Summer School:

Integrated methods to detect polygenic adaptation from genomic data

28 Aug – 30 Aug 2017, WSL Birmensdorf, Switzerland

http://www.ieu.uzh.ch/en/teaching/Polygenic-Adaptation.html

Why this event?

Over the last decade, the genomic revolution has offered the possibility to generate tremendous amounts of data that contain valuable information on the genetic basis of phenotypic traits, such as those linked to human diseases or those involved in species' adaptation to changing environments. Most ecologically and economically relevant traits are controlled by a large number of genes with small individual effects on trait variation, but that are connected with one another through complex developmental, metabolic, and biochemical networks. As a result, it has recently been suggested that most adaptation events in natural populations are reached via correlated changes at multiple genes at a time, for which the name polygenic adaptation has been coined. Detecting polygenic signals of adaptation in genomes is, however, challenging and current genomic approaches often reveal only a small proportion of the genetic determinants of trait variation. We will discuss what relevant information need to be extracted from genomic data to detect signals of polygenic selection and eventually predict phenotypic evolution.

Aims

This Summer School will offer the opportunity to acquire a deeper knowledge of the methods that map genetic to phenotypic or environmental variation and their limitations, and to learn new approaches to analyze genomic data to detect the signature of selection on polygenic traits. You will learn methods which integrate functional data from gene interaction networks, or use information about genetic co-variation among genomic polymorphisms. The basic theory of quantitative and population genetics that underlies many of the approaches presented will be reviewed and a critical overview of the role of epistasis in the evolution of polygenic traits will be provided.

Credits: 1 ECTS

Instructors

Dr. Jeremy Berg (Columbia University, USA)
Dr. Josephine Daub (University Pompeu Fabra, Barcelona, Spain)
Prof. Frédéric Guillaume (University of Zurich, Switzerland)
Prof. Thomas Hansen (University of Oslo, Norway)
Prof. John Mckay (Colorado State University, USA)
Prof. Josh Payne (University of Zurich, Switzerland)
Prof. Peter Visscher (University of Queensland, Australia)
Prof. Sam Yeaman (University of Calgary, Canada)

Schedule

Monday, August 28:

Introduction: 8:00—8:30

Dr. Katalin Csilléry

Modeling the polygenic architecture of quantitative traits and Analysis of signals of polygenic adaptation

Morning: 8:30—12:30

Prof. Frederic Guillaume (1h)

Prof. Sam Yeaman (3h)

Afternoon: 13:30—17:30

Prof. Sam Yeaman (1h)

Dr. Jeremy Berg (3h)

Evening: 18:00—19:00 *(optional class)*

Prof. Frederic Guillaume (How to simulate genotype-phenotype associations with Nemo?)

Tuesday, August 29:

The role of epistasis and gene interaction networks in adaptation

Morning: 8:30—12:30

Prof. Josh Payne (1h)

Prof. Thomas Hansen (3h)

Afternoon: 13:30—16:30

Dr. Josephine Daub (3h)

Evening: 16:30—onward

Wine tasting and dinner, Uerikon am Zürisee (transfer by bus)

Wednesday, August 30:

The principles of genome wide association mapping (GWAS) and phenotype prediction, post-GWAS and applications in plant systems

Morning: 8:30—12:30

Prof. Peter Visscher

Afternoon: 13:30—17:30

Prof. John Mckay

Evening: 17:30—onward

Closing apéro

Information available at:
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Abstracts

Prof. Samuel Yeaman (University of Calgary, Canada) (Monday, August 28)

In my section of the course, we will review some simulation results exploring the importance of genetic redundancy (as per Yeaman 2015) for the evolution of different kinds of genetic architectures. We will then explore how genomic data can be used to search for signatures of convergent adaptation. Students will grapple with some of the statistical problems involved with making inferences about convergent evolution and consider how to treat the problem of false positives in genome scan datasets.

Key references:

Yeaman, S. (2015). Local adaptation by alleles of small effect. *The American Naturalist*, 186: S74-S89.

Yeaman, S., Hodgins, K. A., …, Liepe, K. J. (2016). Convergent local adaptation to climate in distantly related conifers. *Science*, *353:*1431-1433.

Dr. Jeremy Berg (University of Columbia, USA) (Monday, August 28)

In my section of this course, we will focus on a handful of statistical methods developed in the last few years to assess the extent of evidence for polygenic adaptation. Such methods generally leverage information from genome wide association studies about the relationship between genotype and phenotype together with population genetic data about the distribution of allele frequencies both within and between populations. Students will learn about how and why these methods work, when it makes sense to use them, how to interpret their results, and how to identify possible false signals of polygenic adaptation.

Key references:

Berg, J. J., & Coop, G. (2014). A population genetic signal of polygenic adaptation. *PLoS Genet*, 10, e1004412.

Dr. Joshua Payne (University of Zurich, Switzerland) (Tuesday, August 29)

Many cellular functions depend upon intermolecular interactions, such as protein-protein interactions and protein-DNA interactions. I will discuss an example of intermolecular epistasis between a transcription factor – the steroid hormone receptor – and its DNA binding sites (Anderson et al. 2015). Students will be presented with the diversity of techniques used to uncover this instance of intermolecular epistasis, including ancestral protein reconstruction.

Key references:

Anderson, D. W., McKeown, A. N., & Thornton, J. W. (2015). Intermolecular epistasis shaped the function and evolution of an ancient transcription factor and its DNA binding sites. eLife, 4, e07864.

Lynch, M., & Hagner, K. (2015). Evolutionary meandering of intermolecular interactions along the drift barrier. *Proc. Natl. Acad. Sci. U. S. A.*, 112:E30-E38.

Prof. Thomas Hansen (University of Oslo, Norway) (Tuesday, August 29)

I will explain how epistasis is modeled and studied in the standard model of statistical genetics. I will cover the distinction between statistical and functional epistasis, and discuss the relationships between the two. I will cover the standard model of response to selection and discuss how epistasis enters into

this. I will discuss some principles of measurement theory, and show how these apply to the basic parameters of quantitative genetics.

Key references:

Hansen, T. F. (2016). Epistasis. In Nuno de la Rosa, L. & G. B. Müller (Eds.). Evolutionary Developmental Biology: A Reference Guide. Springer.

Hansen, T. F. (2013). Why epistasis is important for selection and adaptation. *Evolution*, 67: 3501-3511.

Dr. Josephine Daub (University of Pompeu Fabra, Spain) (Tuesday, August 29)

Gene set enrichment approaches have originally been developed to discover pathways that play a role in complex diseases. In this course, I will introduce the polysel pipeline, where we apply one of such methods to detect gene sets involved in polygenic adaptation. In addition to running the pipeline ourselves, we will practice how to prepare and inspect data sets that serve as input for the enrichment test and we will discuss how to critically analyze and interpret the test results.

Key references:

Daub, J., Moretti, S., Davydov, I. I., Excoffier, L., & Robinson-Rechavi, M. (2016). Detection of pathways affected by positive selection in primate lineages ancestral to humans. bioRxiv, 044941.

Daub, J. T., Hofer, T., Cutivet, E., Dupanloup, I., Quintana-Murci, L., Robinson-Rechavi, M., & Excoffier, L. (2013). Evidence for polygenic adaptation to pathogens in the human genome. Mol. Biol. Evol., mst080.

Prof. Peter Visscher (University of Queensland, Australia) (Wednesday, August 30)

We will discuss the similarities and differences between human and plant/animal populations in the context of drawing inference about genetic variation and selection for complex traits. We will contrast the inference from pedigree data and GWAS and illustrate those with in-class and practical sessions using empirical data.

Key references:

Vinkhuyzen, A. A., Wray, N. R., Yang, J., Goddard, M. E., & Visscher, P. M. (2013). Estimation and partition of heritability in human populations using whole-genome analysis methods. *Annual review of genetics*, 47:75-95.

Vitti, J. J., Grossman, S. R., & Sabeti, P. C. (2013). Detecting natural selection in genomic data. *Annual review of genetics*, 47:97-120.

Prof. John Mckay (Colorado State University, USA) (Wednesday, August 30)

I will review methods of genome wide phenotype to genotype analysis, including some discussion of strengths and weaknesses. I will then discuss our recent work in identifying causal variants in controlled crosses, by combing re-sequencing and whole genome expression data with the traditional genotype and phenotype matrices. I will also discuss our efforts to use historical climate data to prioritize regions of the genome. Finally, I will discuss the ongoing challenges of functional genetics and validating phenotypic effects of polymorphisms.

Key references:

Lovell, J. T., Mullen, J. L., Lowry, D. B., Awole, K., Richards, J. H., Sen, S., ... & McKay, J. K. (2015). Exploiting differential gene expression and epistasis to discover candidate genes for drought-associated QTLs in Arabidopsis thaliana. *The Plant Cell*, 27:969-983.

Lasky, J. R., Des Marais, D. L., Lowry, D. B., Povolotskaya, I., McKay, J. K., Richards, J. H., ... & Juenger, T. E. (2014). Natural variation in abiotic stress responsive gene expression and local adaptation to climate in Arabidopsis thaliana. *Mol. Biol. Evol*., 31: 2283-2296.