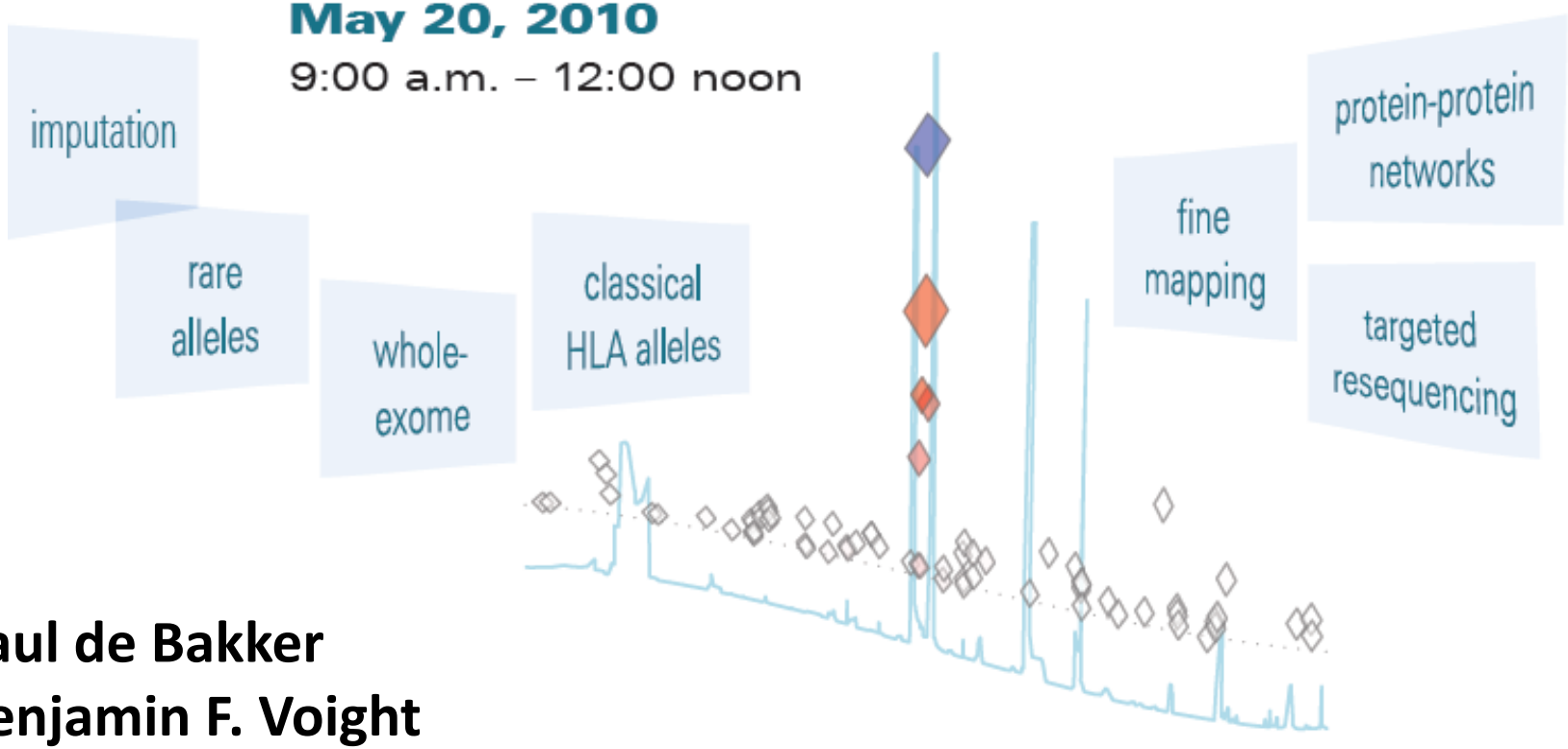
Program of Medical and Population Genetics

2010 Workshop Series

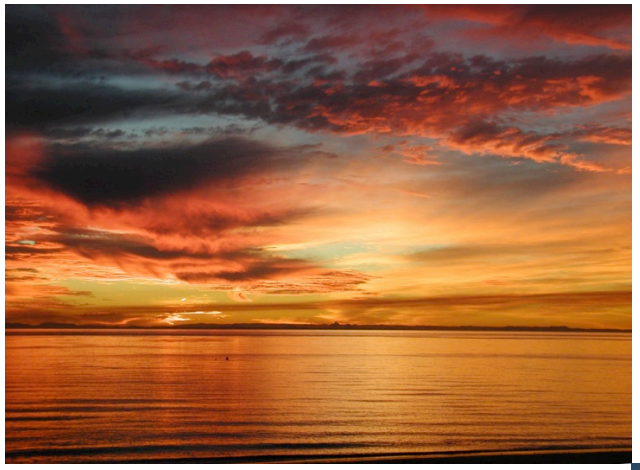
Snapshots of Genome Wide Analysis in Human Disease

May 20, 2010

9:00 a.m. – 12:00 noon



Paul de Bakker
Benjamin F. Voight



Initial catalog of phenotypic associated loci identified via GWAS

Positive improvements to human health

Fundamental understanding of disease

What are the next major pieces?

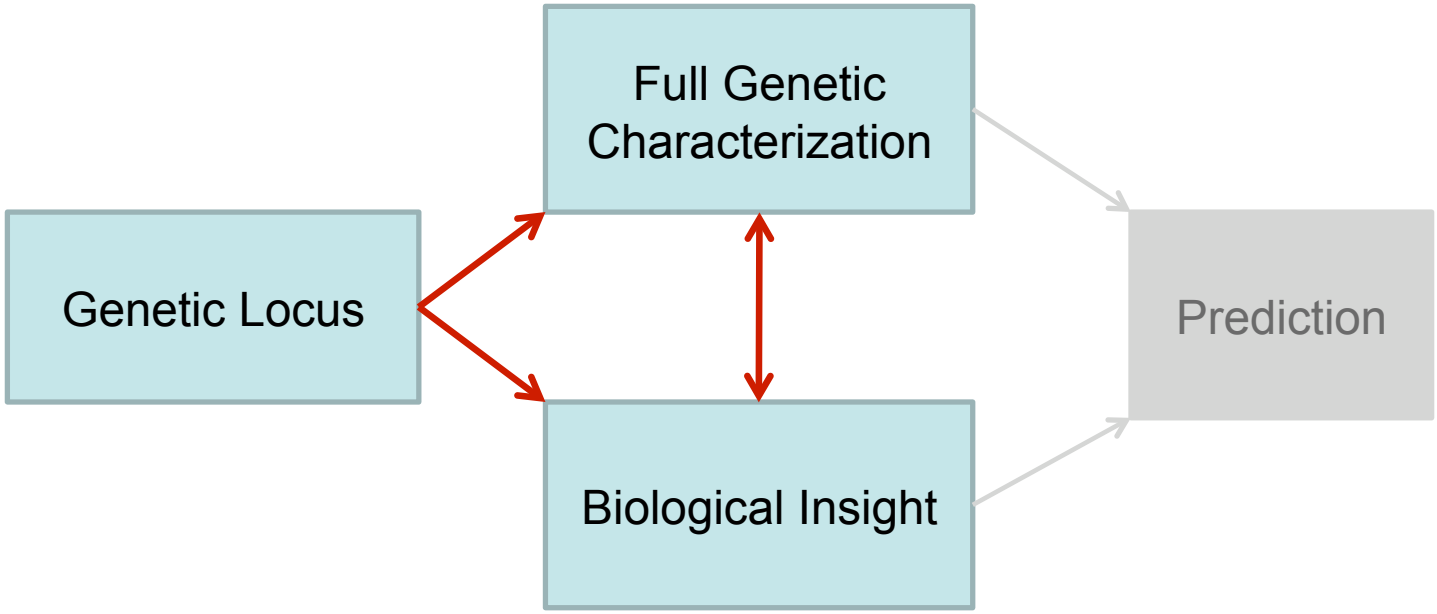
Lessons from the GWAS era

- Characterization
  - Catalog of common SNPs (HapMap)
  - Genotyping arrays (up to 1M SNPs/CNPs)
- Data generation
  - large-scale genotyping, genotype calling, experimental design
  - QC, population stratification, technical artifacts
- Analysis
  - Variant by variant
  - Meta-analysis and replication

These lessons will continue to be relevant in our future endeavors.

And where does that leave us?

- Many hundreds of common SNP associations across the genome
  - often novel loci of unsuspected importance
- Individual variants linked to one or more underlying causal variants
  - generally not known



These are the crucial next steps.

And this is not the end.

Questions

- What analyses are the most important after genome-wide association?
- What strategies are available?
- How can next-generation sequencing technology advance understanding of human disease?

Part I: Analysis of low-frequency variation through sequencing

- Aggregation of low frequency variation

- Incorporation of functional and population genetic data into analysis of genetic data

- Two case studies: Discovery, validation, and analysis of variation from re-sequencing efforts

Part II: Second Generation Analyses

- Imputation with the 1000 Genomes Project
- Fine-mapping of GWAS signals
- Fine-mapping in the HLA loci
- Interpreting associations using protein-protein interaction networks