MSc course: Practical Systems Biology

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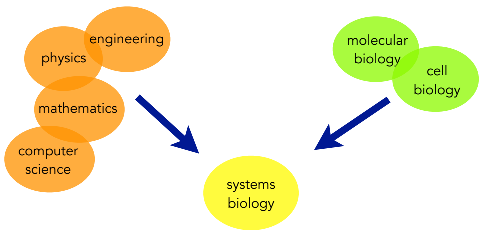
This course will provide *an introduction to systems biology* by focusing on the behaviours expected from interactions between only a few genes, taking examples from microbes to mammals.

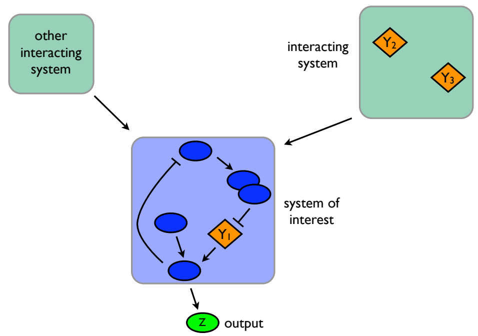
Cells are dynamic systems, and we will build intuition about the types of responses expected from different gene circuits *by running, adapting, and analysing computer simulations.*



SynthSys Centre for Synthetic and Systems Biology

Although systems biology cannot be easily defined, a system can.

By a system, we simply mean some subset of the entire world **whose behaviour, and whose interaction with the rest of the world**, we believe can be sensibly described. (Kuipers, 1994)



These interactions be intra- or extra-cellular.

For many, systems biology started with this 1999 review

From molecular
to modular cell biology

Leland H. Hartwell, John J. Hopfield, Stanislas Leibler and Andrew W. Murray

Cellular functions, such as signal transmission, are carried out by **'modules'** made up of many species of interacting molecules ...

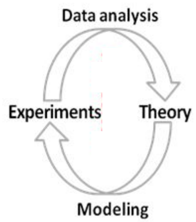
General principles that govern the structure and behaviour of modules may be discovered with help from synthetic sciences such as engineering and computer science, from stronger interactions between experiment and theory in cell biology, and from an appreciation of evolutionary constraints.

Nature, 1999

Initial definitions of systems biology were mostly operational

Systems biology studies biological systems by systematically perturbing them (biologically, genetically, or chemically); monitoring the gene, protein, and informational pathway responses; integrating these data; and ultimately, formulating mathematical models that describe the structure of the system and its response to individual perturbations. (Ideker et al, 2001)

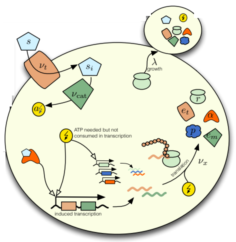
To understand complex biological systems requires the integration of experimental and computational research – in other words a systems biology approach. (Kitano, 2002)



the objective of systems biology [can be] defined as the understanding of network behavior, and in particular their dynamic aspects, which requires the utilization of methematical modeling tightly linked to experiment. (Cassman, 2005)

More inspiring definitions emerged later

What distinguishes systems biology from earlier traditions is the tendency **to define importance** less in operational terms (e.g., necessary or sufficient to produce a behavior) than **in terms of relevance to the goals of a system**. (Lander, 2007)



By discovering how function arises in dynamic interactions, systems biology **addresses the missing links between molecules and physiology**. (Bruggeman and Westerhoff, 2007)

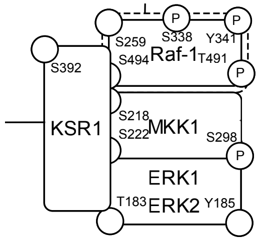
Why do we need systems biology?

The sequencing of the human genome has given us a list of the parts of the cell (the genes and proteins).

We need to understand how these parts interact to generate cellular behaviour if we wish to improve both medicine and biotechnology.

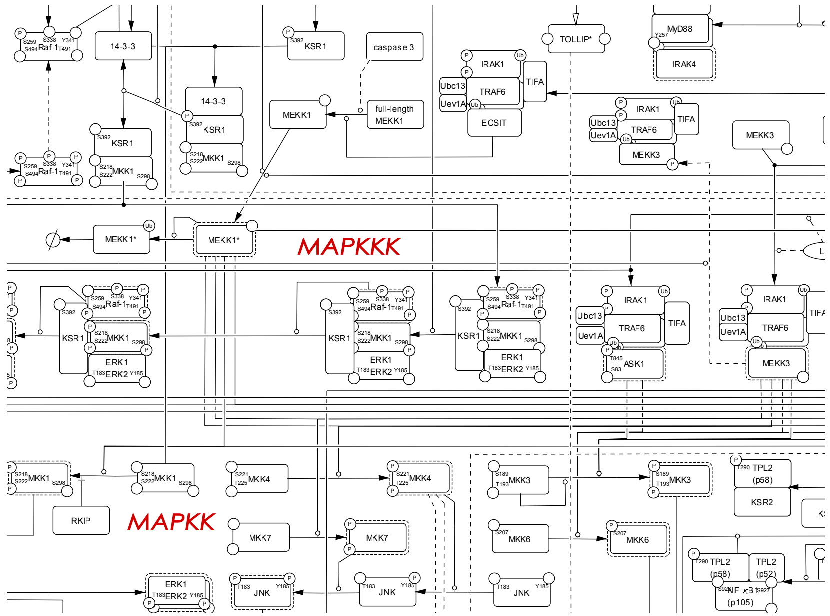
Biology is complex, and understanding cellular behaviours is hard

For example, here are three proteins in a “cascade”: Raf-1 activates MKK1 and MKK1 activates ERK1



These proteins are part of the innate immune response and the figure is taken from a map of the innate immune system by Oda and Kitano.

Zooming out...



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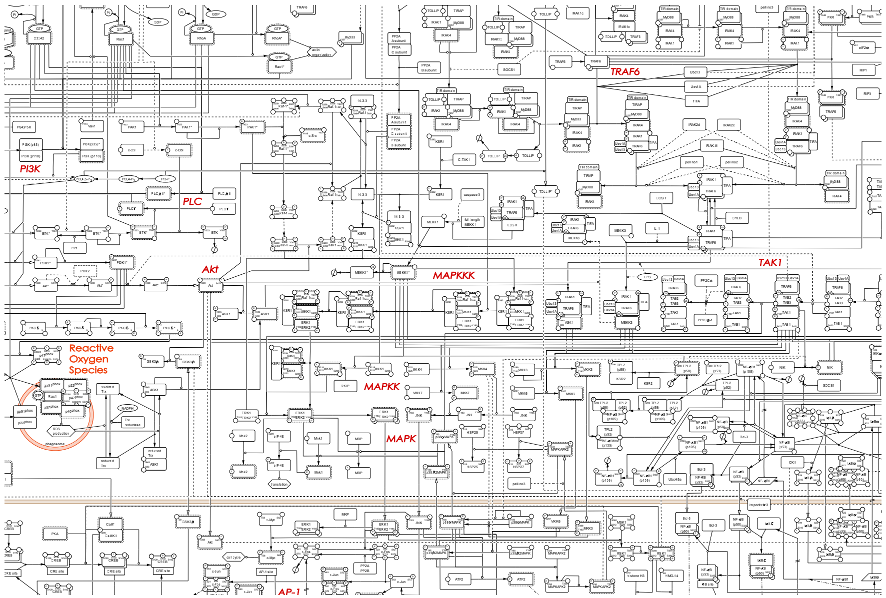

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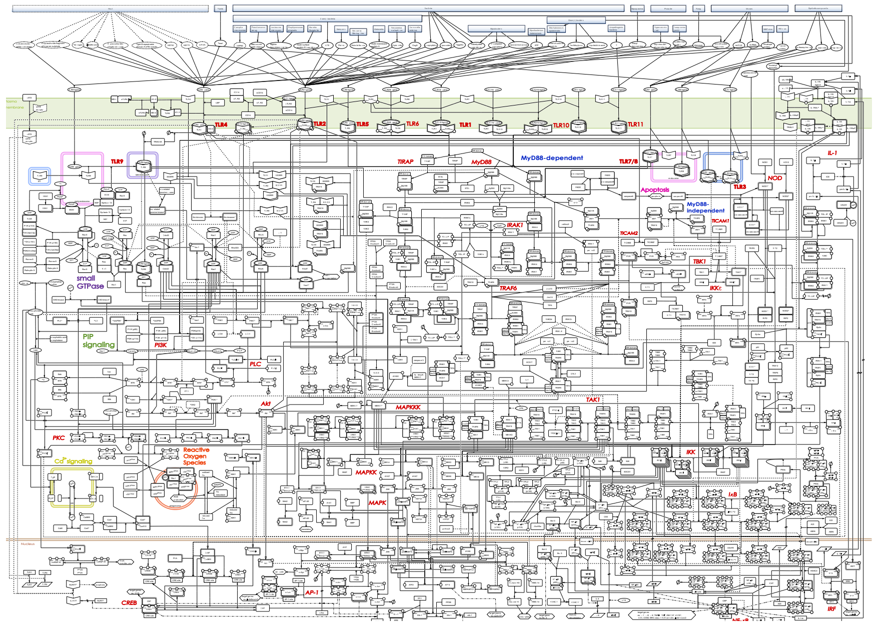
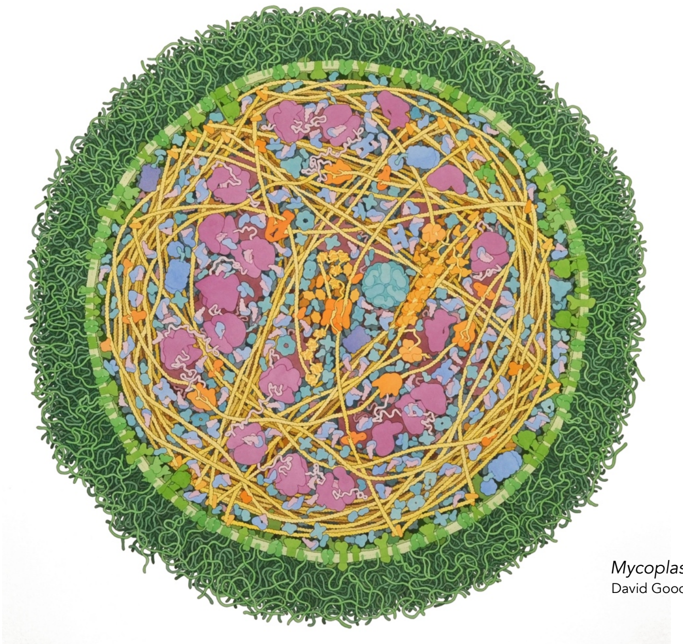


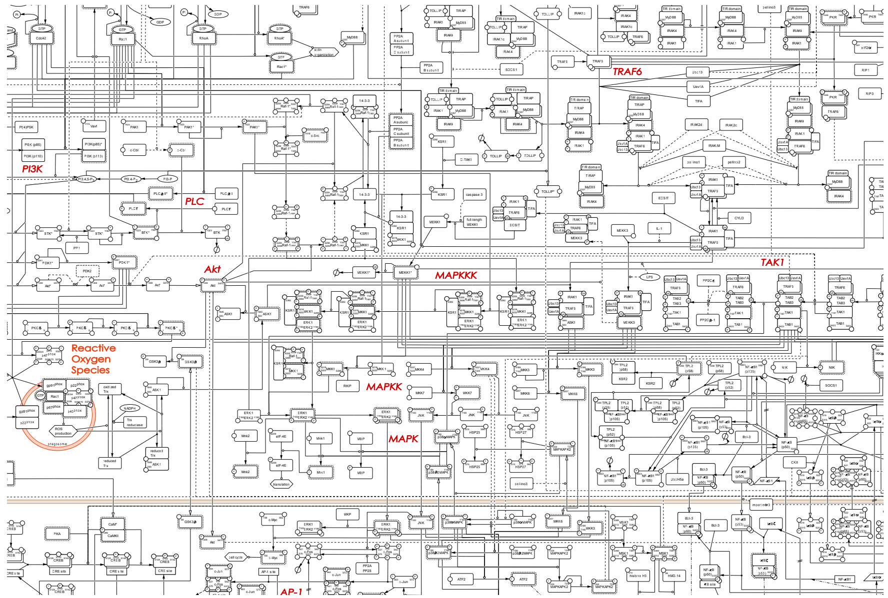
Biology is complex spatially: cells are packed with proteins and other macromolecules

DNA
RNA polymerase
ribosome
lipoglycan



Mycoplasm mycoides
David Goodsell, Scripps Institute

It is because biology is so complex that we need a multidisciplinary approach.



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Outcomes of the course

You will be able to:

(i) design a systems approach – think like a systems biologist

(ii) understand and predict the dynamics of simple modules

(iii) formulate and simulate mathematical models

(iv) write programs in Python to test biological hypotheses

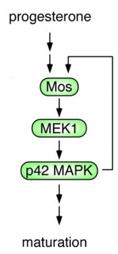
Main learning outcome:

To use the free computer language Python to test biological hypotheses by creating, simulating and analysing mathematical models of biological processes.

Assessment:

Two assignments (step-by-step computational analyses of a model of a biological system – 20% each)

A research project (selecting a model from the literature and simulating and adapting that mode to test a novel hypothesis – 60%)



Structure of the course

Systems biology

- Modelling biochemical networks
- Enzyme kinetics
- Ultrasensitivity and allostery
- Modelling gene expression
- Biochemical switches
- Negative feedback
- Genetic oscillators
- Stochastic gene expression

Python

- Variables
- Loops, lists, and functions
- Plotting data
- Scientific computing with arrays
- Simulating biochemical networks