Genomes and phenotypes

Wolfgang Huber[1,2,⋆]

1. EMBL, Genome Biology Unit, Heidelberg, Germany
2. EMBL, European Bioinformatics Institute, Cambridge, UK
⋆Contact author: whuber@embl.de

Much of what we know about the workings of biological systems has been learned through genetics: either, identifying individuals in a population with remarkable phenotypes and mapping the causal genetic variant; or, systematically perturbing genes and gene products, and spotting the effects this might have. While traditionally the approaches were low-throughput and sometimes haphazard, automation of lab-work, computing and the availability of full genome sequences have enabled systematic, quantitative high-throughput approaches. In particular, I will give an overview over the use of genome-wide RNAi libraries for the mapping of the *phenotypic landscape* of a cell population; and of large-scale combinatorial RNAi perturbation assays to dissect the underlying, "hidden" functional modules. This poses many exciting computational questions, including image analysis, machine learning and inference from high-dimensional data.

References

Boutros, M., L. P. Brás, and W. Huber (2006). Analysis of cell-based RNAi screens. *Genome Biology 7*(7).

Fuchs, F., G. Pau, D. Kranz, O. Sklyar, C. Budjan, S. Steinbrink, T. Horn, A. Pedal, W. Huber, and M. Boutros (2010). Clustering phenotype populations by genome-wide RNAi and multiparametric imaging. *Molecular Systems Biology 6*(370).

Horn, T., T. Sandmann, B. Fischer, E. Axelsson, W. Huber, and M. Boutros (2011). Mapping of signalling networks through synthetic genetic interaction analysis by RNAi. *Nature Methods 8*(4).

Mancera, E., R. Bourgon, A. Brozzi, W. Huber, and L. M. Steinmetz (2008). High-resolution mapping of meiotic crossovers and non-crossovers in yeast. *Nature 454*(7203), 479–485.

Neumann, B. et al. (2010). Phenotypic profiling of the human genome by time-lapse microscopy reveals cell division genes. *Nature 464*(7289), 721–727.

Pau, G., F. Fuchs, O. Sklyar, M. Boutros, and W. Huber (2010). EBImage – an R package for image processing with applications to cellular phenotypes. *Bioinformatics 26*, 979–981.