

Anexo - Documentos comprobatorios



Sanjeet R. Kulkarni, Dean of the Faculty
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Dr. Diogo Melo
 Universidade de São Paulo
 Departamento De Genética E Biologia Evolutiva
 São Paulo, São Paulo, Brazil

March 3, 2020

Dear Dr. Diogo Melo:

I am pleased to offer you an appointment as a Postdoctoral Research Associate in the Lewis-Sigler Institute for Integrative Genomics as part of Princeton's Presidential Postdoctoral Research Fellows Program. The program is intended to recognize and support outstanding early-career stage scholars who will contribute to the University's scholarly excellence and enhance its diversity.

Your 12 month, 100% duty-time salary will be \$53,076, paid monthly. You will also receive an annual research fund of \$2,000 and up to \$2,000 for a computer. The computer will be considered the property of the University and should be returned to the department at the end of your appointment. Moving expense reimbursement will be provided, up to a maximum of \$5,000 for relocation from international and U.S. west coast locations, and up to a maximum of \$3,000 for relocation from all other U.S. locations (exceeding the IRS required 50-mile job site transfer).

Your appointment will be for one year and may start between July 1, 2020 and September 1, 2020, with the possibility of renewal for a second year, assuming satisfactory performance. We will need a written acceptance of this offer to complete the formalities of your appointment. We would very much appreciate your response as soon as possible, and in any case no later than March 1, 2020. Please reply all to the e-mail containing this offer letter to accept this appointment and include a signed copy of the last page as an attachment.

This offer is contingent upon completion of all requirements for the Ph.D. if the Ph.D. is not completed by September 1, 2020, then this PDRA appointment offer is no longer valid.

All Postdoctoral Research Associates in the social sciences, natural sciences, and engineering are required to complete a course in Responsible Conduct in Research (RCR). Our policy for RCR training can be found at <https://oma.princeton.edu/resources/policies-and-procedures/responsible-conduct-research>; contact Kara Dolinski, Director, Genome Databases, Lewis-Sigler Institute for Integrative Genomics., for details.

Final approval of your appointment is contingent upon successful completion of a background check. Information about that process will be shared with you once we have received your acceptance of our offer. Upon approval of your appointment, you will receive a packet of benefits information from the Office of Human Resources. Our benefit policies provide that postdoctoral employees earn two vacation days per month. You will be compensated for any unused vacation time at the end of your appointment up to a limit of 30 days. Please refer to https://dof.princeton.edu/in_researchers for policies relevant to postdoctoral appointments, and to the University's policies for all members of the Princeton community at <http://www.princeton.edu/policy/>.

Princeton University is required to verify that you are eligible for employment under the Immigration Reform and Control Act of 1986. Information on what you must do to prove U.S. citizenship, permanent residency or visa status that authorizes you to work is included with this letter and will also be sent to you along with the formal letter of appointment from the Dean of the Faculty upon acceptance of this offer.

We hope for the good fortune of welcoming you to the Lewis-Sigler Institute for Integrative Genomics, and we have no doubt that you will find Princeton to be a collegial and intellectually enriching environment.

Sincerely,

Sanjeev R. Kulkarni

cc: Julien Ayroles, Assistant Professor of Ecology and Evolutionary Biology and the Lewis-Sigler Institute for Integrative Genomics.

Michael Levine, Anthony B. Evrin '62 Professor in Genomics, Professor of Molecular Biology and the Lewis-Sigler Institute for Integrative Genomics, Director, Lewis-Sigler Institute for Integrative Genomics.

Kara Dolinski, Director, Genome Databases, Lewis-Sigler Institute for Integrative Genomics.

Toni Turano, Deputy Dean of the Faculty

Karen Haskin, Associate Dean for Academic Affairs

Alice Seneres, Assistant Dean of Academic Affairs

Documento 1: Comprovante de bolsa de Pós-Doutorado.



Para uso exclusivo da FAPESP
 Processo: 2019/06559-6
 Data impressão: 07/07/2019 00:06:44
 Folha: _____
 Volume: _____
 Rubrica: _____

FUNDAÇÃO DE AMPARO À PESQUISA DO ESTADO DE SÃO PAULO

TERMO DE OUTORGА E ACEITАО DE BOLSAS NO PAÍS

PROCESSO 2019/06559-6

Pelo presente instrumento, a Fundação de Amparo à Pesquisa do Estado de São Paulo, com sede na Rua Pio XI, nº 1500, Alto da Lapa, São Paulo, Capital, inscrita no CNPJ/MF sob o nº 43.828.151/0001-45, doravante denominada OUTORGANTE, por meio de seu Conselho Técnico-Administrativo, nos termos do Artigo 14, letra "b", da Lei Estadual nº 5.918, de 18 de outubro de 1960, concede ao(s) OUTORGADO(S), a seguir qualificado(s), Bolsa para a realização do Projeto de Pesquisa a seguir especificado, nas instalações e com o apoio da INSTITUIÇÃO SEDE, de acordo com as especificações, cláusulas e condições descritas a seguir e nos Anexos, que passam a ser parte integrante deste Termo.

1. OUTORGADOS

1.1 BOLSISTA: Diogo Amaral Reboucas Melo
 CPF: 329.212.298-89

RG: 350021107-SSP/SP

1.2 ORIENTADOR/SUPERVISOR: Gabriel Henrique Marroig Zambonato
 CPF: 989.457.267-72
 RG: 116197229-IFP/RJ

2. Correspondência

2.1 BOLSISTA: Rua Caraíbas 544 - 122B, Perdizes, São Paulo/SP, CEP 05020-000
 diogro@usp.br

2.2 ORIENTADOR/SUPERVISOR: Rua Fidalga 953 - casa 10, Pinheiros, São Paulo/SP, CEP 05432-070
 gmarroig@usp.br

3. Instituição Sede: Instituto de Biociências/IB
 Universidade de São Paulo/USP

4. Projeto de Pesquisa: Arquitetura genética do crânio de mamíferos

5. Linha de Fomento: Programas Regulares / Bolsas / No País / Pós-Doutorado

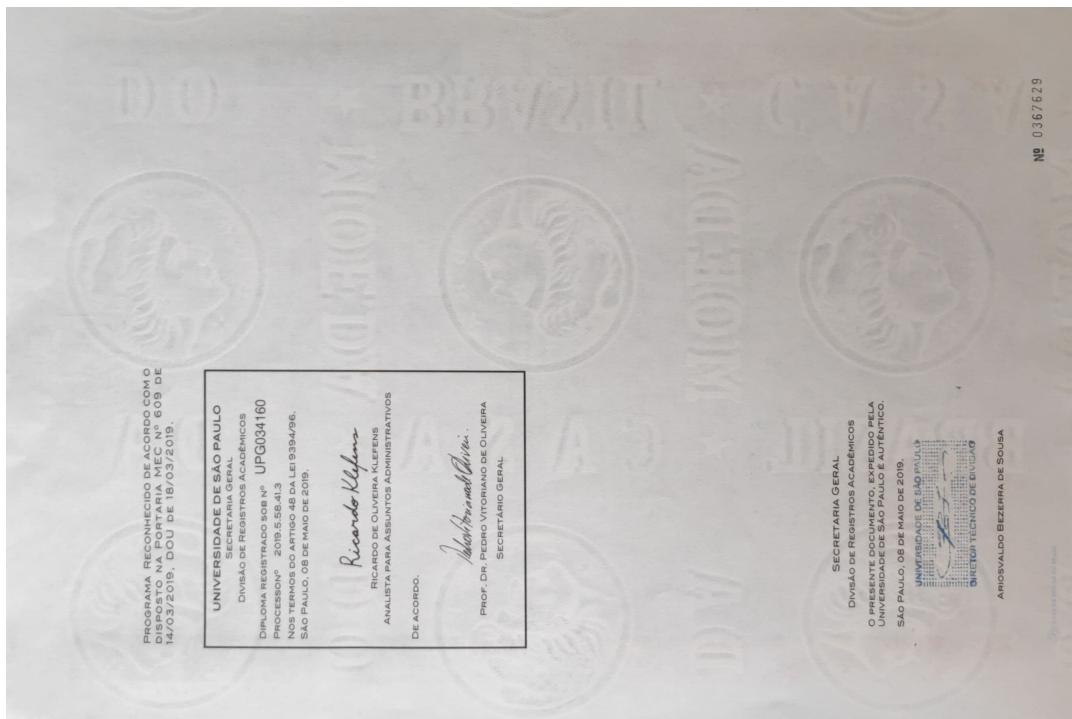
6. Área/Subárea: Genética
 Genética Quantitativa

7. Coordenação: Biologia I

8. Período da vigência: 01/07/2019 a 30/06/2021

9. Relatórios Científicos: 10/07/2021

10. Prestações de Contas: 10/07/2021



Documento 3: Diploma de Doutorado.



Para uso exclusivo da FAPESP
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 Volume: _____
 Rubrica: _____

FUNDAÇÃO DE AMPARO À PESQUISA DO ESTADO DE SÃO PAULO

TERMO DE OUTORGA E ACEITAÇÃO DE BOLSAS NO PAÍS

PROCESSO 2014/26262-4

Pelo presente instrumento, a Fundação de Amparo à Pesquisa do Estado de São Paulo, com sede na Rua Pio XI, nº 1500, Alto da Lapa, São Paulo, Capital, inscrita no CNPJ/MF sob o nº 43.828.151/0001-45, doravante denominada OUTORGANTE, por meio de seu Conselho Técnico-Administrativo, nos termos do Artigo 14, letra "b", da Lei Estadual nº 5.918, de 18 de outubro de 1960, concede ao(s) OUTORGADO(S), a seguir qualificado(s), Bolsa para a realização do Projeto de Pesquisa a seguir especificado, nas instalações e com o apoio da INSTITUIÇÃO SEDE, de acordo com as especificações, cláusulas e condições descritas a seguir e nos Anexos, que passam a ser parte integrante deste Termo.

1. OUTORGADOS

1.1 BOLSISTA: Diogo Amaral Reboucas Melo

CPF: 329.212.298-89

RG: 350021107-SSP/SP

1.2 ORIENTADOR/SUPERVISOR: Gabriel Henrique Marroig Zambonato

CPF: 989.457.267-72

RG: 116197229-IFP/RJ

2. Correspondência

2.1 BOLSISTA: A/C Diogo Melo, Rua Sousa Reis 153 - ap 71, Vila Indiana, São Paulo/SP,
CEP 05586-080
diogro@usp.br

2.2 ORIENTADOR/SUPERVISOR: Rua Fidalga 953 - casa 10, Pinheiros, São Paulo/SP, CEP 05432-070
gmarroig@usp.br

3. Instituição Sede: Instituto de Biociências/IB
Universidade de São Paulo/USP

4. Projeto de Pesquisa: Estimativas Diretas de
Parâmetros Evolutivos Via Análise de Loci de Traços
Quantitativos

5. Linha de Fomento: Programas Regulares / Bolsas / No País / Doutorado

6. Área/Subárea: Genética
Genética Quantitativa

7. Coordenação: Biologia II

8. Período da vigência: 01/04/2015 a 31/03/2018

9. Relatórios Científicos: 10/03/2016, 10/03/2017, 10/04/2018

10. Prestações de Contas: 10/03/2016, 10/03/2017, 10/04/2018

11. Entrega da Ata de Defesa: 15/10/2018



**Milner Centre for Evolution
Department of Biology & Biochemistry**

Bath, BA2 7AY, United Kingdom

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Mobile	+44 (0) 7913.138.388
Fax	+44 (0) 1225 386.779
Email	j.b.wolf@bath.ac.uk

1 November 2016

To whom it may concern,

I hereby express my endorsement of the contents of the final scientific report regarding the research activities developed by Diogo Amaral Reboças Melo during the tenure of his Research Internship Abroad Grant (BEPE-FAPESP number 2015/21811-2), developed under my supervision from 11/05/2016 to 11/09/2016. Diogo also worked under my supervision in a Global Research Scholarship Fund from 11/03/2014 to 30/05/2014. As described in the report, this internship allowed Diogo to familiarize himself with multiple QTL mapping techniques, as well as developing new applications of existing regression models. Diogo also worked on the FAPESP project number 2013/50402-8, which is related to his PhD, being instrumental to the design of a new genotyping array specific for this project. Please feel free to contact me if you require further information.

Sincerely,

A handwritten signature in black ink, appearing to read "Jason B. Wolf".

Jason B. Wolf



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 Processo: 2015/21811-2
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 Folha: _____
 Volume: _____
 Rubrica: _____

FUNDAÇÃO DE AMPARO À PESQUISA DO ESTADO DE SÃO PAULO

TERMO DE OUTORGА E ACEITAÇÃO DE BOLSAS NO EXTERIOR

PROCESSO 2015/21811-2

Pelo presente instrumento, a Fundação de Amparo à Pesquisa do Estado de São Paulo, com sede na Rua Pio XI, nº 1500, Alto da Lapa, São Paulo, Capital, inscrita no CNPJ/MF sob o nº 43.828.151/0001-45, doravante denominada OUTORGANTE, por meio de seu Conselho Técnico-Administrativo, nos termos do Artigo 14, letra "b", da Lei Estadual nº 5.918, de 18 de outubro de 1960, concede aos OUTORGADO(S), a seguir qualificado(s), Bolsa para a realização de Projeto de Pesquisa a seguir especificado, em Instituição no Exterior, com o apoio da INSTITUIÇÃO SEDE, de acordo com as especificações, cláusulas e condições descritas a seguir e nos Anexos, que passa a ser parte integrante deste Termo.

1. OUTORGADOS

1.1 BOLSISTA: Diogo Amaral Reboucas Melo
 CPF: 329.212.298-89
 RG: 350021107-SSP/SP

1.2 ORIENTADOR/SUPERVISOR: Gabriel Henrique Marroig Zambonato
 CPF: 989.457.267-72
 RG: 116197229-IFP/RJ

2. Correspondência

2.1 BOLSISTA: A/C Diogo Melo, Rua Sousa Reis 153 - ap 71, Vila Indiana, São Paulo/SP, CEP 05586-080
 diogro@usp.br

2.2 ORIENTADOR/SUPERVISOR: Rua Fidalga 953 - casa 10, Pinheiros, São Paulo/SP, CEP 05432-070
 gmarroig@usp.br

3. Instituição Sede: Instituto de Biociências/IB
 Universidade de São Paulo/USP

4. Instituição no Exterior: University of Bath
 Bath
 Inglaterra

5. Projeto de Pesquisa: Estimativas Diretas de Parâmetros Evolutivos Via
 Análise de QTL

6. Linha de Fomento: Programas Regulares / Bolsas / No Exterior / Bolsa Estágio de Pesquisa
 no Exterior / BEPE - Doutorado

7. Área/Subárea: Genética
 Genética Quantitativa

8. Coordenação: Biologia II

9. Período da vigência: 11/04/2016 a 10/09/2016

10. Relatórios Científicos: 30/10/2016

11. Prestações de Contas: 30/10/2016



Documento 7: Diploma de Mestrado.



Processo: 2010/04497-9
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Volume: _____
Rubrica: _____

Termo de Outorga

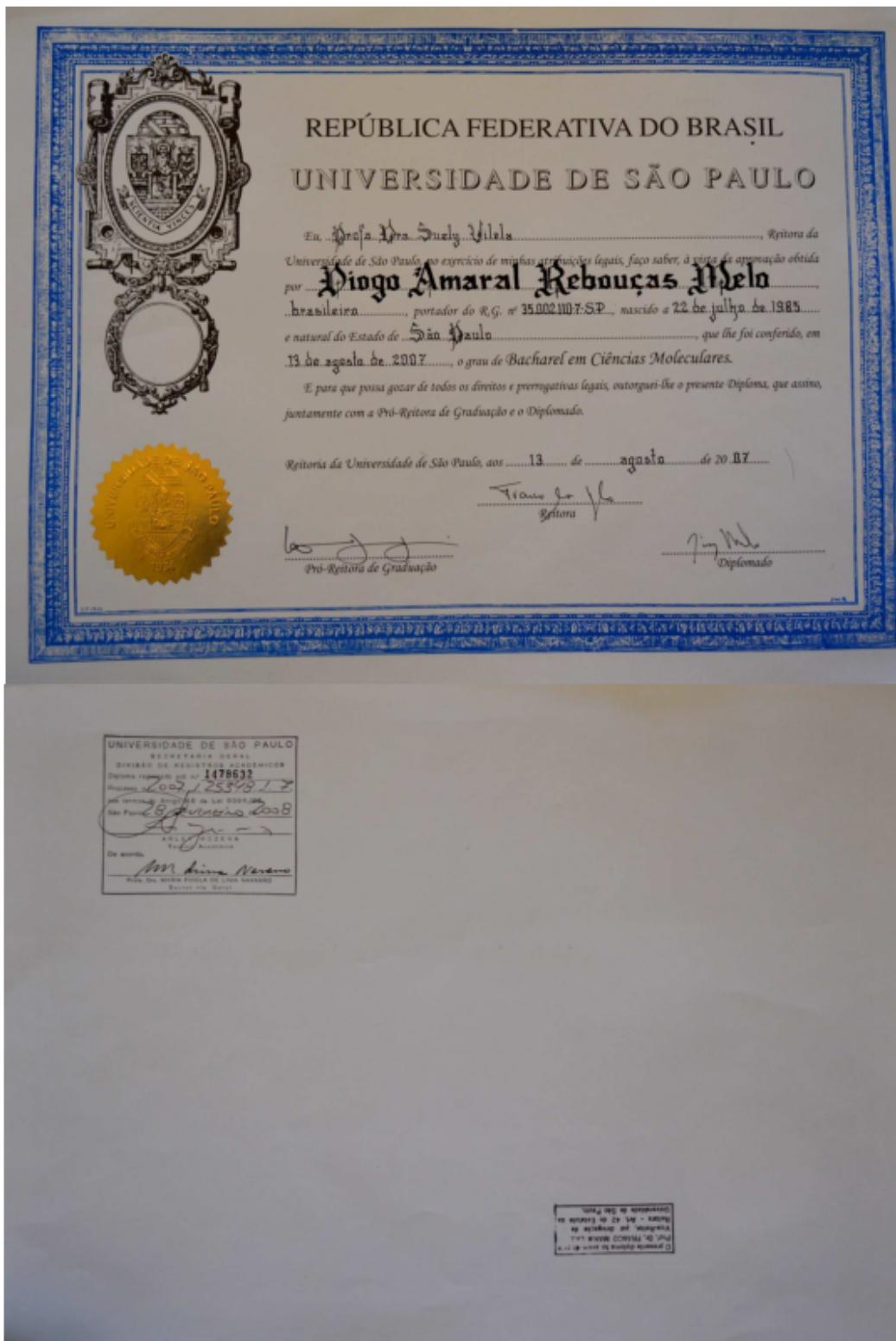
Processo 2010/04497-9

O Conselho Técnico-Administrativo da Fundação de Amparo à Pesquisa do Estado de São Paulo, doravante denominada OUTORGANTE , usando das atribuições que lhe confere o Artigo 14, letra "b" da Lei Estadual no 5.918, de 18 de outubro de 1960, e de acordo com as especificações, cláusulas e condições descritas a seguir e nos Anexos, que são parte integrante deste Termo, concede:	
Outorgado	Diogo Amaral Reboucas Melo CPF: 329.212.298-89
Orientador/Supervisor	Gabriel Henrique Marroig Zambonato CPF: 989.457.267-72
Instituição	Instituto de Biociências/IB/USP
Linha de Fomento	Programas Regulares / Bolsas / No País / Mestrado
Projeto	Evolução Morfológica e Modularidade
Grande Área	Ciências Biológicas
Área	Genética
Sub-área	Genética Quantitativa
Vigência	01/08/2010 a 29/02/2012
Relatórios Científicos até	10/07/2011, 10/03/2012

Observações
- Concessão improrrogável.



Documento 9: Diploma de Curso de Ciências Biológicas.



Documento 10: Diploma de Curso de Ciências Moleculares.



Processo: 2014/01694-9
Data impressão: 20/04/2020 22:14:57
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Volume: _____
Rubrica: _____

Termo de Outorga

Processo 2014/01694-9

O Conselho Técnico-Administrativo da Fundação de Amparo à Pesquisa do Estado de São Paulo, doravante denominada OUTORGANTE , usando das atribuições que lhe confere o Artigo 14, letra "b" da lei Estadual no 5.918, de 18 de outubro de 1960, e de acordo com as especificações, cláusulas e condições descritas a seguir e nos Anexos, que são parte integrante deste Termo, concede:	
OUTORGADO	Diogo Amaral Reboucas Melo CPF: 329.212.298-89
Orientador/Supervisor	Gabriel Henrique Marroig Zambonato CPF: 989.457.267-72
Instituição	Instituto de Biociências/IB/USP
Linha de Fomento	Bolsas Concedidas como Itens Orçamentários em Auxílios / Treinamento Técnico
Projeto	Elaboração de um Pacote em R para uso em pesquisa de genética quantitativa
Área	Genética
Grande Área	Ciências Biológicas
Sub-área	Genética Quantitativa
Vigência	01/03/2014 a 28/02/2015
Relatórios Científicos até	28/02/2015

Observações
- Concessão improrrogável. - Vinculado ao Auxílio à Pesquisa - Projeto Temático 2011/14295-7.



Processo: 2012/20180-0
Data impressão: 20/04/2020 17:06:12
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Termo de Outorga

Processo 2012/20180-0

O Conselho Técnico-Administrativo da Fundação de Amparo à Pesquisa do Estado de São Paulo, doravante denominada OUTORGANTE , usando das atribuições que lhe confere o Artigo 14, letra "b" da lei Estadual no 5.918, de 18 de outubro de 1960, e de acordo com as especificações, cláusulas e condições descritas a seguir e nos Anexos, que são parte integrante deste Termo, concede:	
OUTORGADO	Diogo Amaral Reboucas Melo CPF: 329.212.298-89
Orientador/Supervisor	Gabriel Henrique Marroig Zambonato CPF: 989.457.267-72
Instituição	Instituto de Biociências/IB/USP
Linha de Fomento	Bolsas Concedidas como Itens Orçamentários em Auxílios / Treinamento Técnico
Projeto	Técnicas computacionais em genética quantitativa.
Área	Biologia Geral
Grande Área	Ciências Biológicas
Sub-área	Outra Subárea Biologia Geral
Vigência	01/11/2012 a 31/10/2013
Relatórios Científicos até	30/01/2014

Observações
- Vinculado ao Auxílio à Pesquisa - Projeto Temático 2011/14295-7.

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Reassessing the modularity of gene co-expression networks using the Stochastic Block Model

Diogo Melo, Luisa F. Pallares, Julien F. Ayroles
doi: <https://doi.org/10.1101/2023.05.31.542906>

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Abstract

Finding communities in gene co-expression networks is a common first step toward extracting biological insight from such complex datasets. Most community detection algorithms expect genes to be organized into assortative modules, that is, groups of genes that are more associated with each other than with genes in other groups. While it is reasonable to expect that these modules exist, using methods that assume they exist a priori is risky, as it guarantees that alternative organizations of gene interactions will be ignored. Here, we ask: can we find meaningful communities without imposing a modular organization on gene co-expression networks, and how modular are these communities? For this, we use a recently developed community detection method, the weighted degree corrected stochastic block model (SBM), that does not assume that assortative modules exist. Instead, the SBM attempts to efficiently use all information contained in the co-expression network to separate the genes into hierarchically organized blocks of genes. Using RNA-seq gene expression data measured in two tissues derived from an outbred population of *Drosophila melanogaster*, we show that (a) the SBM is able to find ten times as many groups as competing methods, that (b) several of those gene groups are not modular, and that (c) the functional enrichment for non-modular groups is as strong as for modular communities. These results show that the transcriptome is structured in more complex ways than traditionally thought and that we should revisit the long-standing assumption that modularity is the main driver of the structuring of gene co-expression networks.

Competing Interest Statement

The authors have declared no competing interest.

Documento 13: Artigo *pre-print*: Melo, D., Pallares, L. F., & Ayroles, J. F. (2023). Reassessing the modularity of gene co-expression networks using the Stochastic Block Model. *Biorxiv*, 2023. <https://doi.org/10.1101/2023.05.31.542906>.

New Results [Follow this preprint](#)

Saturating the eQTL map in *Drosophila melanogaster*: genome-wide patterns of cis and trans regulation of transcriptional variation in outbred populations

Luisa F. Pallares, Diogo Melo, Scott Wolf, Evan M. Cofer, Varada Abhyankar, Julie Peng, Julien F. Ayroles

doi: <https://doi.org/10.1101/2023.05.20.541576>

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Posted June 13, 2023.

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Abstract

Decades of genome-wide mapping have shown that most genetic polymorphisms associated with complex traits are found in non-coding regions of the genome. Characterizing the effect of such genetic variation presents a formidable challenge, and eQTL mapping has been a key approach to understand the non-coding genome. However, comprehensive eQTL maps are available only for a few species like yeast and humans. With the aim of understanding the genetic landscape that regulates transcriptional variation in *Drosophila melanogaster*, we developed an outbred mapping panel in this species, the *Drosophila* Outbred Synthetic Panel (Dros-OSP). Using this community resource, we collected transcriptomic and genomic data for 1800 individual flies and were able to map *cis* and *trans* eQTLs for 98% of the genes expressed in *D. melanogaster*, increasing by thousands the number of genes for which regulatory loci are known in this species. We described, for the first time in the context of an outbred population, the properties of local and distal regulation of gene expression in terms of genetic diversity, heritability, connectivity, and pleiotropy. We uncovered that, contrary to long-standing assumptions, a significant part of gene co-expression networks is organized in a non-modular fashion. These results bring the fruit fly to the level of understanding that was only available for a few other organisms, and offer a new mapping resource that will expand the possibilities currently available to the *Drosophila* community. This data is available at DrosophilaeQTL.org.

Competing Interest Statement

The authors have declared no competing interest.

Documento 14: Artigo *pre-print*: Pallares, L. F., Melo, D., Wolf, S., Cofer, E. M., Varada, V., Peng, J., & Ayroles, J. F. (2023). Saturating the eQTL map in *Drosophila melanogaster*: genome-wide patterns of cis and trans regulation of transcriptional variation in outbred populations. *Biorxiv*, 2023. <https://doi.org/10.1101/2023.05.20.541576>.

New Results [Follow this preprint](#)

From GWAS to signal validation: An approach for estimating genetic effects while preserving genomic context

Scott Wolf, Varada Abhyankar, Diogo Melo, Julien F. Ayroles, Luisa F. Pallares
doi: <https://doi.org/10.1101/2023.03.09.531909>

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Posted June 02, 2023.

Abstract

Validating associations between genotypic and phenotypic variation remains a challenge, despite advancements in association studies. Common approaches for signal validation rely on gene-level perturbations, such as loss-of-function mutations or RNAi, which test the effect of genetic modifications usually not observed in nature. CRISPR-based methods can validate associations at the SNP level, but have significant drawbacks, including resulting off-target effects and being both time-consuming and expensive. Both approaches usually modify the genome of a single genetic background, limiting the generalizability of experiments. To address these challenges, we present a simple, low-cost experimental scheme for validating genetic associations at the SNP level in outbred populations. The approach involves genotyping live outbred individuals at a focal SNP, crossing homozygous individuals with the same genotype at that locus, and contrasting phenotypes across resulting synthetic outbred populations. We tested this method in *Drosophila melanogaster*, measuring the longevity effects of a polymorphism at a naturally-segregating cis-eQTL for the *midway* gene. Our results demonstrate the utility of this method in SNP-level validation of naturally occurring genetic variation regulating complex traits. This method provides a bridge between the statistical discovery of genotype-phenotype associations and their validation in the natural context of heterogeneous genomic contexts.

Competing Interest Statement

The authors have declared no competing interest.

Documento 15: Artigo *pre-print*: Wolf, S., Abhyankar, V., Melo, D., Ayroles, J. F., & Pallares, L. F. (2023). From GWAS to signal validation: An approach for estimating genetic effects while preserving genomic context. *Biorxiv*, 2023. <https://doi.org/10.1101/2023.03.09.531909>.

RESEARCH ARTICLE

Characterizing the landscape of gene expression variance in humans

Scott Wolf^{1*}, Diogo Melo^{1,2*}, Kristina M. Garske¹, Luisa F. Pallares^{1,2,3}, Amanda J. Lea^{4,5}, Julien F. Ayroles^{1,2,*}

1 Lewis-Sigler Institute for Integrative Genomics, Princeton University, Princeton, New Jersey, United States of America, **2** Department of Ecology and Evolutionary Biology, Princeton University, Princeton, New Jersey, United States of America, **3** Friedrich Miescher Laboratory of the Max Planck Society, Tübingen, Germany, **4** Department of Biological Sciences, Vanderbilt University, Nashville, Tennessee, United States of America, **5** Child and Brain Development, Canadian Institute for Advanced Research, Toronto, Canada

* These authors contributed equally to this work.
* damelo@princeton.edu (DM); jayroles@princeton.edu (JFA)



OPEN ACCESS

Citation: Wolf S, Melo D, Garske KM, Pallares LF, Lea A, Ayroles JF (2023) Characterizing the landscape of gene expression variance in humans. PLoS Genet 19(7): e1010833. <https://doi.org/10.1371/journal.pgen.1010833>

Editor: James J. Cai, Texas A&M University, UNITED STATES

Received: January 5, 2023

Accepted: June 15, 2023

Published: July 6, 2023

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: <https://doi.org/10.1371/journal.pgen.1010833>

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Data Availability Statement: Code for reproducing all analyses and figures, along with a walk-through, is available at github.com/ayroles-lab/expressionVariance-code. All relevant data are within the paper and its Supporting Information

Abstract

Gene expression variance has been linked to organismal function and fitness but remains a commonly neglected aspect of molecular research. As a result, we lack a comprehensive understanding of the patterns of transcriptional variance across genes, and how this variance is linked to context-specific gene regulation and gene function. Here, we use 57 large publicly available RNA-seq data sets to investigate the landscape of gene expression variance. These studies cover a wide range of tissues and allowed us to assess if there are consistently more or less variable genes across tissues and data sets and what mechanisms drive these patterns. We show that gene expression variance is broadly similar across tissues and studies, indicating that the pattern of transcriptional variance is consistent. We use this similarity to create both global and within-tissue rankings of variation, which we use to show that function, sequence variation, and gene regulatory signatures contribute to gene expression variance. Low-variance genes are associated with fundamental cell processes and have lower levels of genetic polymorphisms, have higher gene-gene connectivity, and tend to be associated with chromatin states associated with transcription. In contrast, high-variance genes are enriched for genes involved in immune response, environmentally responsive genes, immediate early genes, and are associated with higher levels of polymorphisms. These results show that the pattern of transcriptional variance is not noise. Instead, it is a consistent gene trait that seems to be functionally constrained in human populations. Furthermore, this commonly neglected aspect of molecular phenotypic variation harbors important information to understand complex traits and disease.

Author summary

Gene expression variance, or the variation in the level of gene expression within a population, can have significant impacts on physiology, disease, and evolutionary adaptations. While the average level of gene expression is typically the focus of research, the variation

Evolution, 2023, XX(XX), 1–13
<https://doi.org/10.1093/evolut/qpac052>
 Advance access publication 22 December 2022
 Original Article



Morphological integration during postnatal ontogeny: implications for evolutionary biology

Alex Hubbe, PhD^{1,2}, Fabio A. Machado, PhD³, Diogo Melo, PhD⁴, Guilherme Garcia, PhD⁵, Harley Sebastião, PhD⁶, Arthur Porto, PhD^{6,7}, James Cheverud, PhD⁸, Gabriel Marroig, PhD⁹

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Abstract

How covariance patterns of phenotypes change during development is fundamental for a broader understanding of evolution. There is compelling evidence that mammalian cranium covariance patterns change during ontogeny. However, it is unclear to what extent variation in covariance patterns during ontogeny can impact the response to selection. To tackle this question, we explored: (a) the extent to which covariance patterns change during postnatal ontogeny; (b) in which ontogenetic stages covariance patterns differ the most; and (c) the extent to which the phenotypic covariance pattern at different ontogenetic stages can be explained by the same processes determining additive genetic covariance. We sampled the postnatal ontogenetic series for both marsupials and placentals. Within each ontogenetic series, we compared covariance matrices (**P**-matrices) at different ontogenetic stages. Furthermore, we compared these **P**-matrices to two target matrices [adult **P**-matrix and an additive genetic covariance matrix (**G**-matrix)]. Our results show that for all ontogenetic series, covariance patterns from weaning onward are conserved and probably shaped by the same processes determining the **G**-matrix. We conclude that irrespective of eventual differences in how selection operates during most of the postnatal ontogeny, the net response to such pressures will probably not be affected by ontogenetic differences in the covariance pattern.

Keywords: development, **G**-matrix, **P**-matrix, Marsupialia, Placentalia

Developmental processes change the amount and distribution of morphological variation through time (Mitteroecker & Bookstein, 2009; Zelditch et al., 2006). Not surprisingly, this is well documented for the mammalian cranium (Atchley, 1984; Coleman et al., 1994; Goswami et al., 2012; Hallgrímsson et al., 2009; Mitteroecker & Bookstein, 2009; Mitteroecker et al., 2012; Nonaka & Nakata, 1984; Sydney et al., 2012; Zelditch, 1988; Zelditch & Carmichael, 1989; Zelditch et al., 1992, 2006), which is a common model system for investigating the evolution of complex structures [e.g., Goswami (2006); Haber (2015); Machado et al., (2018)]. Yet, there is little evidence on how these documented differences along ontogeny would affect evolution.

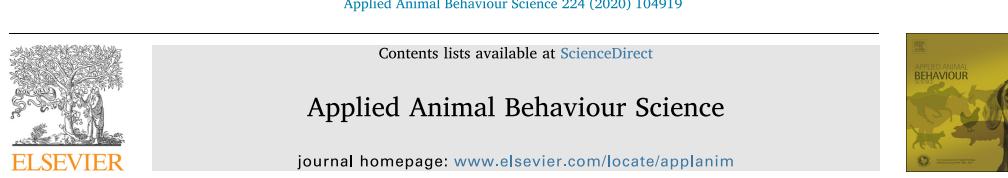
Since natural selection is contingent on the availability and organization of morphological variation (Lande, 1979; Lande & Arnold, 1983), differences in the amount and structure of variation across life history stages can affect how populations respond to selection (Wasserman et al., 2021). For example, consider a scenario in which a pair of traits are associated (i.e., high integration *sensu* Olson & Miller, 1958) in the

juvenile phase, but in the adult phase, these traits are much less integrated [Figure 1; e.g., Sydney et al. (2012)]. If selection operates on a single trait at the juvenile stage, evolutionary responses will be aligned with the major direction of variation of juveniles, leading to a correlated response in the second trait, even in the absence of trait association in the adult phase. Furthermore, in this scenario, the reconstruction of selection using the adult stage would suggest that selection is acting on multiple traits simultaneously, while in fact, it is acting on a single trait earlier in development. Conversely, if the covariance patterns are relatively stable throughout ontogeny, selection would produce evolutionary responses that are similar across ontogenetic stages. Therefore, understanding how the variance is distributed on different ontogenetic stages can provide further insight about how complex phenotypes might evolve in response to natural selection. This knowledge has also broader implications since complex phenotypes play, for instance, an important role in ecological interactions (Assis et al., 2022; Saccheri & Hanski, 2006), and population's extinction risk (Forester et al., 2022).

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Received May 2, 2022; accepted December 2, 2022
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Documento 17: Artigo: Hubbe, A., Machado, F. A., Melo, D., Garcia, G., Sebastião, H., Porto, A., Cheverud, J., & Marroig, G. (2022). Morphological integration during postnatal ontogeny: implications for evolutionary biology. *Evolution*. <https://doi.org/10.1093/evolut/qpac052>.



Are cats less stressed in homes than in shelters? A study of personality and faecal cortisol metabolites



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ARTICLE INFO

Keywords:
Feline personality
Individual differences
Faecal cortisol metabolites
Cat owners
Shelter adoption

ABSTRACT

Personality is defined by characteristics of individuals and describes and accounts for temporally stable patterns of affect, cognition and behaviour traits. The study of cat behaviour and personality can minimize potential problems in the relationship between cats and their owners and decrease abandonment and maltreatment. People generally adopt animals according to the individual's appearance, age or sex. Personality assessments can help make adoptions successful by identifying ideal subjects for potential owners. A personality assessment called "Meet Your Match"™ (MYM), developed by the American Society for the Prevention of Cruelty to Animals (ASPCA) and validated for our cat sample was used in this study. To evaluate stress, we measured faecal cortisol metabolites (FCMs) of cats in shelters and after adoption. In an effort to improve adoption and cat adaptation in new homes, our goals were 1) to evaluate the relationship between personality and cortisol levels; 2) to confirm if MYM assessment is consistent through situations; and 3) to investigate how moving from the shelter to the owners' homes affects FCM levels. The subjects for our first goal were 53 sheltered cats. For the second and the third goals, we followed 15 of the original 53 after the adoption. No correlation was found between personality dimensions (agreeableness $p = 0.878$; openness $p = 0.141$; extraversion $p = 0.942$) and FCM levels. MYM assessment was consistent through different localities. There was a slight, but significant ($p = 0.0072$), decrease of FCM levels at owners' home. However, most subjects ($n = 11$) did not present changes that were significantly different from zero. Our study underlined the usefulness of the MYM personality assessment and confirmed a lack of correlation between personality and cortisol levels in cats. It is a further step towards incorporating a more objective approach to the adoption process in shelters to improve the pairing of humans and cats.

1. Introduction

Personality research ranges from invertebrates (Carere et al., 2018) to primates (Freeman and Gosling, 2010). Definitions of personality point to those characteristics of individuals that describe and account for temporally stable patterns of affection, cognition, and behaviour (Siegford et al., 2003; Gosling, 2008; Uher, 2011; Gartner and Weiss, 2013; MacKay and Haskell, 2015). Research in animal personality joined efforts to unravel the dimensions that compose each species' personality traits. Human personality, for example, is composed of five dimensions as shown in the Five Factor Model (John and Srivastava, 1999). Being the most popular pets in households, dogs and cats are also being studied (Jones and Gosling, 2005; Gartner and Weiss, 2013). Most studies are based on surveys with caretakers and focus on

personality measurements, genetics and the relationship between personality and its health effects in captive and confined individuals (Gartner, 2015). Recent studies have investigated cat personality dimensions (Gartner and Weiss, 2013; Gartner et al., 2014; Kaleta et al., 2016; Bennett et al., 2017; Ha and Ha, 2017; Litchfield et al., 2017) and, so far, have unfolded a number of them, such as affection, energy, sociability and curiosity (Gartner, 2015).

As complex and intricate as human-animal interactions can be (Bradshaw, 2013), potential issues in the relationship between cats and their owners — such as abandonment or mistreatment (Genaro, 2004) — can be mitigated with the aid of knowledge obtained from studies about cat behaviour and personality, the monitoring of cat populations, and educational actions (Hiby et al., 2014). Unsuccessful adoptions are a multi-causal event and are related to: aggression between cats in

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<https://doi.org/10.1016/j.applanim.2019.104919>
Received 15 January 2019; Received in revised form 22 October 2019; Accepted 20 November 2019
Available online 28 November 2019
0168-1591/© 2020 Elsevier B.V. All rights reserved.

Documento 18: Artigo: Fukimoto, N., Melo, D., Palme, R., Zanella, A. J., & Mendonça-Furtado, O. (2020). Are cats less stressed in homes than in shelters? A study of personality and faecal cortisol metabolites. *Applied Animal Behaviour Science*, 104919. <https://doi.org/10.1016/j.applanim.2019.104919>.



Journal of Heredity, 2019, 1–15
 doi:10.1093/jhered/esz011
 Symposium Article
 Advance Access publication April 15, 2019



Symposium Article

Genomic Perspective on Multivariate Variation, Pleiotropy, and Evolution

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Received August 30, 2018; First decision November 8, 2019; Accepted February 13, 2019.

Corresponding Editor: Anne Bronikowski

Abstract

Multivariate quantitative genetics provides a powerful framework for understanding patterns and processes of phenotypic evolution. Quantitative genetics parameters, like trait heritability or the G-matrix for sets of traits, can be used to predict evolutionary response or to understand the evolutionary history of a population. These population-level approaches have proven to be extremely successful, but the underlying genetics of multivariate variation and evolutionary change typically remain a black box. Establishing a deeper empirical understanding of how individual genetic effects lead to genetic (co)variation is then crucial to our understanding of the evolutionary process. To delve into this black box, we exploit an experimental population of mice composed from lineages derived by artificial selection. We develop an approach to estimate the multivariate effect of loci and characterize these vectors of effects in terms of their magnitude and alignment with the direction of evolutionary divergence. Using these estimates, we reconstruct the traits in the ancestral populations and quantify how much of the divergence is due to genetic effects. Finally, we also use these vectors to decompose patterns of genetic covariation and examine the relationship between these components and the corresponding distribution of pleiotropic effects. We find that additive effects are much larger than dominance effects and are more closely aligned with the direction of selection and divergence, with larger effects being more aligned than smaller effects. Pleiotropic effects are highly variable but are, on average, modular. These results are consistent with pleiotropy being partly shaped by selection while reflecting underlying developmental constraints.

Keywords: G-matrix, genetic architecture, genome prediction, genotype–phenotype map, horseshoe prior, QTL mapping

Individuals are composed of a complex array of traits that are interconnected through shared genetic, physiological, and developmental processes. Consequently, evolution is inherently a multivariate process, wherein suites of traits interact to determine an individual's fitness, which generates selection that cascades to the genomic level through the genotype–phenotype relationship leading to heritable changes across generations (Lande and Arnold 1983; Klingenberg

2008; Melo et al. 2016). Therefore, understanding evolutionary change in response to selection requires an understanding of the relationship between genotypic variation and multivariate traits. The quantitative genetics framework was developed to achieve this goal, historically relying on statistical measurement of genetic covariation between traits as a summary of their genetic "connectedness." The covariances estimated using this framework can be used

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Documento 19: Artigo: Melo, D., Marroig, G., & Wolf, J. B. (2019). Genomic Perspective on Multivariate Variation, Pleiotropy, and Evolution. *Journal of Heredity*, 4, 479–493. <https://doi.org/10.1093/jhered/esz011>.

BRIEF COMMUNICATION

 doi:10.1111/evo.13864

SSE
SOCIETY FOR THE STUDY OF EVOLUTION

Measuring the magnitude of morphological integration: The effect of differences in morphometric representations and the inclusion of size

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Received March 4, 2019
Accepted October 3, 2019

The magnitude of morphological integration is a major aspect of multivariate evolution, providing a simple measure of the intensity of association between morphological traits. Studies concerned with morphological integration usually translate phenotypes into morphometric representations to quantify how different morphological elements covary. Geometric and classic morphometric representations translate biological form in different ways, raising the question if magnitudes of morphological integration estimates obtained from different morphometric representations are compatible. Here we sought to answer this question using the relative eigenvalue variance of the covariance matrix obtained for both geometric and classical representations of empirical and simulated datasets. We quantified the magnitude of morphological integration for both shape and form and compared results between representations. Furthermore, we compared integration values between shape and form to evaluate the effect of the inclusion or not of size on the quantification of the magnitude of morphological integration. Results show that the choice of morphological representation has significant impact on the integration magnitude estimate, either for shape or form. Despite this, ordination of the integration values within representations is relatively the same, allowing for similar conclusions to be reached using different methods. However, the inclusion of size in the dataset significantly changes the estimates of magnitude of morphological integration, hindering the comparison of this statistic obtained from different spaces. Morphometricians should be aware of these differences and must consider how biological hypothesis translate into predictions about integration in each particular choice of representation.

KEY WORDS: Covariance matrix, canidae, eigenvalue variance, P matrix, skull.

ORIGINAL ARTICLE

doi:10.1111/evo.13304



SSE
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The evolution of phenotypic integration: How directional selection reshapes covariation in mice

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Received February 7, 2017
Accepted June 10, 2017

Variation is the basis for evolution, and understanding how variation can evolve is a central question in biology. In complex phenotypes, covariation plays an even more important role, as genetic associations between traits can bias and alter evolutionary change. Covariation can be shaped by complex interactions between loci, and this genetic architecture can also change during evolution. In this article, we analyzed mouse lines experimentally selected for changes in size to address the question of how multivariate covariation changes under directional selection, as well as to identify the consequences of these changes to evolution. Selected lines showed a clear restructuring of covariation in their cranium and, instead of depleting their size variation, these lines increased their magnitude of integration and the proportion of variation associated with the direction of selection. This result is compatible with recent theoretical works on the evolution of covariation that take the complexities of genetic architecture into account. This result also contradicts the traditional view of the effects of selection on available covariation and suggests a much more complex view of how populations respond to selection.

KEY WORDS: Artificial selection, body size, cranium, experimental evolution, G-matrix, morphological integration, P-Matrix.

Evolutionary change can only occur in the presence of variation, and when dealing with complex multivariate phenotypes (consisting of multiple traits) the patterns and magnitude of genetic covariation between traits can radically influence the course of evolution (Lande 1979; Felsenstein 1988). The standing genetic covariation of a given population depends on its evolutionary history, and can be altered by selection, drift, mutation, and recombination (Turelli and Barton 1994; Jones et al. 2004, 2014). These changes in covariation, in turn, can alter how a population responds to further selection or other evolutionary processes. So, if we are to understand how populations evolve and how the current phenotypic diversity observed in nature came to be, then the question of how genetic variation changes under various evolutionary processes becomes central to biology (Mitchell-Olds et al. 2007).

How a single trait responds to directional selection is a well-studied problem (Falconer and Mackay 1996). In general, we expect the response to selection to gradually erode genetic variation, as the many loci influencing a given trait go to fixation and, in the absence of mutation, preclude further evolutionary change (Bulmer 1971). If mutation is present and of sufficient magnitude, the variation removed by selection can be replenished and the rate of evolutionary change remains constant, at least for a time.

A theory on how directional selection and covariation interact to produce the response to selection on multiple traits was proposed by Lande (1979). This author related the standing genetic

*These authors contributed equally to this work.

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Evolution

Documento 21: Artigo: Penna, A., Melo, D., Bernardi, S., Oyarzabal, M. I., & Marroig, G. (2017). The evolution of phenotypic integration: How directional selection reshapes covariation in mice. *Evolution*, 10, 2370–2380. <https://doi.org/10.1111/evo.13304>.

Insights from Systems Biology in Physiological Studies: Learning from Context

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Key Words

Physiology • Systems biology • Context • Epistasis • Top-down • Genetic background • Modularity • Interolog

Abstract

Systems biology presents an integrated view of biological systems, focusing on the relations between elements, whether functional or evolutionary, and providing a rich framework for the comprehension of life. At the same time, many low-throughput experimental studies are performed without influence from this integrated view, whilst high-throughput experiments use low-throughput results in their validation and interpretation. We propose an inversion in this logic, and ask which benefits could be obtained from a holistic view coming from high-throughput studies—and systems biology in particular—in interpreting and designing low-throughput experiments. By exploring some key examples from the renal and adrenal physiology, we try to show that network and modularity theory, along with observed patterns of association between elements in a biological system, can have profound effects on our ability to draw meaningful conclusions from experiments.

Introduction

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Low-throughput studies in experimental biology are a traditional approach in science and have been responsible for tremendous advances, from new medications to a better understanding of human behaviour. When Otto Loewi, in 1921, showed that acetylcholine was a neurotransmitter, he was using low-throughput techniques to show that one substance could perform a specific action, transmitting a message from one cell to the next [1]. Indeed, research in physiology still uses very similar approaches to identify new molecular pathways, proteins that could be targets for new drugs, mutations in genes that are good candidates for triggering diseases, and so on. Often, low-throughput studies are considered by the academic community as of higher quality when compared to high-throughput

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Modularity: Genes, Development, and Evolution

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Annu. Rev. Ecol. Evol. Syst. 2016; 47:463–86

First published online as a Review in Advance on September 7, 2016

The *Annual Review of Ecology, Evolution, and Systematics* is online at ecolsys.annualreviews.org

This article's doi:
10.1146/annurev-ecolsys-121415-032409

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Keywords

macroevolution, genotype–phenotype map, G-matrix, adaptive landscape, morphological integration

Abstract

Modularity has emerged as a central concept for evolutionary biology, thereby providing the field with a theory of organismal structure and variation. This theory has reframed long-standing questions and serves as a unified conceptual framework for genetics, developmental biology, and multivariate evolution. Research programs in systems biology and quantitative genetics are bridging the gap between these fields. Although this synthesis is ongoing, some major themes have emerged, and empirical evidence for modularity has become abundant. In this review, we look at modularity from a historical perspective, highlighting its meaning at different levels of biological organization and the different methods that can be used to detect it. We then explore the relationship between quantitative genetic approaches to modularity and developmental genetic studies. We conclude by investigating the dynamic relationship between modularity and the adaptive landscape and how this relationship potentially shapes evolution and can help bridge the gap between micro- and macroevolution.

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Documento 23: Artigo: Melo, D., Porto, A., Cheverud, J. M., & Marroig, G. (2016). Modularity: genes, development and evolution. *Annual Reviews of Ecology, Evolution, And Systematics*, 1, 463–486.
<https://doi.org/10.1146/annurev-ecolsys-121415-032409>.

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Cite this article: Costa TM, Hebets EA, Melo D, Willemart RH. 2016 Costly learning: preference for familiar food persists despite negative impact on survival. *Biol. Lett.* **12**: 20160256. <http://dx.doi.org/10.1098/rsbl.2016.0256>

Received: 28 March 2016

Accepted: 22 June 2016

Subject Areas:
behaviour

Keywords:
dietary conservatism, harvestman,
maladaptive, neophobia, optimal foraging

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Electronic supplementary material is available at <http://dx.doi.org/10.1098/rsbl.2016.0256> or via <http://rsbl.royalsocietypublishing.org>.

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Animal behaviour

Costly learning: preference for familiar food persists despite negative impact on survival

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Animals often rely on events in their environment that provide information (i.e. experience) to alter their future decision-making in ways that are presumed to be beneficial. Such experience-based learning, however, does not always lead to adaptive decision-making. In this study, we use the omnivorous harvestman *Heteromitobates discolor* to explore the role of past diet on subsequent food choice and survival. We first tested whether a short-term homogeneous diet (rotten crickets, fresh crickets or dog food) influenced subsequent food choice (rotten cricket versus fresh cricket). We next examine the impact of diet on survival. We found that following experience with a homogeneous cricket diet, adult harvestmen displayed a learned preference for familiar food, regardless of whether it was rotten or fresh crickets; individuals experiencing dog food were equally likely to choose rotten versus fresh crickets. We additionally found that individuals that ate rotten crickets suffered shorter survival than those that ate fresh crickets. Together, our results suggest that the diet an individual experiences can lead to maladaptive food preferences—preferences that ultimately result in reduced longevity.

1. Introduction

Early modelling of foraging behaviour focused heavily on optimality, with models that predicted an animal's behaviour based on relative costs and benefits of alternative tactics [1]. These models assumed that animals have complete information about their environment; an unlikely assumption that led to proponents arguing for the importance of incomplete information and the role of experience in leading to behavioural changes [1]. More recently, it has been contended that formal theoretical modelling can be misleading or even wrong, as it often neglects the underlying mechanisms of behaviour, including psychological mechanisms such as learning and decision rules [2,3]. Additionally, many simple models do not incorporate the spatio-temporal heterogeneity, or complexity, of natural environments [3].

Indeed, animals are known to deviate from optimal decision-making across behavioural contexts—they are impulsive, they may not behave in ways that maximize rewards, and they may value alternative options irrationally (reviewed in [2,3]). One potential explanation for how and why animals engage in non-optimal decision-making may rely, at least in part, on the fact that animals often update their decision-making based on experience, or the processing of new information [4]—they learn. Additionally, seemingly irrational behaviour observed under simplified environmental conditions may be better understood

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Documento 24: Artigo: Costa, T. M., Hebets, E. A., Melo, D., & Willemart, R. H. (2016). Costly learning: preference for familiar food persists despite negative impact on survival. *Biology Letters*, 7, 20160256. <https://doi.org/10.1098/rsbl.2016.0256>.

Paleobiology, page 1 of 24
DOI: 10.1017/pab.2015.49



A case study of extant and extinct Xenarthra cranium covariance structure: implications and applications to paleontology

Alex Hubbe, Diogo Melo, and Gabriel Marroig

Abstract.—Most of the mammalian diversity is known only from fossils, and only a few of these fossils are well preserved or abundant. This undersampling poses serious problems for understanding mammalian phenotypic evolution under a quantitative genetics framework, since this framework requires estimation of a group's additive genetic variance–covariance matrix (G matrix), which is impossible, and estimating a phenotypic variance–covariance matrix (P matrix) requires larger sample sizes than what is often available for extinct species. One alternative is to use G or P matrices from extant taxa as surrogates for the extinct ones. Although there are reasons to believe this approach is usually safe, it has not been fully explored. By thoroughly determining the extant and some extinct Xenarthra (Mammalia) cranium P matrices, this study aims to explore the feasibility of using extant G or P matrices as surrogates for the extinct ones and to provide guidelines regarding the reliability of this strategy and the necessary sample sizes. Variance–covariance and correlation P matrices for 35 cranium traits from 16 xenarthran genera (12 extant and 4 extinct) were estimated and compared between genera. Results show xenarthran P -matrix structures are usually very similar if sample sizes are reasonable. This study and others developed with extant therian mammals suggest, in general, that using extant G or P matrices as an approximation to extinct ones is a valid approach. Nevertheless, the accuracy of this approach depends on sample size, selected traits, and the type of matrix being considered.

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Accepted: 12 November 2015

Supplemental materials deposited at Dryad: doi:10.5061/dryad.6br16

Introduction

The evolution of continuous traits is critically dependent on the genetic variance available in populations. Moreover, since traits in multicellular complex organisms often are not genetically independent (due to pleiotropy, epistasis, and linkage disequilibrium), these organisms cannot be regarded as a collection of independent parts being changed by evolutionary processes. Instead, an organism must be understood as a coherent whole, with relationships described by a covariance structure. Thus, traits usually evolve in a correlated way, and to fully understand the evolution of complex structures (like the mammalian skull) we need to deal with the inheritance of such multidimensional phenotypes (Fisher 1930; Wright 1931; Lande 1979; Lande and Arnold 1983; Falconer and MacKay 1996). Quantitative genetics provides a framework with which to understand multivariate

phenotypic character evolution, and this framework has been used to study many evolutionary questions in several extant and some extinct species, from plants to vertebrates (e.g., Lande 1979; Cheverud 1984; Lofsvold 1986; Arnold 1992; Steppan 1997; Goswami 2006; Goswami et al. 2014; Hansen and Houle 2008; Webster and Zelditch 2011; Porto et al. 2013; Armbruster et al. 2014; Haber 2015). Under this framework it is fundamental to determine the additive genetic variance–covariance matrix (hereafter G matrix), since it interacts with evolutionary processes to determine the rate and direction of evolution (Lande 1979; Lande and Arnold 1983; Cheverud 1984).

The G matrix is a symmetric square matrix in which each row/column represents a phenotypic trait measured in a population. The G matrix describes the additive genetic variance of each trait (i.e., unstandardized measure of heritability) on the diagonal and

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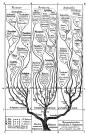
REVISED **EvoIQG - An R package for evolutionary quantitative genetics [version 3; referees: 2 approved, 1 approved with reservations]**

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v3 First published: 30 Sep 2015, 4:925 (doi: [10.12688/f1000research.7082.1](https://doi.org/10.12688/f1000research.7082.1))
Second version: 27 Jun 2016, 4:925 (doi: [10.12688/f1000research.7082.2](https://doi.org/10.12688/f1000research.7082.2))
Latest published: 08 Nov 2016, 4:925 (doi: [10.12688/f1000research.7082.3](https://doi.org/10.12688/f1000research.7082.3))

Abstract
We present an open source package for performing evolutionary quantitative genetics analyses in the R environment for statistical computing. Evolutionary theory shows that evolution depends critically on the available variation in a given population. When dealing with many quantitative traits this variation is expressed in the form of a covariance matrix, particularly the additive genetic covariance matrix or sometimes the phenotypic matrix, when the genetic matrix is unavailable and there is evidence the phenotypic matrix is sufficiently similar to the genetic matrix. Given this mathematical representation of available variation, the `\text{EvoIQG}` package provides functions for calculation of relevant evolutionary statistics; estimation of sampling error; corrections for this error; matrix comparison via correlations, distances and matrix decomposition; analysis of modularity patterns; and functions for testing evolutionary hypotheses on taxa diversification.

 This article is included in the Phylogenetics channel.

 This article is included in the RPackage channel.

Open Peer Review

Referee Status: ✓ ✓ ?

	Invited Referees	1	2	3
REVISED		✓		
version 3	report			
published				
08 Nov 2016				
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Fitness Trade-offs Result in the Illusion of Social Success

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<http://dx.doi.org/10.1016/j.cub.2015.02.061>

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SUMMARY

Cooperation is ubiquitous across the tree of life, from simple microbes to the complex social systems of animals [1]. Individuals cooperate by engaging in costly behaviors that can be exploited by other individuals who benefit by avoiding these associated costs. Thus, if successful exploitation of social partners during cooperative interactions increases relative fitness, then we expect selection to lead to the emergence of a single optimal winning strategy in which individuals maximize their gain from cooperation while minimizing their associated costs [2]. Such social “cheating” appears to be widespread in nature [3], including in several microbial systems [4–11], but despite the fitness advantages favoring social cheating, populations tend to harbor significant variation in social success rather than a single optimal winning strategy. Using the social amoeba *Dictyostelium discoideum*, we provide a possible explanation for the coexistence of such variation. We find that genotypes typically designated as “cheaters” [12] because they produce a disproportionate number of spores in chimeric fruiting bodies do not actually gain higher fitness as a result of this apparent advantage because they produce smaller, less viable spores than putative “losers.” As a consequence of this trade-off between spore number and viability, genotypes with different spore production strategies, which give the appearance of differential social success, ultimately have similar realized fitness. These findings highlight the limitations of using single fitness proxies in evolutionary studies and suggest that interpreting social trait variation in terms of strategies like cheating or cooperating may be misleading unless these behaviors are considered in the context of the true multidimensional nature of fitness.

RESULTS AND DISCUSSION

Social Success in *D. discoideum*

D. discoideum live as single-celled amoebae in terrestrial habitats, but when their food is depleted, large numbers ($\sim 10^5$) of individuals aggregate to form a multicellular fruiting body [13, 14]. The fruiting body is comprised of dead stalk cells that sacrifice themselves to hold aloft a ball of viable spores. Importantly, because fruiting bodies can contain a mixture of different genotypes, this is expected to lead to selection for exploitative social “cheaters,” which in *D. discoideum* have historically been defined simply as those strains that are overrepresented in the spore population of chimeric fruiting bodies [12, 15–20]. Consistent with earlier experiments [21, 22], we found that a set of genotypes isolated from a small geographic area in North Carolina [23] showed highly significant quantitative genetic variation (i.e., among-strain variation, H^2) in the relative number of spores produced by each strain after amoebae were mixed in a 50:50 ratio and allowed to undergo chimeric development ($H^2 = 0.35$, credible interval (CI) = [0.16, 0.62]; see Figure S1). This resulted in a linear (transitive) dominance hierarchy ($t_{tri} = 0.73$, $p < 0.001$; see [24]) with clear cheaters and “losers” when defined solely in terms of spore numbers. These observations thus raise a critical question: what processes maintain such variation in apparent social success in this species?

Trade-offs Exist between Spore Size, Number, and Viability

One mechanism by which variation in social success could persist is if fitness gains during social competition are offset by inherent costs in another context (e.g., social traits expressed in a non-social context or through pleiotropic links between different social traits or social and non-social traits). Such trade-offs could potentially lead to the coexistence of diverse social behaviors, where different strategies have similar overall fitness, and hence the variation is nearly neutral and persists at mutation-selection balance [25]. It is also possible that the traits mediating social interactions are shaped primarily by selection in a non-social context, which incidentally gives rise to variation in social fitness, but only as a neutral byproduct.

Current Biology 25, 1–5, April 20, 2015 ©2015 The Authors 1

Documento 27: Artigo: Wolf, J. B., Howie, J. A., Parkinson, K., Gruenheit, N., Melo, D., Rozen, D., & Thompson, C. R. L. (2015). Fitness Trade-offs Result in the Illusion of Social Success. *Current Biology*, 8, 1086–1090. <https://doi.org/10.1016/j.cub.2015.02.061>.



Directional selection can drive the evolution of modularity in complex traits

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Edited by Stevan J. Arnold, Oregon State University, Corvallis, OR, and accepted by the Editorial Board December 2, 2014 (received for review December 9, 2013)

Modularity is a central concept in modern biology, providing a powerful framework for the study of living organisms on many organizational levels. Two central and related questions can be posed in regard to modularity: How does modularity appear in the first place, and what forces are responsible for keeping and/or changing modular patterns? We approached these questions using a quantitative genetics simulation framework, building on previous results obtained with bivariate systems and extending them to multivariate systems. We developed an individual-based model capable of simulating many traits controlled by many loci with variable pleiotropic relations between them, expressed in populations subject to mutation, recombination, drift, and selection. We used this model to study the problem of the emergence of modularity, and hereby show that drift and stabilizing selection are inefficient at creating modular variational structures. We also demonstrate that directional selection can have marked effects on the modular structure between traits, actively promoting a restructuring of genetic variation in the selected population and potentially facilitating the response to selection. Furthermore, we give examples of complex covariation created by simple regimes of combined directional and stabilizing selection and show that stabilizing selection is important in the maintenance of established covariation patterns. Our results are in full agreement with previous results for two-trait systems and further extend them to include scenarios of greater complexity. Finally, we discuss the evolutionary consequences of modular patterns being molded by directional selection.

variational modularity | G-matrix | quantitative genetics | pleiotropy | phenotypic correlations

Modularity, the organizational pattern found in many organisms, can be defined as the tendency for some parts to be more associated with each other than with other parts of the same organism. This type of modular organization can manifest at many levels, for example, between the bases of an RNA molecule (1), in the interaction between proteins (2), or in the covariance structure of continuous morphological traits (3). In each case, the type of association is different, but the modular pattern remains (4). Traits measured on a continuous scale that covary with each other can frequently be divided into variational modules. A variational module is characterized by higher correlations between traits in the same module and lower correlations between traits of different modules.

Modularity is an important concept in understanding the evolution of many biological systems. At the individual level, tension in producing a full, coherent organism, and having each of its parts performing a separate task subject to different selective pressures and requirements, shapes the association between traits (5). At the same time, the existing pattern of association also influences the response to a given selective pressure: Traits that are associated tend to change together (6, 7). The evolutionary consequences of these correlations are twofold. On the one hand, traits that perform a common function will tend to change in an orchestrated fashion, although interfering less with traits in other modules at the same time. On the other hand, if natural selection

promotes changes in only one trait of a module, the other traits within this module will suffer an indirect selection pressure and change as well, even if this response leads to lower fitness (8). This indirect response in other traits is due to their genetic correlation with the selected trait. Understanding how traits become associated, or correlated, is therefore a central question in evolutionary biology.

The question of how modular patterns evolve in each level of complexity is still open to intense scrutiny (9–11). In morphological systems, one condition for the evolution of variational patterns is the existence of genetic variation in the association between traits in a population. Pavlicev et al. (12) have presented empirical evidence of this variation by showing the existence of relationship quantitative trait loci (rQTLs). These rQTLs are genomic regions that show variation in epistatic effects, altering pleiotropic relations and the correlation between phenotypic traits. Using this concept and the multivariate breeder's equation, Pavlicev et al. (13) proposed a simple deterministic model for the evolution of association or dissociation between two traits in response to directional and stabilizing selection.

The variational pattern of genetic associations between continuous morphological traits is expressed in the additive genetic covariance matrix, called the G-matrix (8, 14). Covariance expressed in the G-matrix is the result of the sum and interaction of genetic effects on many traits, such as pleiotropic and epistatic effects, and shared development, leading to heritable variation and covariation. This variation interacts with evolutionary processes, such as drift and selection. The multivariate breeder's equation relates a population's G-matrix with its response to a given directional selection pressure (14). Under certain conditions,

EVOLUTION

Significance

Modularity, the tendency for the parts of many biological systems to be organized into semi-independent groups, is crucial to the understanding of diversification and the interaction between a population and its environment. In particular, a population's response to selection is dependent on its modularity pattern, which, in turn, is molded by selection. How these modular patterns evolve is therefore a central question in biology. We show, using novel individual-level simulations, that directional selection is very efficient at restructuring variation and creating modular patterns in continuous traits and that stabilizing selection can maintain established patterns.

Author contributions: D.M. and G.M. designed research; D.M. and G.M. performed research; D.M. contributed new reagents/analytic tools; D.M. analyzed data; and D.M. and G.M. wrote the paper.

The authors declare no conflict of interest.

This article is a PNAS Direct Submission. S.J.A. is a guest editor invited by the Editorial Board.

Freely available online through the PNAS open access option.

Data deposition: Full simulation runs and code are available from the Dryad Digital Repository: doi.org/10.5061/dryad.3cb81. Code is also available at github.com/fem-usp/evomod_r. R package for analyzing results can be found at github.com/fem-usp/evomod_r.

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This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1322632112/-DCSupplemental.

www.pnas.org/cgi/doi/10.1073/pnas.1322632112

PNAS Early Edition | 1 of 6

Documento 28: Artigo: Melo, D., & Marroig, G. (2015). Directional selection can drive the evolution of modularity in complex traits. *Proceedings of the National Academy of Sciences*, 2, 470–475. <https://doi.org/10.1073/pnas.1322632112>.

ORIGINAL ARTICLE

doi:10.1111/j.1558-5646.2011.01555.x

MODULARITY, NOISE, AND NATURAL SELECTION

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Received April 14, 2011

Accepted November 24, 2011

Most biological systems are formed by component parts that are to some degree interrelated. Groups of parts that are more associated among themselves and are relatively autonomous from others are called modules. One of the consequences of modularity is that biological systems usually present an unequal distribution of the genetic variation among traits. Estimating the covariance matrix that describes these systems is a difficult problem due to a number of factors such as poor sample sizes and measurement errors. We show that this problem will be exacerbated whenever matrix inversion is required, as in directional selection reconstruction analysis. We explore the consequences of varying degrees of modularity and signal-to-noise ratio on selection reconstruction. We then present and test the efficiency of available methods for controlling noise in matrix estimates. In our simulations, controlling matrices for noise vastly improves the reconstruction of selection gradients. We also perform an analysis of selection gradients reconstruction over a New World Monkeys skull database to illustrate the impact of noise on such analyses. Noise-controlled estimates render far more plausible interpretations that are in full agreement with previous results.

KEY WORDS: Adaptation, models/simulations, morphological evolution, pleiotropy, quantitative genetics, selection—natural.

The study of biological systems and its component parts, whether molecules, cells, tissues, organisms and its forming parts, and even species and their interactions, is rapidly converging to the central theme of modularity. This refers to the connections among some of the component parts of a biological system (genes or morphological traits, for example) and the lack of such associations among other parts of the same system. (Olson and Miller 1958; Berg 1960; Wagner et al. 2007). The notion that interacting parts are not independent is intuitive and appears early in the history of Biology (see Mayr 1982). Therefore, modularity is quickly becoming one of the central questions in modern biology (Wagner et al. 2007; Klingenberg 2008) and a point of convergence of various specialties and areas (Mathematics, Statistics, Genetics and Genomics, Evolutionary Biology, Ecology, Biochemistry, and Physiology).

In biology, several types of modules have been recognized, including (1) functional, consisting of characters or features that

act together on performing a task or function and are quasi-autonomous in relation to other functional sets; (2) developmental, which corresponds to parts of an embryo that are relatively autonomous with respect to pattern formation and differentiation, or an autonomous signaling cascade; (3) variational, composed of characters that vary together and are relatively independent of other such sets (Wagner et al. 2007).

The study of modularity is centered on statistical estimation of association among traits (Olson and Miller 1958; Berg 1960). Whether such association is measured by correlation, covariance, or distance/similarity measures, it is usually represented by matrices. Even if a particular system or network does not present a modular structure or is not being interpreted under this theory, associations among traits, parts, genes, or lineages will still be quantified by statistical association or dissociation matrices among these elements. We will focus here on correlation or covariance matrices (from now on C-matrix) among variables, although the

Selection Response Decomposition (SRD): A New Tool for Dissecting Differences and Similarities Between Matrices

Gabriel Marroig · Diogo Melo · Arthur Porto · Harley Sebastião · Guilherme Garcia

Received: 13 July 2010/Accepted: 24 December 2010
© Springer Science+Business Media, LLC 2011

Abstract Genetic and phenotypic variance/covariance matrices are a fundamental measure of the amount of variation and the pattern of association among traits for current investigations in evolutionary biology. Still, few methods have been developed to accomplish the goal of pinpointing in which traits two matrices differ most, hampering further works on the field. We here described a novel method for dissecting matrix comparisons. This method is called Selection Response Decomposition and is an extension of the random skewers in the sense that evolutionary responses produced by known simulated selection vectors are unfolded and then compared in terms of the direct and indirect responses to selection for any trait. We also applied the method in diverse case studies, illustrating its potential. Both theoretical matrices and empirical biological data were used in the comparisons made. In the theoretical ones, the method was able to

determine exactly which traits were responsible for the known a priori differences between the matrices, as well as where matrices remained similar to each other. Similar support could be observed in comparisons carried on between matrices produced from empirical biological data, since reasonable and detailed interpretations could be made regarding matrix comparisons. SRD represents an excellent tool for matrix comparisons and should provide quantitative evolutionary biology with a new method for analyzing and comparing variance/covariance patterns.

Keywords V/CV matrix · Random skewers · G-matrix · Selection gradient

Introduction

Evolution in complex systems, where many traits share a common genetic basis and/or interact to perform some function together, results from the interaction between evolutionary processes and within-population patterns and magnitudes of association among traits. Genetic and phenotypic variance/covariance (G- and P-matrices) and correlation matrices are a critical quantitative measure of association among traits in a system and, therefore, play a central role in evolutionary biology (Arnold et al. 2001). This led, in the past decades, to a research program focused on estimating G- and P- matrices and comparing them among populations and/or species (Steppan et al. 2002). While some debate sparked around the subject of how to compare those matrices (Cheverud 1988; Roff 1997; Phillips and Arnold 1999; Houle et al. 2002; Cheverud and Marroig 2007), few methods were developed to pinpoint where (in which traits) any pair of matrices differ and where they remain essentially similar.

Electronic supplementary material The online version of this article (doi:[10.1007/s11692-010-9107-2](https://doi.org/10.1007/s11692-010-9107-2)) contains supplementary material, which is available to authorized users.

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Published online: 22 February 2011

 Springer

Documento 30: Artigo: Marroig, G., Melo, D., Porto, A., Sebastião, H., & Garcia, G. (2011). Selection Response Decomposition (SRD): A New Tool for Dissecting Differences and Similarities Between Matrices. *Evolutionary Biology*, 2, 225–241. <https://doi.org/10.1007/s11692-010-9107-2>.

Chapter 11

How Does Modularity in the Genotype–Phenotype Map Shape Development and Evolution?



Diogo Melo

Abstract Traits do not evolve independently, as genetic and developmental associations affect the variation that is expressed in populations and that is available for evolutionary change. In this chapter, we explore the causes and consequences of structured variation, introducing the concept of modularity, exploring some possible causes for modular organization in different levels, and, finally, discussing how the introduction of new variation can evolve.

11.1 Evolution and Variation

Hence if man goes on selecting, and thus augmenting, any peculiarity, he will almost certainly modify unintentionally other parts of the structure, owing to the mysterious laws of correlation. Darwin (1872)

Evolution proceeds by many different processes, all of which depend on the variation present in natural populations. The probability of fixation or loss of a neutral variant due to drift depends on its frequency in a population. The increase or decrease via natural selection of the frequency of an allele that has an effect on fitness depends on the standing variation in that locus. Therefore, the fate of a new variant depends on the population in which the new variant appears, whether it is neutral or not. Advantageous variants that are quite frequent may be lost in small populations, while even the smallest advantage in fitness can guarantee that a rare variant will be fixed in very large populations. In an analogous way, the change in the distribution of a phenotype in a population depends on its standing variation, and the details of this variation can profoundly alter the evolutionary process. For example, consider a hypothetical selection regime that operates as to increase the length of the left arm of the individuals in a population. Individuals that have a long left arm leave more

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© Springer Nature Switzerland AG 2019
J. M. Martín-Durán, B. C. Vellutini (eds.), *Old Questions and Young Approaches to Animal Evolution, Fascinating Life Sciences*,
https://doi.org/10.1007/978-3-030-18202-1_11 237

Modularity and Integration

APA Assis, BMA Costa, DM Rossoni, D Melo, and G Marroig, Universidade de São Paulo, CEP São Paulo, Brazil

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Glossary

Developmental module Performs a specific role in developmental processes and corresponds to a set of cells, genes, or tissues that are relatively independent with respect to pattern formation and differentiation, or an autonomous developmental signaling pathway.

Evolutionary modules Sets of phenotypic elements evolving in coordinated fashion, because the elements are inherited together or because they are jointly selected.

Functional module Sets of traits or features that interact to perform some discrete function or task.

Genetic architecture Refers to the pattern of genetic effects that underlie the variation for a given set of phenotypic characters and its variational properties. A description of genetic architecture may include statements about gene and allele number, the distribution of allelic and mutational effects, and patterns of pleiotropy, dominance, and epistasis.

Genetic modules Sets of traits that are modular due to pleiotropy or linkage disequilibrium.

Genotype–phenotype map Depicts relationship between genetic variation and phenotypic variation; that is, it specifies which locus or loci affects each trait or traits.

Internal stabilizing selection Stabilizing selection due to the interaction of the phenotype with other internal characteristics of an organism, and is related to the need for

coadaptation of traits to one another rather than to the external environment.

Linkage disequilibrium The nonrandom association of alleles at different loci.

Morphological integration Refers to the cohesion or association among morphological traits that are related functionally and/or developmentally. Traits that are integrated tend to covary together, and so this results in higher correlation between these traits when compared to traits that are not integrated.

Pleiotropy A single locus affecting two or more phenotypic traits.

Quasi-independence (quasi-autonomy) A lower than average grade of connectedness, for example, the elements of modules are highly interconnected, while being less connected to other modules. This 'quasi independence' may allow one character to change without affecting others.

Quantitative Trait Loci (QTL) Refers to DNA loci that affect quantitative traits.

Variational modules Set of covarying traits that vary relatively independently of other sets of traits. The reason for this relative independence of different sets of traits, or modules, is that pleiotropic loci with effects on traits belonging to different modules are less frequent than those within modules. These modules are recognized by higher correlations between traits in the same module and lower correlations between traits of different modules.

What Is Modularity and Integration?

Biology is rapidly embracing the challenge of dealing with multidimensional hierarchical systems as a way of moving forward and addressing questions that range from the genetic basis of diseases, behavior, or morphology, the ecological structure of communities, or the evolution of any of these features. To face this challenge we need both theoretical developments and methods capable of dealing with such complexity. At the core of all this lies the concept of modularity. In Biology, modularity refers to the pattern and magnitude of association among elements in a system. This pattern emerges whenever a high connectivity between some elements in the system exists, forming modules, and at the same time these same elements are more loosely associated to other elements that compose other modules. Modularity depends on the ability of a system to organize semi-autonomous parts, or even discrete elements, into a coherent whole. Modularity can be studied at nearly every scale of biological organization; and it has been described in a variety of contexts and observed in many model systems, in a wide range of disciplines and specialties. These include proteins (Han *et al.*, 2004), genes (Litvin *et al.*, 2009), cells (Hartwell

et al., 1999; Wagner, 1996), organs (Schlosser and Wagner, 2004), and ecosystems (Montoya *et al.*, 2006).

Here, we address modularity in the context of morphological quantitative traits and discuss the influence of genetic, functional, and developmental factors at this level. In this context, different parts of organisms can behave as modules because they exhibit some degree of independence, and are internally organized, reflecting their developmental origins and functions, as we will see later (Cheverud, 1996; Klingenberg 2004).

Most of our current understanding of character correlations and on the evolution of complex continuous traits is influenced by the concept of morphological integration (Olson and Miller, 1951, 1958). Olson and Miller (1951, 1958) coined the term morphological integration to describe high levels of phenotypic correlation within subsets of morphological traits. Today, these sets of integrated traits related functionally and/or developmentally are termed modules. In a remarkable work addressing morphological variation and correlation in plants, Raissa Berg (1960) described a similar concept known as 'correlation pleiades.' As with morphological integration, correlation pleiades are based on the presence of high levels of



Diogo Melo <diogro@gmail.com>

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Documento 33: Certificado de apresentação em Congresso.

GR Gordon Research Conference Certificate of Participation

November 28th 2023

Diogo Melo
Princeton University
Lewis-Sigler Institute
Princeton New Jersey
United States

This letter certifies your participation as a(n) Attendee at the Gordon Research Conference on Ecological and Evolutionary Genomics held 07/30/2023 - 08/04/2023 at Bryant University in Smithfield, Rhode Island, United States.

Poster Entitled: Longitudinal sequencing reveals polygenic and epistatic nature of genomic response to selection



Dr. Nancy Ryan Gray
President and Chief Executive Officer
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The Organizing Committee of the **II Joint Congress on Evolutionary Biology** certifies that:

Mr. Diogo Melo

has presented the following poster:

Genetic architecture and the evolution of variational modularity

on the occasion of the **II Joint Congress on Evolutionary Biology**

(August 19-22, 2018 - Corum, Montpellier - France).

Two handwritten signatures are shown side-by-side. The signature on the left appears to be "Ophélie RONCE" and the one on the right appears to be "Yannis MICHAKALIS".

Ophélie RONCE & Yannis MICHAKALIS

Organizing Committee

Documento 35: Certificado de apresentação em Congresso.

Detailed Programme

Thursday, July 28th

- S10-01 **Microbiome research and the eco-immunity of biological individuals**
Chiu, Lynn C. (University of Bordeaux, FRA)
- S10-02 **Tiny changes, big effects: the impact of microexons on neuronal differentiation, function and evolution**
Irimia, Manuel (Centre for Genomic Regulation, Barcelona, ESP)
- S10-03 **Early animal evolution – Insights from exceptionally preserved Cambrian fossils**
Ma, Xiaoya (Natural History Museum, London, GBR)
- S10-04 **The Evolution of pleiotropy and modularity**
Melo, Diogo (University of São Paulo, BRA); Marroig, Gabriel (University of São Paulo, BRA)

- 09.00 – 10.40 Symposium S11:
Ancestral reconstruction of proteins, networks and genomes in plants and animals

SAL C

Organizers: Jerome Salse and Koen Geuten
Chair: Jerome Salse

- S11-01 **Ancestral complex and network evolution of MADS domain proteins and the origin of flowering plant lineages**
Geuten, Koen (University of Leuven, BEL)
- S11-02 **Lineage-specific radiations and the evolution of the genetic tool-kit**
Brockington, Sam (University of Cambridge, GBR)
- S11-03 **Reconstruction of the ancestral repertoire of proteins domains suggests modern genomes are deprived of building blocks**
Bornberg-Bauer, Erich (Westfälische Wilhelms-Universität, DEU)
- S11-04 **Paleogenomics in plants and animals to unveil evolutionary forces**
Salse, Jerome (INRA, FRA)

- 09.00 – 10.40 Symposium S12:
Process thinking for evo-devo

K3/K4

Organizer: Johannes Jaeger
Chair: Johannes Jaeger

- S12-01 **Process Thinking for Evo-Devo: an Introduction**
Jaeger, Johannes (KLI, AUT)
- S12-02 **Explanatory idealization and developmental processes**
DiFrisco, James (KLI, AUT)
- S12-03 **Inheritance of Process: A dynamical systems view of development and evolution**
Monk, Nick (University of Sheffield, GBR)
- S12-04 **A damped oscillator drives posterior gap gene expression in Drosophila melanogaster**



CERTIFICATE OF ATTENDANCE

This hereby certifies that Diogo Melo, Anna Penna, María Inés Oyarzabal, Gabriel Marroig presented the following Contributed Presentation at the EVOLUTION 2015:

Changes in multivariate covariance structures under directional selection



Reinaldo A. de Brito
Evolution 2015
Chair, Local Organizing Committee
evolmeeting2015@gmail.com

Documento 37: Certificado de apresentação em Congresso.



CERTIFICATE OF ATTENDANCE

This hereby certifies that Diogo Melo, Gabriel Marroig presented the following Contributed Presentation at the EVOLUTION 2015:

The effect of directional selection on pleiotropy and modularity

Reinaldo A. de Brito
Evolution 2015
Chair, Local Organizing Committee
evolmeeting2015@gmail.com



Documento 38: Certificado de apresentação em Congresso.

*V Brazilian Meeting on Simulational Physics
Ouro Preto, 01-03 August 2007*

Belo Horizonte, 03 August 2007

Diogo Amaral

Has attended the *IV Brazilian Meeting on Simulational Physics* and presented the posters entitled "**Transição de fase ordem-desordem em membranas na presença de dissociação**".

João Antônio Plascak
João Antônio Plascak

Chairman

UNIVERSIDADE FEDERAL DE OURO PRETO
Campus Morro do Cruzeiro
35400-000 Ouro Preto – MG – Brazil

UNIVERSIDADE FEDERAL DE MINAS GERAIS
Campus da Pampulha C. P. 702
30123-970 Belo Horizonte – MG -Brazil

Documento 39: Certificado de apresentação em Congresso.

 Gmail

Diogo Melo <diogro@gmail.com>

NIMBioS Tutorial: The Search for Selection - June 18-22, 2018

1 message

cwelsh@nimbios.org <cwelsh@nimbios.org>
 Reply-To: admimb@nimbios.org
 To: diogro@gmail.com
 Cc: admimb@nimbios.org, admimb@nimbios.org

Thu, Mar 1, 2018 at 4:51 PM

 **NIMBioS** National Institute for Mathematical and Biological Synthesis

1122 Volunteer Blvd, Suite 106
 University of Tennessee
 Knoxville, TN 37996-3410
 Phone: (865) 974-9334
 Fax: (865) 974-9300

Dear Mr. Diogo Melo,

It is my pleasure to invite you to participate in the Search for Selection tutorial (<http://www.nimbios.org/tutorials/selection>) sponsored by the National Institute for Mathematical and Biological Synthesis (NIMBioS) and organized by J. Bruce Walsh.

The meeting is scheduled for June 18-22, 2018, at NIMBioS on the University of Tennessee campus in Knoxville, Tennessee, USA. We expect you will want to arrive by the evening of the 17th and depart afternoon or evening on the 22nd. The tutorial will end around noon on the 22nd, so plan on flights out after 2 pm.

NIMBioS will provide your lodging for five nights (Sun June 17 - Thu June 21) and breakfast and lunch each day of the tutorial, including dinner on the 22nd. Interested in lodging later? Please let us know at a later date. Most participants will be in University of Tennessee dorms, a few may be staying in nearby hotel. In addition to lodgings and breakfast/lunch, we offer you up to \$500 toward your travel expenses. Flights must be economy class on a U.S. carrier. If the fare is less than \$500, we can book your trip for you and pay for it directly. Jennifer Spar, NIMBioS Event and Travel Coordinator, (jspar@nimbios.org, 865-974-9317) can work with you on this. If >\$500, you will need to book yourself and submit a reimbursement form after the tutorial to receive this support. If driving a personal vehicle, reimbursement is at \$0.47/mi.

If flying, you should fly in and out of Tyson-McGhee Airport (TYS). You will need to take a taxi from the airport to campus, a roughly 20-min drive with fare of ~\$35. For those driving, we will provide more information about parking later.

Please ACCEPT or DECLINE this invitation by clicking on the appropriate link below no later than March 23rd. If you will not be able to attend, please let us know as soon as possible. We have a number of people on the waiting list for this event.

If you accept the invitation, you will be directed to our online registration system. If you already have an account, please log in. If you have never used ADNIMB before, your username will be the email address this invitation was sent to, and you will be able to set your password at the login screen.

All participants must fill out (1) a User Profile and (2) a Dietary, Travel and Reimbursement (DTR) Form through the online registration system by March 23rd. When your user profile is complete, the DTR Form will be made accessible on the system's Main Menu. Note that you can accept the invitation and log back in later to complete your DTR form. We cannot reimburse any expenses if you have not completed the DTR form. We do not need your social security number if we are not arranging your travel or reimbursing you.

If you experience any problems using the online registration system, please contact us at admimb@nimbios.org or (865) 974-9334.

By clicking ACCEPT, you are authorizing NIMBioS to use your image(s), both with and without identification, for NIMBioS publicity, promotional and advertising purposes.

Click the button below to accept this invitation:

ACCEPT

Click the button below to decline this invitation:

DECLINE

(If clicking the button did not work, try copying and pasting the link below into your browser.)

Accept:
<https://admimb.nimbios.org/Invitations/response/type:confirm/ticket:3c0aca93e633edacb8b6b0893ee310ec5ddd5925>

Decline:
<https://admimb.nimbios.org/Invitations/response/type:decline/ticket:3c0aca93e633edacb8b6b0893ee310ec5ddd5925>

International travelers: please let us know if you need a more formal invitation to use when applying for a visa. You should travel on a WB or B-1 visa. Also, let us know if you plan to extend your trip before or after the tutorial. We are open to that, but you will need to cover your own expenses outside the tutorial.

Federal employees: let us know if you need a more formal invitation that includes language specifying in-kind support. We can generally cover your lodging and meals during the tutorial directly, but your agency may prefer to invoice us rather than NIMBioS providing any reimbursement directly to you.

We will send directions and additional information one week before your meeting.

Please free to contact me or especially Jennifer Spar (NIMBioS Event and Travel Coordinator, jspar@nimbios.org, 865-974-9317) if you have any questions about the logistics of your visit to NIMBioS.

Sincerely,



Christopher Welsh, PhD
 Deputy Director, NIMBioS
 1122 Volunteer Blvd., Suite 106
 University of Tennessee
 Knoxville, TN 37996-3410
 (office) 865-974-9334 (fax) 865-974-9300
cwelsh@nimbios.org
www.nimbios.org



CERTIFICATE OF COMPLETION

April 24, 2015, Els Hostalets de Pierola (Barcelona, Spain).

WE HEREBY CERTIFY that **Diogo Melo** has successfully completed the postgraduate course "**Introduction to Network Tools in Biosciences - 2nd Edition**", organized by Transmitting Science, the Institut Català de Paleontologia M. Crusafont and the Centre de Restauració i Interpretació Paleontològic. This course was held from April 20 to April 24, 2015, at the premises of the Centre de Restauració i Interpretació Paleontològic, Els Hostalets de Pierola, Barcelona (Spain), and has been taught by Dr. Diego Rasskin-Gutman (Institut Cavanilles de Biodiversitat i Biologia Evolutiva, Spain) and Dr. Borja Esteve-Altava (Institut Cavanilles de Biodiversitat i Biologia Evolutiva, Spain).

Length of the course: 34 hours on-site. This course is equivalent to 3.5 ECTS (European Credit Transfer System).

CERTIFICAMOS ante quién corresponda que **Diogo Melo** ha superado satisfactoriamente el curso de postgrado "**Introduction to Network Tools in Biosciences - 2nd Edition**" organizado por Transmitting Science, el Institut Català de Paleontologia M. Crusafont y el Centre de Restauració i Interpretació Paleontològic. Este curso tuvo lugar en las instalaciones del Centre de Restauració i Interpretació Paleontològic en Els Hostalets de Pierola, Barcelona (España) del 20 al 24 de Abril de 2015, y fue impartido por el Dr. Diego Rasskin-Gutman (Institut Cavanilles de Biodiversitat i Biología Evolutiva, España) y el Dr. Borja Esteve-Altava (Institut Cavanilles de Biodiversitat i Biología Evolutiva, España).

Total horas lectivas: 34 horas presenciales. Este curso se corresponde a 3,5 ECTS.

Dr. D. Rasskin-Gutman
Instructor
Institut Cavanilles de
Biodiversitat i
Biología Evolutiva

Dr. B. Esteve-Altava
Instructor
Institut Cavanilles de
Biodiversitat i
Biología Evolutiva

Dr. S. De Esteban-Trivigno
Course director
Transmitting Science



Transmitting Science, S.L.U. – NIF B65731903 – NIF-IVA ESB65731903
C/ Gardenia, 2 – Urb. Can Claramunt – 08784 Piera (Barcelona) – Spain
Inscrita en el Registro Mercantil de Barcelona, Tomo 43061, Folio 54, Sección General, Hoja B-420066, Inscripción I
info@transmittingscience.org • www.transmittingscience.org

Documento 41: Certificado de curso de extensão.

4/18/2020

Gmail - SFI Complex Systems Summer School 2008 - Notice



Diogo Melo <diogro@gmail.com>

SFI Complex Systems Summer School 2008 - Notice

1 message

Santa Fe Institute <summerschool@santafe.edu>
To: diogro@gmail.com

Fri, Sep 12, 2008 at 5:00 PM

Diogo MELO
Rua Sousa Reis 153, ap 71
Sao Paulo
SP
05586-080
Brazil
via e-mail

Dear Diogo MELO:

On behalf of CSSS Co-Directors Miguel Fuentes and Pablo Marquet, I am pleased to inform you that you have been selected to participate in the Complex Systems Summer School in San Carlos de Bariloche, Argentina, from December 1 through December 14, 2008. You have been chosen from among many qualified applicants because of your unusually strong application. We hope that you will accept this invitation to attend the school.

No tuition is charged for the program. We will also cover your housing and meals for the duration of the school.

PROGRAM COMMITMENTS: 1) Participants are expected to attend all program sessions for the duration of the program. 2) Participants are expected to complete two online surveys, before and after the program; the anonymous results are used to help in our program evaluation. 3) Participants are expected to complete a collaborative group project by the deadline established by the program directors.

LOGISTICS: You should plan to arrive in Bariloche by 4:00 p.m. on Monday, December 1 and to depart on Monday morning, December 15. Please review the travel and logistical information posted on the CSSS wiki at <http://www.santafe.edu/events/workshops/index.php/CSSS_2008_Argentina>. The wiki will be updated as new information becomes available.

To accept this invitation and reserve your space at the school, you must register online at <http://www.santafe.edu/education/application/csss08_bariloche> no later than Friday, October 3, 2008. If you are unable to attend, please e-mail me directly at your earliest convenience, but no later than Oct. 3.

Please introduce yourself to other participants by posting a picture and completing the template under your name at the CSSS wiki at <http://www.santafe.edu/events/workshops/index.php/CSSS_2008_Argentina-Participants> after creating your own login.

Once you have registered, please take a few moments to complete the CSSS pre-survey online at <<http://www.santafe.edu/sfiforms/>> . Your user name is your e-mail address, and the password is f33db4ck.

Congratulations on your acceptance, and we look forward to seeing you this December in Bariloche. In the meantime, if you have any questions, please do not hesitate to contact me.

Best wishes,
Lee Goodwin
CSSS Application Coordinator
(505) 946-2746
goodwin@santafe.edu

[Ref: diogro@gmail.com]

<https://mail.google.com/mail/u/0/?ik=8dda739d52&view=pt&search=all&permthid=thread-f%3A1280573075166373545&simpl...> 1/1

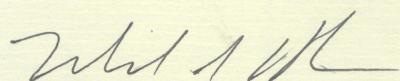


Documento 43: Certificado de curso de extensão.

Course in NEUROBIOLOGY

UNESP Rio Claro December 10-12 (2007)

This certifies that Diogo A. R. Melo completed the 24 hour graduate course in Neurobiology at UNESP Rio Claro. The course included lectures, problem solving and computer simulations.



Prof Michael S Hedrick, PhD



Prof Tobias Wang, PhD

Documento 44: Certificado de curso de extensão.

10/6/23, 9:38 AM

Course Details | Office of the Registrar

Office of the Registrar

COURSE DETAILS

Programming for Biology

2023-2024 Fall**EEB 330****DISTRIBUTION AREA:**

QCR

GRADING BASIS:Graded A-F, P/D/F,
Audit**INSTRUCTORS:**

- [Diogo Melo](#)

LINKS:

- [Books](#)
- [Evaluations](#)

Description:

In this course you will learn two of the most popular programming languages in biology, R and python, along with current bioinformatics tools for dealing with genomic datasets. We will cover the basics of programming logic, along with project and data management skills. Special focus will be given to processing and curation of large tabular and genomic datasets. This course will serve as a practical introduction to programming, giving students the tools they need to succeed in their projects and showing how simple computational tools can liberate them to pursue the questions they are passionate about.

Sample Reading List:

- Steven H. D. Haddock, Casey W. Dunn, *Practical Computing for Biologists*
- Vince Buffalo, *Bioinformatics Data Skills: Reproducible and Robust Research*
- Hadley Wickham, *Advanced R*

Reading/Writing Assignments:

There will not be writing assignments. Students will be expected to complete coding assignments during the semester.

Requirements/Grading:**Term Assessments:**

- Project(s) - 20%
- Participation - 15%
- Programming assignments - 30%

Final Assessments:

- Final paper or project - 35%

Other Requirements:

- Not Open to First Year Undergraduates.

Other Information:

20% of final grad will be from precept projects

Schedule/Classroom Assignment:

CLASS NUMBER	SECTION	MEETINGS	ENROLLMENT	STATUS
22711	L01	M W, 1:30 pm – 2:50 pm, McCosh Hall 62	Enrolled: 23 Limit: 26	
23241	P01	W, 3:30 pm – 4:20 pm, Jadwin Hall 111	Enrolled: 12 Limit: 13	

D E C L A R A Ç Ã O

Declaro, para os devidos fins e atendendo à solicitação formal do interessado, que o **Dr. DIOGO AMARAL REBOUÇAS MELO (Nº USP 4579712)** ministrou a disciplina BIZ 5791 – Escrita Científica, 8 créditos, carga horária total de 120h, junto ao Programa de Pós-Graduação em Ciências Biológicas (Zoologia) deste Instituto, no 1º semestre de 2021.

Declaro, ainda, que o interessado foi colaborador na disciplina BIP 5701 – Escrita Científica, 8 créditos, carga horária total de 120h, neste Instituto, no 1º semestre de 2020.

São Paulo, 1 de dezembro de 2023.



HELDER ROSSI SANTOS SOUZA

Chefe Administrativo de Serviço Substituto
Secretaria de Pós-Graduação - IBUSP

CERTIFICADO

A COMISSÃO ORGANIZADORA DO CURSO DE FÉRIAS
EM GENÉTICA E EVOLUÇÃO CERTIFICA QUE

DIOGO AMARAL REBOUÇAS MELO

MINISTROU O MINICURSO "BIOLOGIA EVOLUTIVA", COM CARGA HORÁRIA DE 6 HORAS,
DURANTE O 1º CURSO DE FÉRIAS EM GENÉTICA E EVOLUÇÃO, REALIZADO NO INSTITUTO DE BIOCIÊNCIAS DA
UNIVERSIDADE DE SÃO PAULO, DE 10 A 14 DE FEVEREIRO DE 2020.



CURSO DE FÉRIAS EM
GENÉTICA E EVOLUÇÃO
Instituto de Biociências - USP



USP
Universidade de São Paulo
Instituto de Biociências

Paulo Cesar Ricardo

COMISSÃO ORGANIZADORA DO CURSO
DE FÉRIAS EM GENÉTICA E EVOLUÇÃO

merari dr farias

PROFA. DRA. MERARI DE FÁTIMA
RAMIRES FERRARI

Documento 47: Certificado de curso ministrado.



DECLARAÇÃO

Declaro para os devidos fins que o **PROF. DR. DIOGO AMARAL REBOUÇAS MELO** ministrou como Docente Colaborador, juntamente com a Profa. Dra. Tiana Kohlsdorf e a Profa. Dra. Monique Nouailhetas Simon, a disciplina intitulada "Modularidade: Conectando Padrões e Processos em Evolução Multivariada", regularmente credenciada junto ao Programa de Pós-Graduação em Biologia Comparada do Departamento de Biologia da Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto da Universidade de São Paulo na cidade de Ribeirão Preto, no período de 20 a 24 de maio de 2019.

Declaro, ainda, que a referida disciplina possui 02 (dois) créditos no total de 30 (trinta) horas.

Ribeirão Preto, 01 de dezembro de 2023.

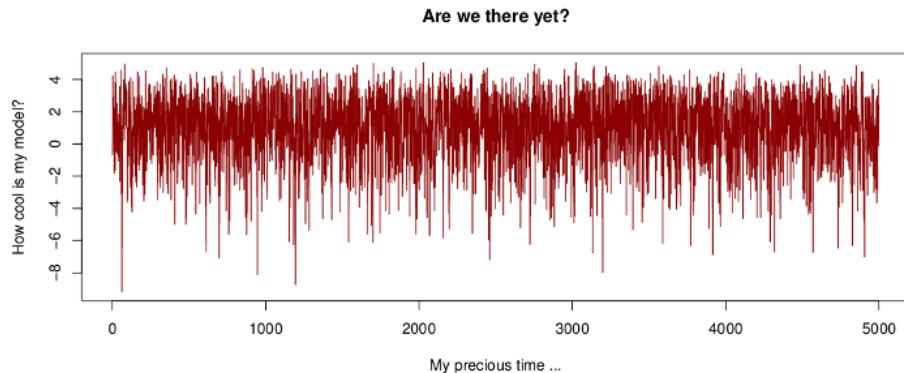
Documento assinado digitalmente
 MILTON GROOPPO JUNIOR
Data: 01/12/2023 13:07:09-0300
Verifique em <https://validar.itd.gov.br>

PROF. DR. MILTON GROOPPO JUNIOR
Coordenador Programa de Pós-Graduação Biologia Comparada

Fone/Fax: (016) 3315-3704
Av. Bandeirantes, 3900 - 14040-901
Ribeirão Preto – SP - Brasil

Documento 48: Certificado de curso ministrado.

Curso MCMC passo a passo



Venha aprender uma visão prática de métodos Monte Carlo para inferência Bayesiana e aplicações usando models comparativos filogenéticos!

Palestrantes: Daniel Caetano (University of Arkansas)
Diogo Melo (Universidade de São Paulo)

Datas e local: 24 a 27 de Julho de 2017 no Instituto de Biociências, USP, São Paulo

Publico alvo: Pessoas que já utilizam ou pretendem utilizar métodos que implementam MCMC. Conhecimento prático com linguagem R é importante para acompanhar o curso.

Inscrição: Encaminhe email para 'diogro+mcmc@gmail.com' com o título "Inscrição workshop" até dia 14/07/2017. Favor enviar breve texto sobre o interesse no curso e tipo de métodos Bayesianos que você utiliza. Indicar se possui experiência com a linguagem R.

Documento 49: Certificado de curso ministrado.



VII Semana Temática de Oceanografia
Oceanografia 2020: Cenários e Perspectivas
Instituto Oceanográfico da Universidade de São Paulo

UNIVERSIDADE DE SÃO PAULO



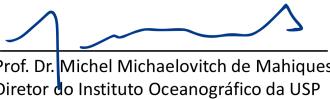
INSTITUTO OCEANOGRÁFICO

Universidade de São Paulo

CERTIFICADO

Diogo Melo

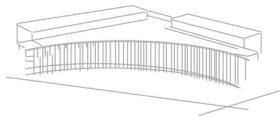
Participou como ministrante do curso “Introdução à manipulação de dados com a linguagem R” promovido pelo Instituto Oceanográfico da Universidade de São Paulo, realizado no período de 27 a 30 de agosto de 2012, com carga horária de 12 horas.


Prof. Dr. Michel Michaelovitch de Mahiques
Diretor do Instituto Oceanográfico da USP


Prof. Dr. Marcos César de Oliveira Santos
Orientador da Comissão Organizadora

Documento 50: Certificado de curso ministrado.

PRINCETON UNIVERSITY



Lewis-Sigler Institute for Integrative Genomics

Carl Icahn Laboratory
Princeton, New Jersey 08544www.princeton.edu/genomicsJulien Ayroles, Ph.D.
Princeton UniversityNovember 30th 2023

Subject: Confirmation of Teaching Roles of Diogo Melo

To Whom It May Concern,

I am writing to confirm that Diogo Melo has served as a Teaching Assistant and Lecturer within the Department of Ecology and Evolutionary Biology at Princeton University.

During his tenure with us, Diogo has been involved in the following courses:

- Teaching Assistant for "Human Genomics: The Past, Present, and Future of the Human Genome" In this role, Diogo demonstrated exceptional ability in assisting with course preparation, conducting tutorial sessions, and providing support to students throughout the course duration.
- Teaching Assistant for "Epidemiology: An Ecological and Evolutionary Perspective" Diogo's contributions were integral to the course's success, where he was responsible for guiding students through complex concepts and facilitating engaging discussions.
- Lecturer for "Programming for Biology" As a Lecturer, Diogo took on a more prominent role by leading this course. His expertise in biology and programming allowed him to create a comprehensive and accessible curriculum, which he delivered with great proficiency and enthusiasm.

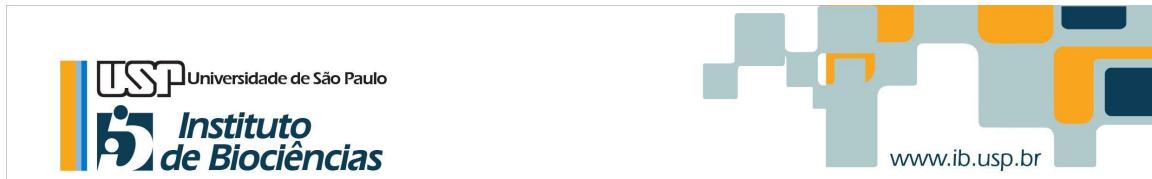
Diogo Melo's dedication and expertise have been invaluable to our department. His ability to convey complex scientific ideas in an understandable and engaging manner has consistently received positive feedback from students and faculty alike.

Should you require any further information, please do not hesitate to contact me.

Sincerely,

Julien Ayroles, Ph.D.
Assistant Professor
Department of Ecology and Evolutionary Biology
Princeton University

Documento 51: Certificado de monitoria e de curso ministrado.



São Paulo, 1 de dezembro de 2023

Prezado Diogo Amaral Reboucas Melo,

Escrevo para registrar e agradecer pela sua importante contribuição para a disciplina "**Biologia Evolutiva**" **BIO 0312**, oferecida para o curso de graduação em Ciências Biológicas no Instituto de Biociências da USP, da qual fui um dos professores responsáveis. Sua contribuição nos anos 2012, 2013 e 2019 foi fundamental, ao oferecer apoio para os alunos na forma de horários de atendimento, ajudando nas atividades práticas (que são de importância central para a disciplina), desenvolvendo o material didático, e participando das discussões para o planejamento da disciplina.

Destaco sua dedicação, ao reservar várias horas para acompanhar as aulas nos diferentes períodos, e pensar sobre a disciplina, sua importância e formas de melhorá-la, em conjunto com a equipe de docentes.

Cordialmente,

A handwritten signature in black ink, appearing to read 'Diogo Meyer'.

Prof. Dr. Diogo Meyer

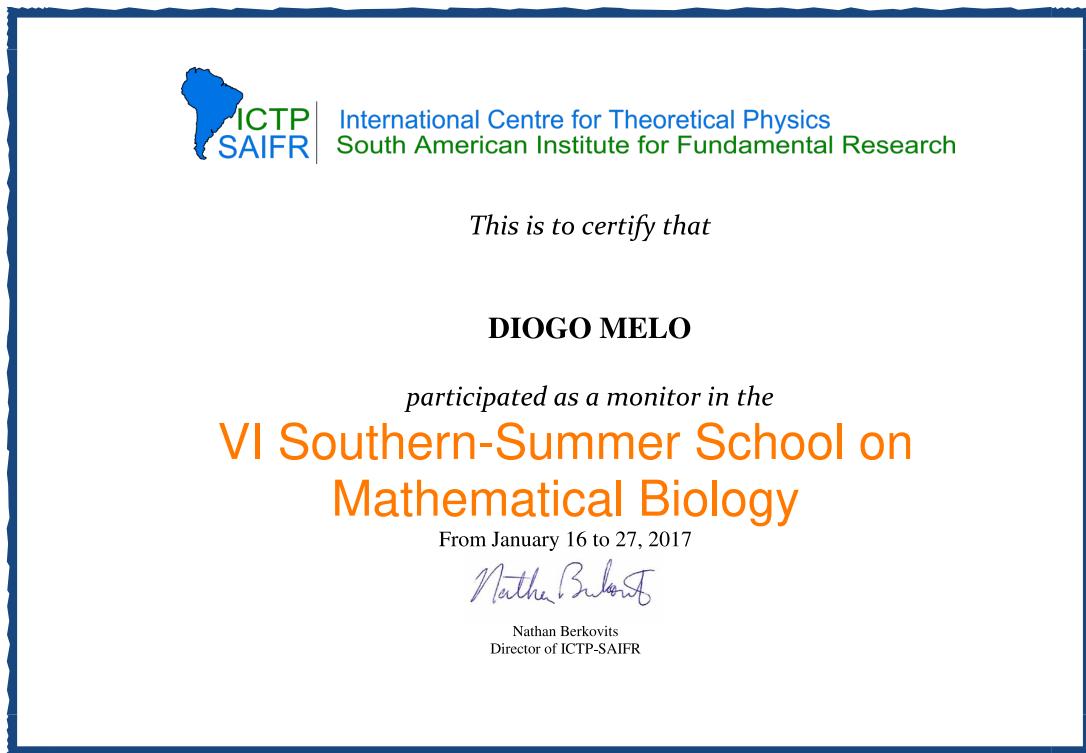
Responsável por BIO 0312



Documento 52: Certificado de monitoria.

 <p>IB-USP Universidade de São Paulo Instituto de Biociências</p>  <p>www.ib.usp.br</p>	 <p>IB-USP Universidade de São Paulo Instituto de Biociências</p>  <p>www.ib.usp.br</p>
<p style="text-align: center;">DECLARAÇÃO</p> <p>Declaro para os devidos fins que Diogo Amaral Rebouças Melo participou como monitor da disciplina BIE5782 – Uso da Linguagem R para Análise de Dados Ecológicos, ministrada entre 19 de março a 09 de abril de 2012 para os alunos do Programa de Pós-Graduação em Ecologia do IB-USP, sob minha responsabilidade. Na ocasião, o referido pesquisador auxiliou os alunos em plantões presenciais, ajuda no fórum online, avaliação de propostas, correção de exercícios e trabalhos finais, totalizando 40 horas-aula.</p> <p>São Paulo, 15 de junho de 2012.</p> <p>Prof. Dr. Alexandre Adalardo de Oliveira</p>	
<p>Declaro para os devidos fins que Diogo Amaral Rebouças Melo participou como monitor da disciplina BIE5782 – Uso da Linguagem R para Análise de Dados Ecológicos, ministrada entre 04 a 22 de março de 2013 para os alunos do Programa de Pós-Graduação em Ecologia do IB-USP, sob minha responsabilidade. Na ocasião, o referido pesquisador auxiliou os alunos em plantões presenciais, ajuda no fórum online, avaliação de propostas, correção de exercícios e trabalhos finais, e desenvolvimento da plataforma notar (sistema para notas automatizadas de exercícios), totalizando 50 horas-aula.</p> <p>São Paulo, 15 de junho de 2013.</p> <p>Prof. Dr. Alexandre Adalardo de Oliveira</p>	
 <p>Rua do Matão • Travessa 14 • nº 321 • Cidade Universitária • São Paulo • SP • CEP 05508-090 • Brasil</p>  <p>IB-USP Universidade de São Paulo Instituto de Biociências</p>  <p>www.ib.usp.br</p>	 <p>Rua do Matão • Travessa 14 • nº 321 • Cidade Universitária • São Paulo • SP • CEP 05508-090 • Brasil</p>  <p>IB-USP Universidade de São Paulo Instituto de Biociências</p>  <p>www.ib.usp.br</p>
<p style="text-align: center;">DECLARAÇÃO</p> <p>Declaro para os devidos fins que Diogo Amaral Rebouças Melo participou como monitor da disciplina BIE5782 – Uso da Linguagem R para Análise de Dados Ecológicos, ministrada entre 24 de março a 11 de abril de 2014 para os alunos do Programa de Pós-Graduação em Ecologia do IB-USP, sob minha responsabilidade. Na ocasião, o referido pesquisador auxiliou os alunos em plantões no fórum online, totalizando 20 horas-aula.</p> <p>São Paulo, 18 de junho de 2014.</p> <p>Prof. Dr. Alexandre Adalardo de Oliveira</p>	
 <p>Rua do Matão • Travessa 14 • nº 321 • Cidade Universitária • São Paulo • SP • CEP 05508-090 • Brasil</p>	

Documento 53: Certificado de monitoria.



Documento 54: Certificado de monitoria em curso de extensão.



UNIVERSIDADE DE SÃO PAULO

DEPARTAMENTO DE ECOLOGIA

Rua do Matão - Travessa 14 nº 321 - CEP 05508-900

Cidade Universitária - São Paulo - Brasil

<http://www.ib.usp.br>

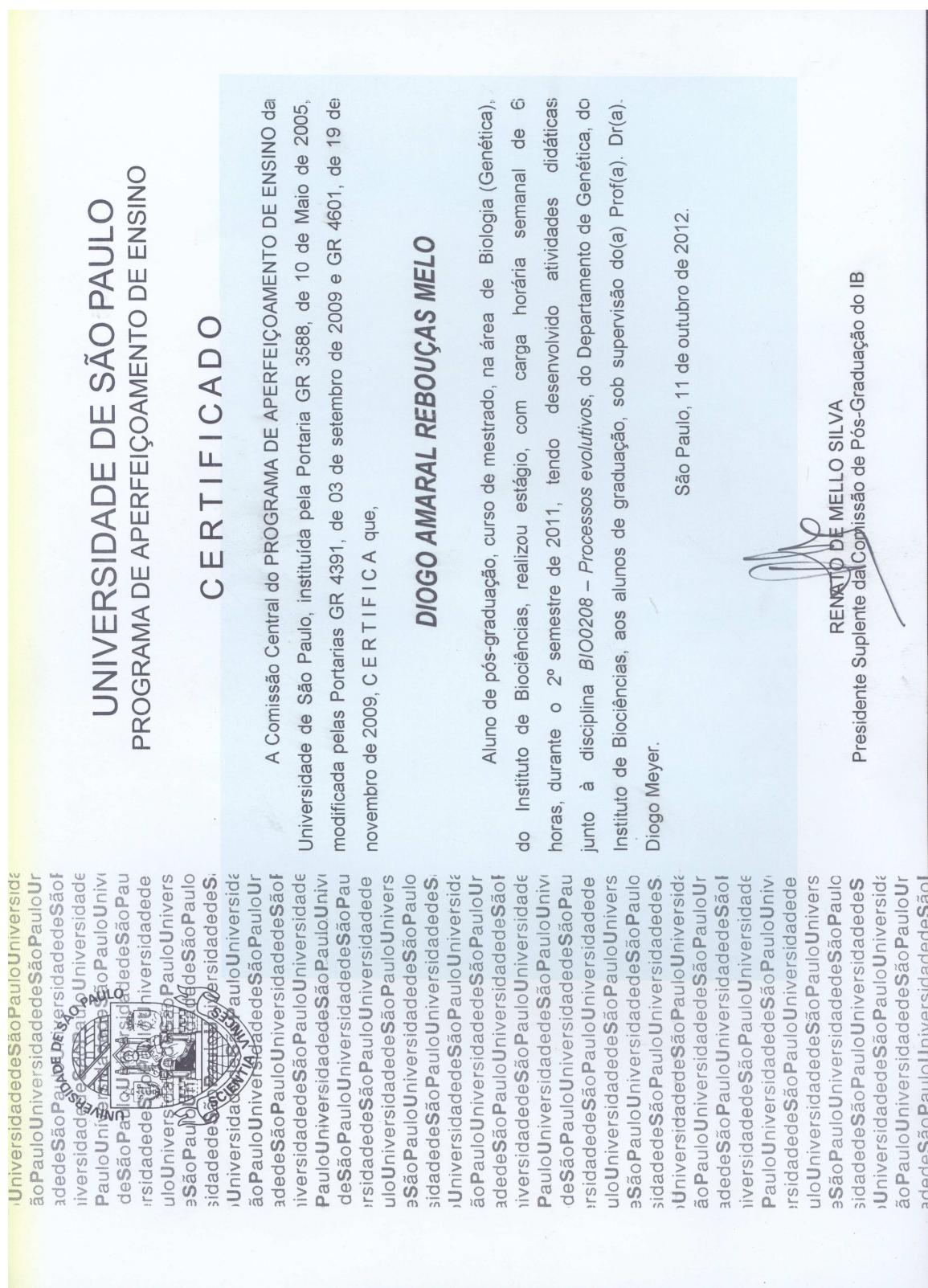
São Paulo, 1 de agosto de 2015

CERTIFICADO

Certifico que o estudante de doutorado Diogo Melo participou como monitor da disciplina “Ecologia da Mata Atlântica”, oferecida pelo Programa de Pós-graduação em Ecologia da Universidade de São Paulo e realizada no período de 6 a 31 de julho de 2015 na Reserva de Desenvolvimento Sustentável da Barra do Uma, Peruíbe, São Paulo. Aproveito a oportunidade para manifestar meu sincero agradecimento por sua colaboração e dedicação.

Dr. Glauco Machado
Coordenador do Curso de Campo
Ecologia da Mata Atlântica

Documento 55: Certificado de monitoria em disciplina de pós-graduação.



Documento 56: Certificado de monitoria PAE em disciplina de graduação.