

## LOGICAL REASONING IN HUMAN GENETICS, 2015

### GENERAL AGENDA

**DATE and TIME:** August 10-14, 2015, 9:30AM-5:00PM

Course may end early on Friday afternoon

**PLACE:** Oulu, Finland (building/room to be announced)

### OBJECTIVES AND NATURE

This course is designed to examine the conceptual, empirical, and theoretical approaches to understanding the complex cause and effect relationships underlying human variation. Despite a century of quantitative research on evolutionary biology and genetics, our hypotheses about the phenogenetic (genotype + environment + culture → phenotype) relationships underlying human variation seem poorly focused and often based on unnecessarily naïve models. In this course we will review the logical basics of evolutionary biology, genetic epidemiology, gene mapping. ‘Logical’ refers to the nature of the controlling structures of genomes and evolution, as well as of the reasoning processes by which inferences are made. Logical thinking helps integrate these three disciplines to address questions of causality in human genetics (and genetics and evolution generally).

It is hoped that through this course, students will be stimulated to develop critical thinking and logical reasoning skills to try and learn from what existing results tell us about the architecture of disease—and, importantly, to question the assumptions underlying their experimental approaches, so as to develop better study designs based on better hypotheses for future studies. The reason studies are not finding the clear causal effects that are often promised is usually because the question was poorly posed or incompletely thought out, not because of technical or analytical errors. In fact, many of the most important recent findings, often of many genes (and environmental factors) with little individual effect, have been a major success, because they have shown that the causal landscape is more complex than had been widely hoped and expected, but this is in fact consistent with biological and evolutionary theory.

The basic structure is given below, but this is only a general outline. The details are subject to change.

## Monday 10<sup>th</sup> of August: Philosophical and Evolutionary Background

- Introductions
  - Welcome
  - Faculty Introductions
  - Student introductions
- What is ‘logical’ about this course or about science?

*Coffee (10.45AM-11.00AM)*

- How reliable are our criteria for determining causation?
- Doubt: Scientific inference in a probabilistic world
- Evolution and the Darwinian method: Why should traits be ‘genetic’?

*Lunch (12.30PM-1.30PM)*

- Just like peas! Genetic epidemiology of simple traits?
- But....not simple like peas after all

*Coffee (3.00PM-3.15PM)*

- Phenogenetics and the consequences of evolution by phenotype
- Human variation and evolution
- Discussion: how do today’s topics apply to *your* interests?

## Tuesday 11<sup>th</sup> of August: Analytical methods

- Dichotomous traits – linkage analysis

*Coffee*

- Quantitative traits – linkage analysis

*Lunch*

- Dichotomous traits – LD analysis and joint linkage/LD analysis

*Coffee*

- Quantitative traits – LD analysis and joint linkage/LD analysis
- Discussion: how do today’s topics apply to *your* interests?

### **Wednesday 12<sup>th</sup> of August: Complex traits and the evolution of genetic architecture**

- Detectance, mapping, study design, linkage and LD analysis of complex traits
- Historical overview of GWAS and HapMap (he said/she said)

*Coffee*

- Complexity: some illustrative results to date
- Not all inheritance is Mendelian, but it's all evolutionary (somatic mutation)

*Lunch*

- Complexity: other issues, concepts, and subtleties
- Projects and results – real world examples

*Coffee*

- GWAS and consortia and biobanks and other technological panaceas
- Complexity made simply: developmental biology and issues it raises
- Discussion: how do today's topics apply to *your* interests?

### **Thursday 13<sup>th</sup> of August: Simulation as a tool of choice**

- Evolution revisited – phenogenetic traits and how they got here
- Quantitative evolutionary genetic modeling

*Coffee*

- ForSim: A tool to simulate highly complex phenotypes under evolutionary population genetic models (basic description)

*Lunch*

- Quantitative epidemiological modeling
- SimQTL: A tool to simulate complex phenotypes under epidemiological models (basic description)

*Coffee*

- Software for analysis of simulated data – Autogscan, etc...
- Some specific studies relevant to EU and Finland
- Discussion: how do today's topics apply to *your* interests?

### **Friday 14<sup>th</sup> of August: Examples and discussion – study design and analysis issues**

- Sample applications of these programs to research problems and questions

- Controlled experiments and what they tell us

*Coffee*

- Natural Experiments in human genetics – a better alternative to GWAS
- Real-world results from different approaches with an eye to the future

*Lunch*

- Some thoughts on approaching complex problems
- Strange issues, violating ‘common sense’, and what they may mean

*Coffee*

- Summary overview: our understanding of ‘truth’
- Questions and Discussion