		10	6.5	1.4E-4	9.1E-2
GOTERM_MF_FAT	tetrapyrrole_binding	RT		8	5.2	1.5E-4	1.9E-2
GOTERM_MF_FAT	iron_ion_binding	RT		11	7.1	4.3E-4	3.9E-2
GOTERM_BP_FAT	defense_response_to_bacterium	RT		7	4.5	8.9E-4	3.4E-1
GOTERM_BP_FAT	response_to_drug	RT		9	5.8	1.5E-3	4.0E-1
GOTERM_BP_FAT	regulation_of_response_to_external_stimulus	RT		7	4.5	5.2E-3	7.7E-1
GOTERM_BP_FAT	taxis	RT		7	4.5	5.4E-3	7.2E-1
GOTERM_BP_FAT	chemotaxis	RT		7	4.5	5.4E-3	7.2E-1
GOTERM_CC_FAT	hemoglobin_complex	RT		3	1.9	5.7E-3	2.6E-1
GOTERM_MF_FAT	oxygen_transporter_activity	RT		3	1.9	5.8E-3	3.5E-1

富集分析 | DAVID | 工具选择

- Highly recommended
- Recommended

	Gene ID conversion tool	Gene name batch viewer	Gene functional classification	Functional annotation chart	Functional annotation clustering	Functional annotation table
Convert gene IDs from one type to another	■					
Diagnose and fix problems of gene IDs		■				■
Explore gene names in batch		■	■			■
Discover enriched functionally related gene groups			■	■		
Display relationship of many-genes-to-many-terms on 2D view.				■	■	■
Initial glance of major biological functions associated with gene list	■		■	■		
Identify enriched (overrepresented) annotation terms				■	■	
Visualize genes on BioCarta and KEGG pathway maps				■		
Link gene–disease associations				■		
Highlight protein functional domains and motifs			■	■		
Redirect to related literatures				■		■
List interacting proteins				■	■	■
Cluster redundant and heterozygous annotation terms						
Search other functionally similar genes in genome, but not in list	■	■	■	1	1	
Search other annotations functionally similar to one of my interests				■		
Read all annotation contents associated with a gene						■



教学提纲

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序列标识 | 徽标



序列标识

定义

序列标识图是显示序列保守区域的共有序列、每个位置上各个氨基酸或核苷酸出现的频率以及各个位点上的序列信息量的一种可视化方法。

含义

根据序列保守区域的多序列比对来绘制序列标识图。

在一个标识图像里，由大小不一的字符形成的一个堆栈代表序列保守区域的一个位点。每个核苷酸或氨基酸的高度和它在对应位点上出现的频率成比例。堆栈的总高度代表对应位点上的序列信息，以比特（bit）为单位。在每个堆栈里，字符按其出现的频率大小自上而下排列。所以，位于各个堆栈最上方的字符组成保守区域的共识序列。



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序列标识图是显示序列保守区域的共有序列、每个位置上各个氨基酸或核苷酸出现的频率以及各个位点上的序列信息量的一种可视化方法。

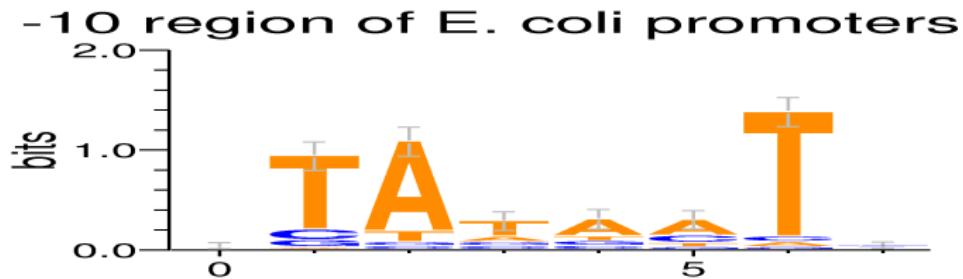
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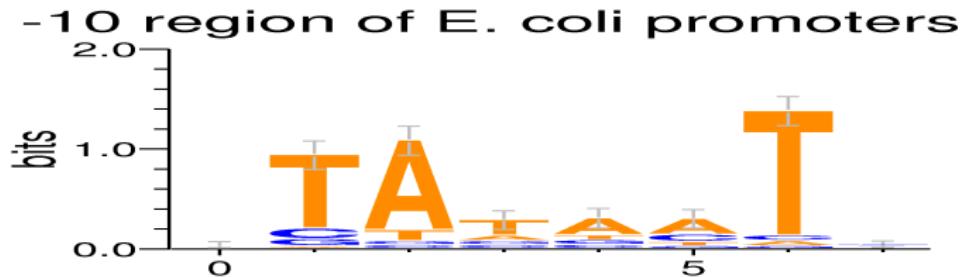
序列标识



序列标识 (sequence logo)

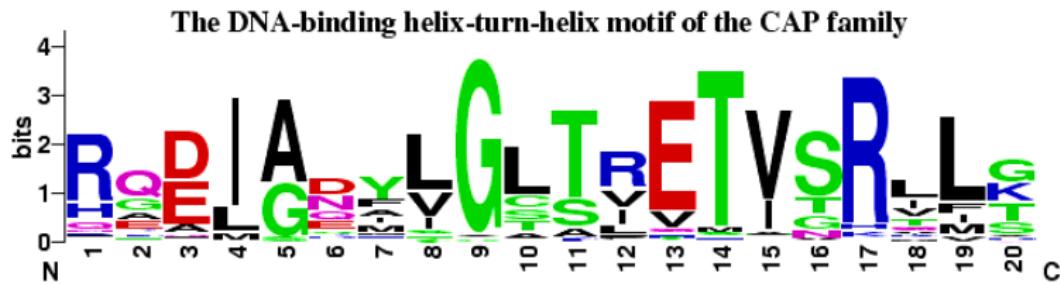
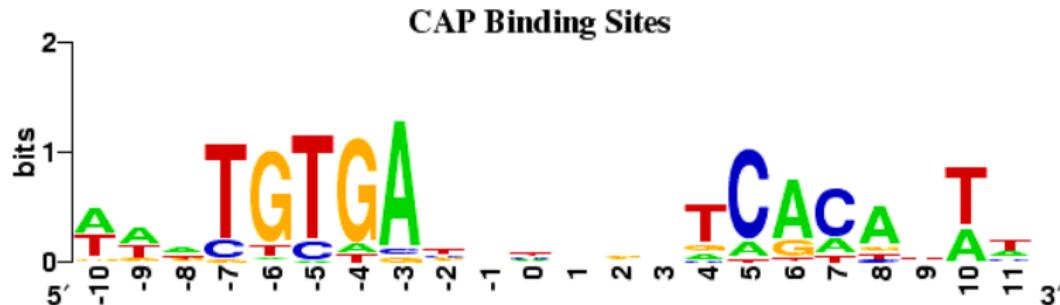
- 数据：多序列比对信息
- 横轴：序列坐标位置
- 纵轴：比特，计量单位
- 总高度：信息量/保守性
- 相对高度：相对频率
- 位置自上而下：频率由大到小
- 制作工具：WebLogo, enoLOGOS, Skylign

序列标识

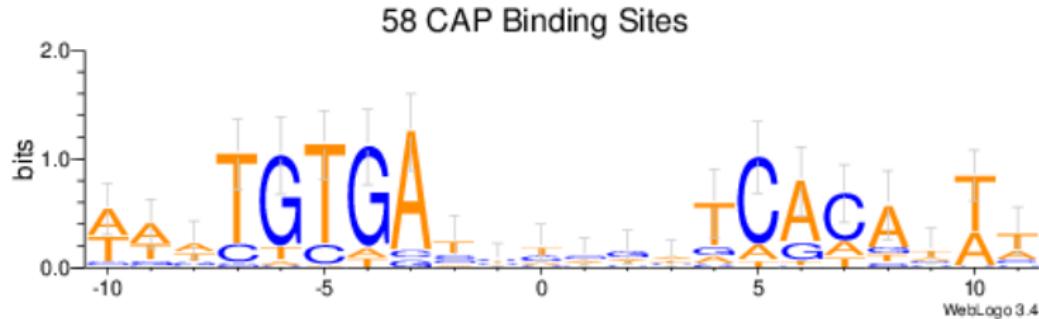


序列标识 (sequence logo)

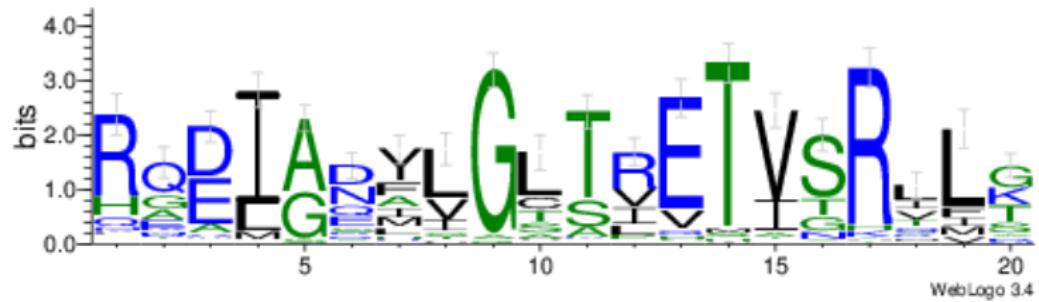
- 数据：多序列比对信息
- 横轴：序列坐标位置
- 纵轴：比特，计量单位
- 总高度：信息量/保守性
- 相对高度：相对频率
- 位置自上而下：频率由大到小
- 制作工具：WebLogo, enoLOGOS, Skylign



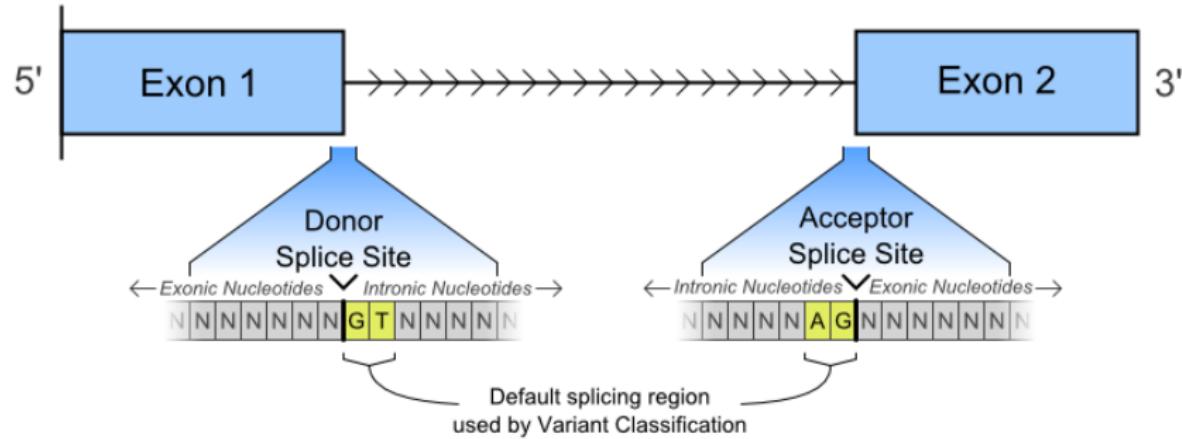
序列标识 | 着色 | WebLogo3



The DNA-binding helix-turn-helix motif of the CAP family

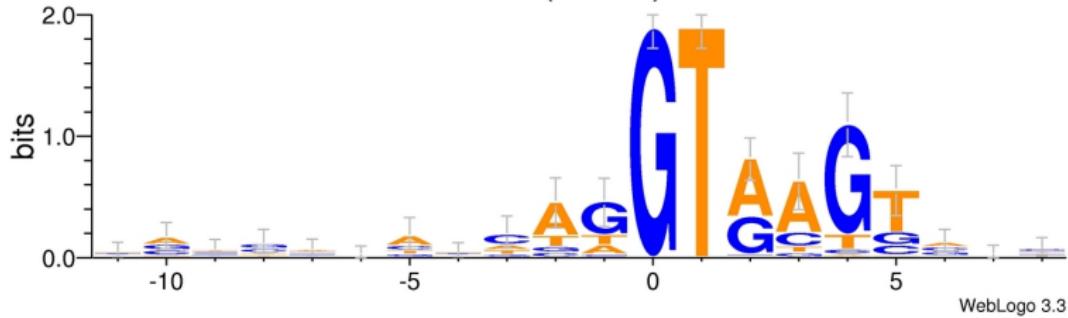


序列标识 | 剪接



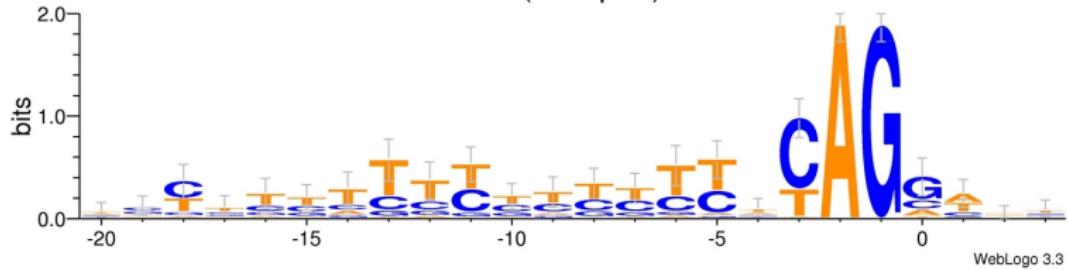
序列标识 | 实例

Exon-Intron (Donor) Sites



WebLogo 3.3

Intron-Exon (Acceptor) Sites



WebLogo 3.3



教学提纲

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知识点——基因组功能的高级注释

- 变异位点的注释——用途，注释内容，注释工具
- 基因集富集分析——功能，分析工具
- 序列标识——含义，制作工具



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基础知识

- 组装版本和坐标系统
- 常用格式
- 坐标的逻辑运算

高级注释

- 变异位点的注释
- 基因集富集分析
- 制作序列标识

分析平台

- Galaxy
- GenePattern

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- Get Data
- Text Manipulation
- Convert Formats
- Operate on Genomic Intervals
- Phenotype Association
- Statistics
- Graph/Display Data
- NGS Toolbox
- ...



Galaxy | 界面

Galaxy Analyze Data Workflow Shared Data Visualization Cloud Help User

工具

search tools

[Get Data](#)

[Lift-Over](#)

[Text Manipulation](#)

[Convert Formats](#)

[FASTA manipulation](#)

[Filter and Sort](#)

[Join, Subtract and Group](#)

[Extract Features](#)

[Fetch Sequences](#)

[Fetch Alignments](#)

[Get Genomic Scores](#)

[Operate on Genomic Intervals](#)

[Statistics](#)

[Graph/Display Data](#)

[Regional Variation](#)

[Multiple regression](#)

[Multivariate Analysis](#)

Galaxy is an open source, web-based platform for data intensive biomedical research. If you are new to Galaxy [start here](#) or consult our [help resources](#).

Galaxy 101

Start small

The very first tutorial you need

历史

Unnamed history 1.5 MB

历史已空，请单击左边窗格中‘获取数据’



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- UCSC liftOver tool：支持 BED 和 “chrN:start-end” 格式的输入
- Galaxy（基于 UCSC liftOver tool）：支持 BED、GFF 和 GTF 格式的输入
- CrossMap：支持 SAM/BAM、Wiggle/BigWig、BED、GFF/GTF 和 VCF 格式的输入，输出对应格式
- NCBI Remap：支持 BED、GFF、GTF 和 VCF 等格式的输入
- Ensembl assembly converter（2015 年退休，CrossMap 继位）：支持 BED、GFF、GFT 和 PSL 格式的输入，但输出都是 GFF 格式的
- pyliftover：仅支持点坐标（point coordinates）的转换，无法对区段（ranges）坐标进行转换



Galaxy 演示 | 坐标转换 | liftOver

hg19 ⇒ hg18

获取输入



hg19 ⇒ hg18

① 获取输入

- 输入文件：hg19 坐标

② 数据处理

使用 Galaxy 的“坐标转换”工具

③ 保存输出



hg19 ⇒ hg18

① 获取输入

- 输入文件：hg19 坐标

② 数据处理

- 设置参数：hg19 ⇒ hg18

③ 保存输出



hg19 ⇒ hg18

① 获取输入

- 输入文件：hg19 坐标

② 数据处理

- 设置参数：hg19 ⇒ hg18

③ 保存输出



hg19 ⇒ hg18

① 获取输入

- 输入文件：hg19 坐标

② 数据处理

- 设置参数： $hg19 \Rightarrow hg18$

③ 保存输出



hg19 ⇒ hg18

① 获取输入

- 输入文件：hg19 坐标

② 数据处理

- 设置参数：hg19 ⇒ hg18

③ 保存输出

- 过滤结果：MAPPED VS. UNMAPPED



hg19 \Rightarrow hg18

① 获取输入

- 输入文件：hg19 坐标

② 数据处理

- 设置参数： $hg19 \Rightarrow hg18$

③ 保存输出

- 过滤结果：MAPPED VS. UNMAPPED



Galaxy 演示 | 格式转换 | BED ⇌ GFF

BED ⇌ GFF

● 获取输入



BED ⇌ GFF

① 获取输入

- 输入文件：BED

② 数据处理

③ 保存输出



BED ⇌ GFF

① 获取输入

- 输入文件：BED

② 数据处理

BED → GFF

GFF → BED

③ 保存输出



BED ⇌ GFF

① 获取输入

- 输入文件：BED

② 数据处理

- ① BED ⇒ GFF
- ② GFF ⇒ BED

③ 保存输出



BED ⇌ GFF

① 获取输入

- 输入文件：BED

② 数据处理

- ① BED ⇒ GFF

- ② GFF ⇒ BED

③ 保存输出



BED ⇌ GFF

① 获取输入

- 输入文件：BED

② 数据处理

① BED ⇒ GFF

② GFF ⇒ BED

③ 保存输出



BED ⇌ GFF

① 获取输入

- 输入文件：BED

② 数据处理

- ① BED ⇒ GFF
- ② GFF ⇒ BED

③ 保存输出

- 查看结果：互相比较



BED ⇌ GFF

① 获取输入

- 输入文件：BED

② 数据处理

- ① BED ⇒ GFF
- ② GFF ⇒ BED

③ 保存输出

- 查看结果：互相比较



- Galaxy 中的 “Operate on Genomic Intervals” 工具集
- BEDTools: a powerful toolset for genome arithmetic
- BEDOPS: the fast, highly scalable and easily-parallelizable genome analysis toolkit



外显子 vs. SNP

① 获取输入



外显子 vs. SNP

① 获取输入

- exon
- SNP

② 数据处理

③ 保存输出



外显子 vs. SNP

① 获取输入

- exon
- SNP

② 数据处理

③ 保存输出



外显子 vs. SNP

① 获取输入

- exon
- SNP

② 数据处理

- subtract
- join

③ 保存输出



外显子 vs. SNP

① 获取输入

- exon
- SNP

② 数据处理

- subtract
- join

③ 保存输出



外显子 vs. SNP

① 获取输入

- exon
- SNP

② 数据处理

- subtract
- join

③ 保存输出



外显子 vs. SNP

① 获取输入

- exon
- SNP

② 数据处理

- subtract
- join

③ 保存输出

正在运行



外显子 vs. SNP

① 获取输入

- exon
- SNP

② 数据处理

- subtract
- join

③ 保存输出

- 解析结果



外显子 vs. SNP

① 获取输入

- exon
- SNP

② 数据处理

- subtract
- join

③ 保存输出

- 解析结果



问题

- 找到含有至少 N (2) 个 SNP 的外显子。

输入

- 外显子数据 (BED 格式)
- SNP 数据 (BED 格式)

输出

- 满足要求的外显子信息 (BED 格式)



问题

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问题

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- SNP 数据 (BED 格式)

输出

- 满足要求的外显子信息 (BED 格式)



外显子数据

①	chr1	10	20	exon1	0	+
②	chr1	30	40	exon2	0	+
③	chr1	50	60	exon3	0	-
④	chr1	65	75	exon4	0	+
⑤	chr1	85	95	exon5	0	-



SNP 数据

①	chr1	11	12	snp1	0	+
②	chr1	15	16	snp2	0	+
③	chr1	17	18	snp3	0	+
④	chr1	24	25	snp4	0	+
⑤	chr1	33	34	snp5	0	+
⑥	chr1	37	38	snp6	0	+
⑦	chr1	44	45	snp7	0	+
⑧	chr1	54	55	snp8	0	+
⑨	chr1	57	58	snp9	0	-



Finding exons with the highest number (≥ 10) of SNPs

Join-Group-Filter-Compare-Sort

- Input: Get exons, SNPs; UCSC Table Browser
- Join[Operate on Genomic Intervals]: Join exons with SNPs
- Group: Count the number of SNPs per exon
- Filter: Filter exons that have ten or more SNPs
- Compare two Datasets: Recover exon information
- Sort: Sort the start and end coordinates
- Visualize: Display data in genome browser



Finding exons with the highest number (≥ 10) of SNPs

Join-Group-Filter-Compare-Sort

- ① Input: Get exons, SNPs; UCSC Table Browser
- ② Join[Operate on Genomic Intervals]: Join exons with SNPs
- ③ Group: Count the number of SNPs per exon
 - ④ Sort: Sort by the number of SNPs in descending order
 - ⑤ Filter: Filter exons with at least 10 SNPs
 - ⑥ Compare: Compare the results with the original exons
 - ⑦ Sort: Sort the filtered exons by their genomic position



Finding exons with the highest number (≥ 10) of SNPs

Join-Group-Filter-Compare-Sort

- ① Input: Get exons, SNPs; UCSC Table Browser
- ② Join[Operate on Genomic Intervals]: Join exons with SNPs
- ③ Group: Count the number of SNPs per exon
- ④ Filter: Filter exons that have ten or more SNPs
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- ③ Count: Count the number of SNPs per exon
- ④ Sort: Sort by the number of SNPs per exon
- ⑤ Filter: Filter exons with ≥ 10 SNPs
- ⑥ Cut: Cut the top 10 exons
- ⑦ Sort: Sort by the number of SNPs per exon



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Finding 10 exons with the highest number of SNPs

Join-Group-Sort-SelectFirst-Join-Cut-Sort

- Input: Get exons, SNPs; UCSC Table Browser
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- Sort: Sort exons by SNPs count
- Select first: Select top ten
- Join[Join two Datasets]: Recover exon information
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BEDTools-shell-BEDTools

考虑链性

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Workflow : create, modify, rerun, share

① Save: Rename the history as "Exons and SNPs"

② Workflow: Extract workflow from history

③ Workflow: Share workflow with others and modify history



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- ⑤ Share: Share or publish workflow
- ⑥ Create: Create workflows from scratch (e.g. Find the 50 longest exons)



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- 4 基因组注释常用格式
- 5 基因组坐标的逻辑运算
- 6 总结与答疑
- 7 引言
- 8 变异位点的注释

- 9 基因集富集分析
- 10 序列标识
- 11 总结与答疑
- 12 引言
- 13 Galaxy 分析平台
- 14 Galaxy 使用演示
- 15 **总结与答疑**
- 16 复习思考题



知识点——Galaxy 分析平台

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知识点

- ① hg19 和 mm10 分别代表什么含义？hg19 是和 GRCh37 相对应，还是和 GRCm38 相对应？
- ② 常见的基因组坐标系统是哪两种，举例进行说明。
- ③ 简述 BED 格式前 6 列的含义，能解释实际的 BED 记录。
- ④ 基于基因组坐标的常见逻辑运算模式有哪些，画图进行解释。
- ⑤ 简述序列标识的含义，能解释实际的序列标识图。

