Mathematical modelling introduction

basic models of biological networks

why do we make models?

nature and complexity – static pattern formation, simple mechanisms

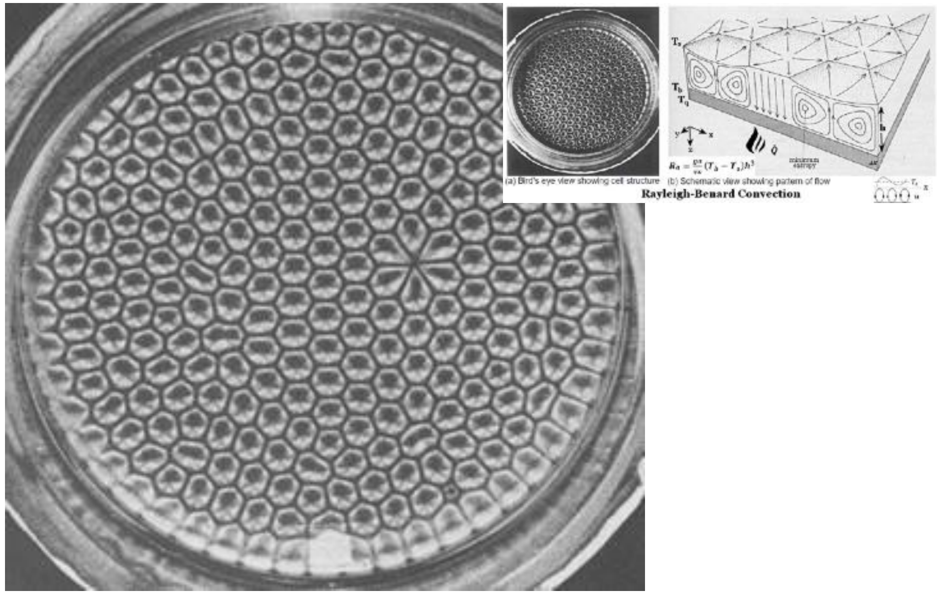
Lämmel, M., Meiwald, A., Yizhaq, H. *et al*. Aeolian sand sorting and megaripple formation. *Nature Phys* **14**, 759–765 (2018).

nature and complexity – dynamic pattern formation, simple mechanisms, physicochemical systems

Belousov-Zhabotinski reaction

waves of chemicals in a chemical reaction

in a lab petri dish



Rayleigh-Bénard convection

pattern formation in water film exposed to temperature gradient

nature and complexity – dynamic pattern formation, simple mechanisms, collectives of agents


a bird flock of starlings


ants making a bridge


a school of fish

nature and complexity – static pattern formation, unknown mechanisms

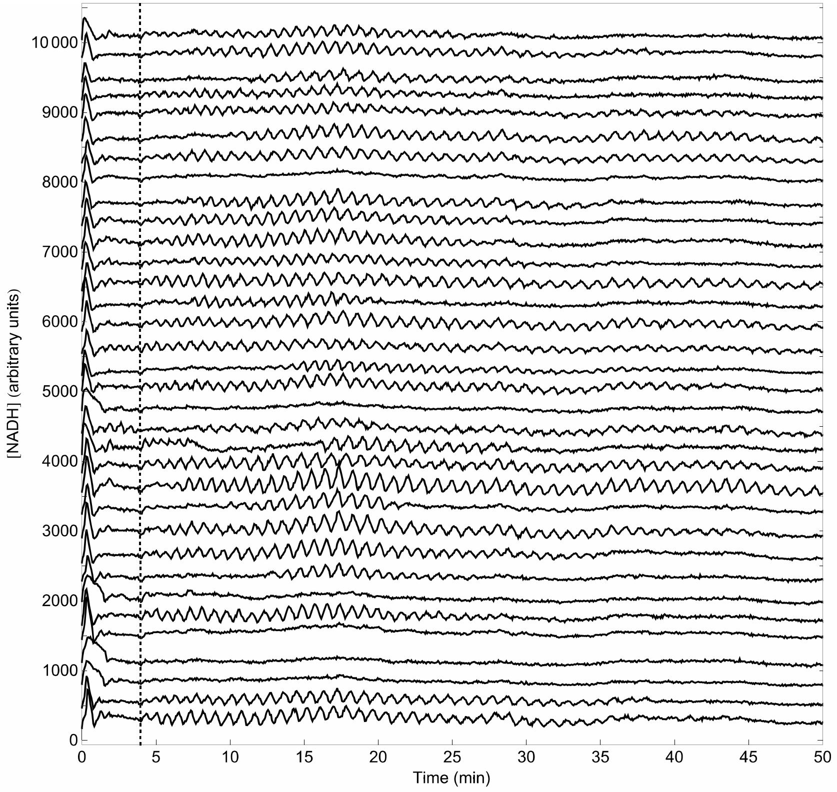
computer generated
Barnsley fern
https://en.wikipedia.org/wiki/Barnsley_fern

nature and complexity – dynamic pattern formation, complex mechanisms

[*C. elegans* worm development]

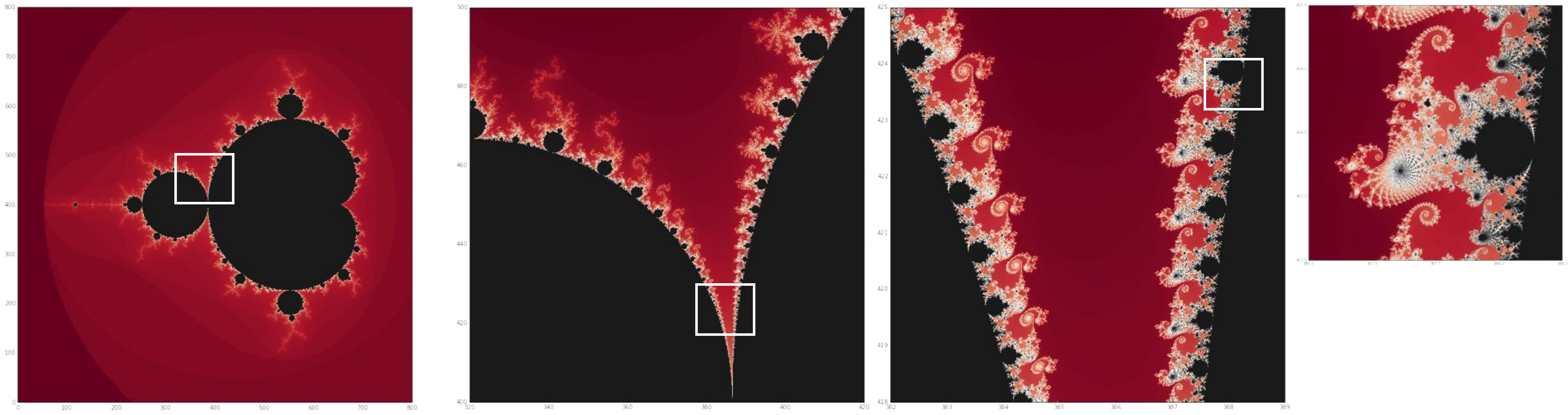
servable oscillations should dampen initially, but subsequently should reappear as the synchronization becomes effective. Fig. 1 shows that reappearance was observed. Because the oscillations in the mixed cell populations were sustained (over 30 cycles; data not shown) and of the same amplitude as before mixing, the re-emergence of oscillations cannot be explained as an interference pattern due to a slight frequency difference between the two subpopulations. This finding and the observation that it takes some time before the oscillations re-emerge after mixing, is at variance with earlier reports concerning transient oscillations in mixed cell populations [7, 17]. This difference with the previous studies may well arise from the rather subtle dependence of the dynamic behaviour of yeast metabolism on the history of the yeast cells [6, 7].

The requirements for any intercellular-signalling mechanism are, (a) the signal has to be sensed by the cells; (b) the signal has to be emitted; and (c) the signal has to pass through the



oscillating yeast cells, communicating with each other

mathematics and complexity – fractals, Mandelbroth set



nature and complexity

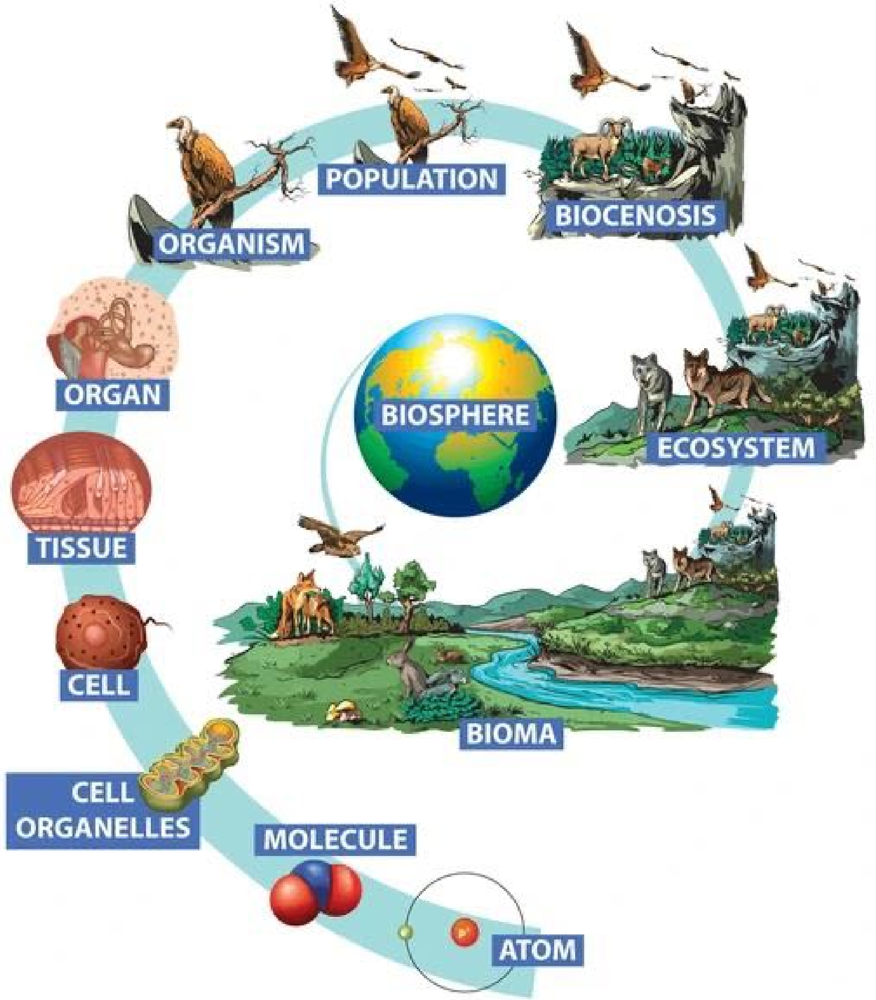
complex behavior emerges from interactions

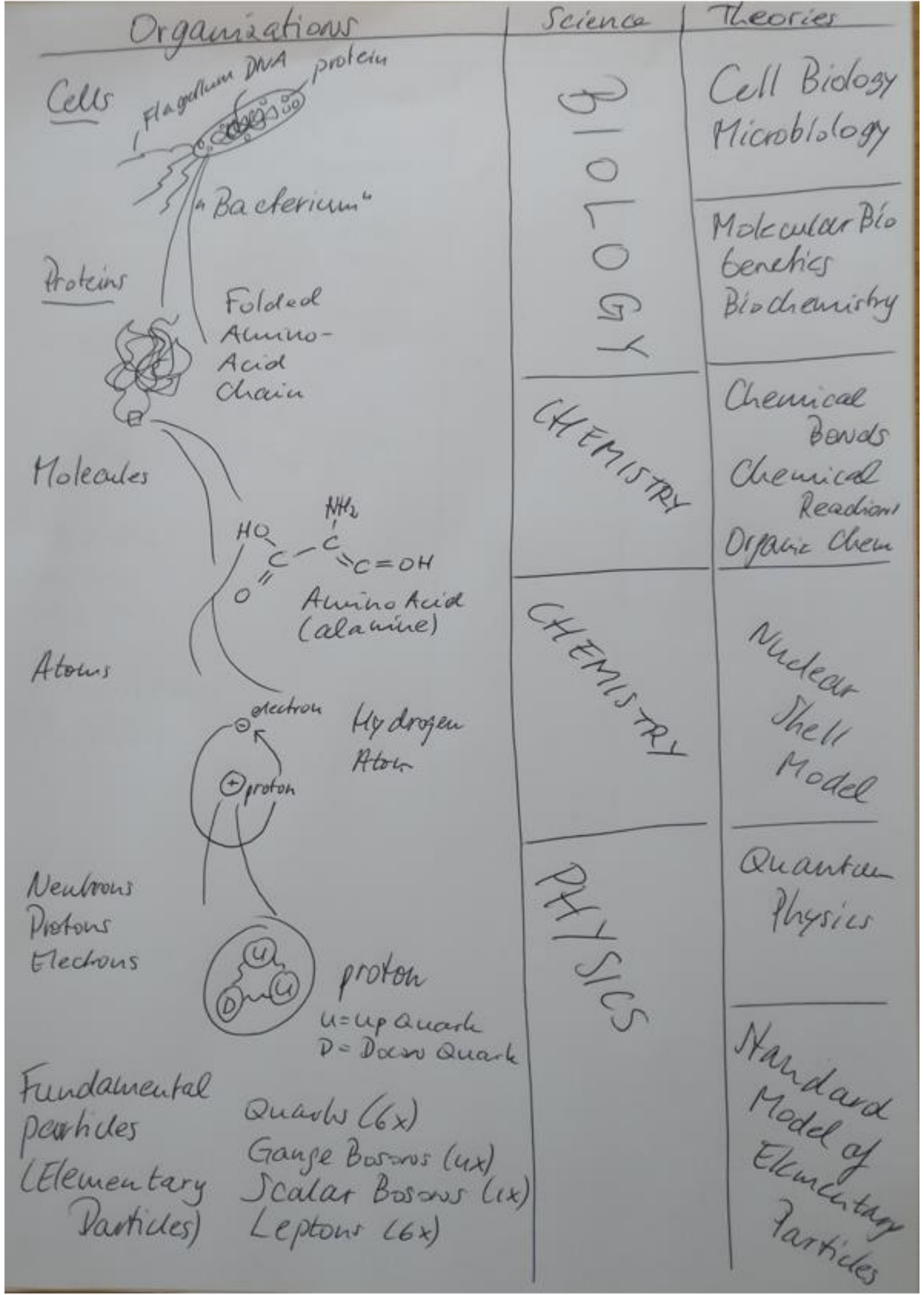
pattern formation

self-organisation

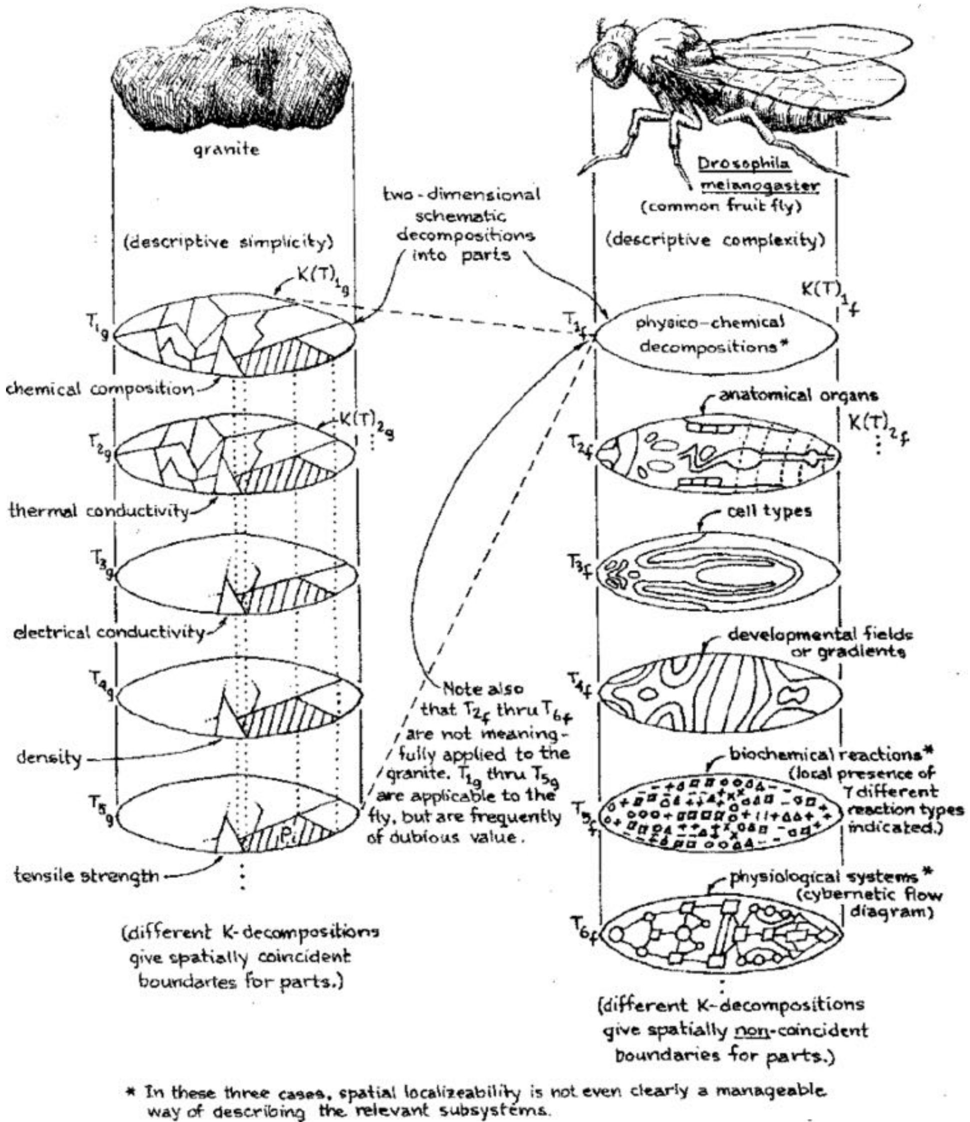
underlying mechanisms vary from simple to complex how is nature organised such that complexity can arise?

nature – a nested hierarchy

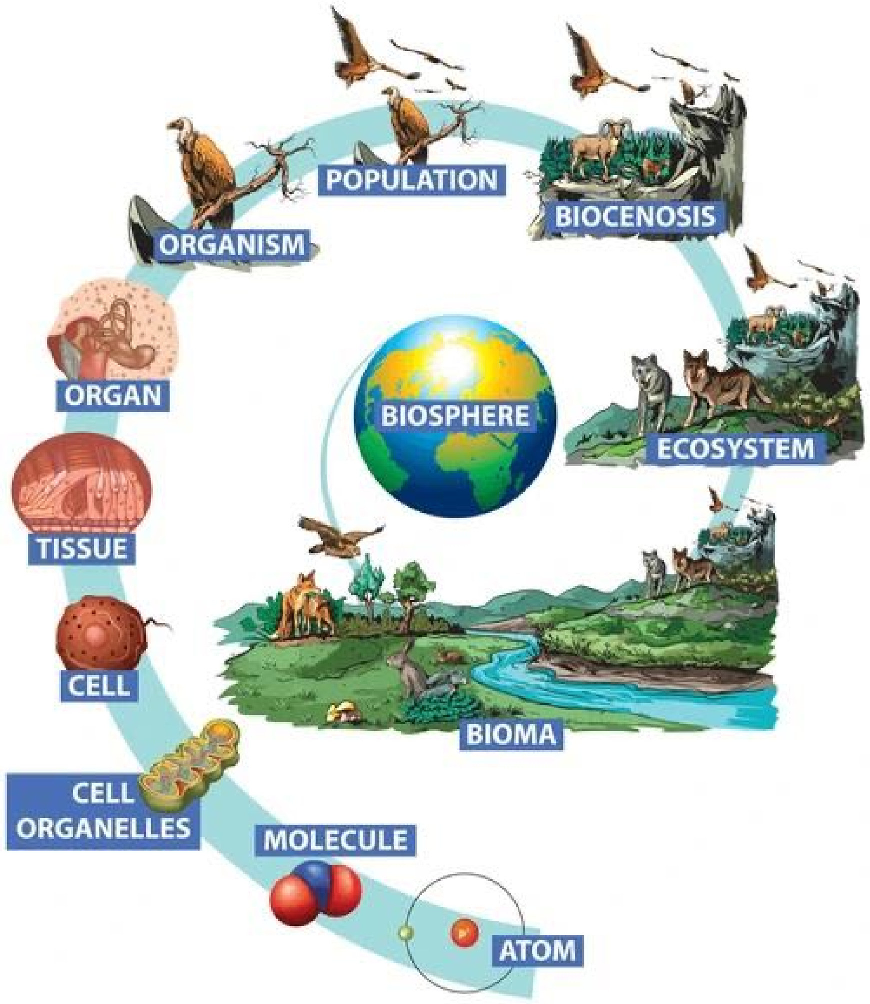




Complexity – systems vary in complexity



Complexity emerges from interactions between the lower level constituents of systems

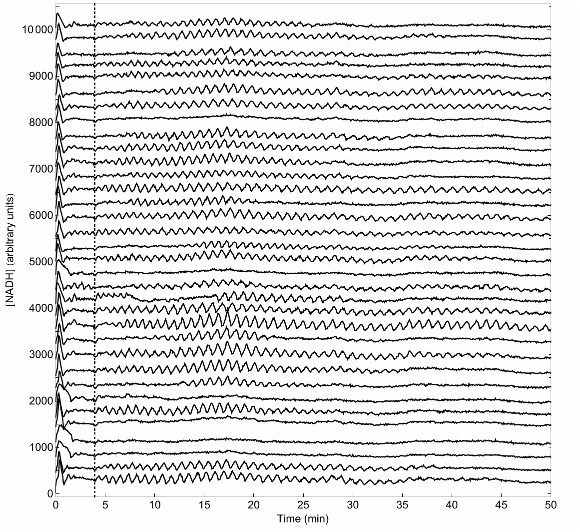


why do we make models?

- to forecast; to make predictions
- to engineer new technologies and medicine
- to understand the principles of nature
- ....
- ....

many models aim to predict the emergent behavior of systems, given their parts and interactions

chemical reactions
and diffusion

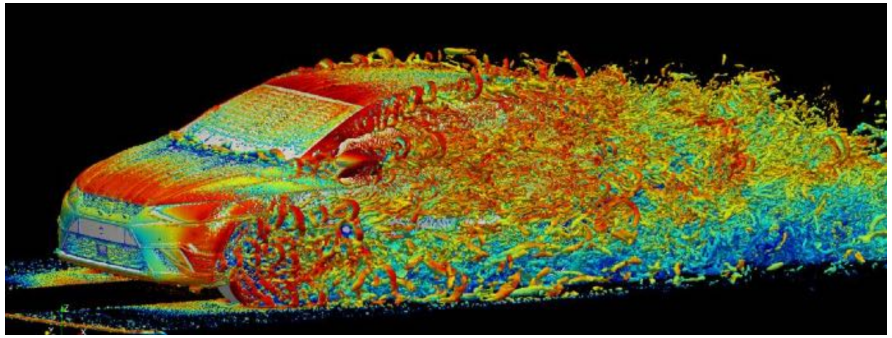


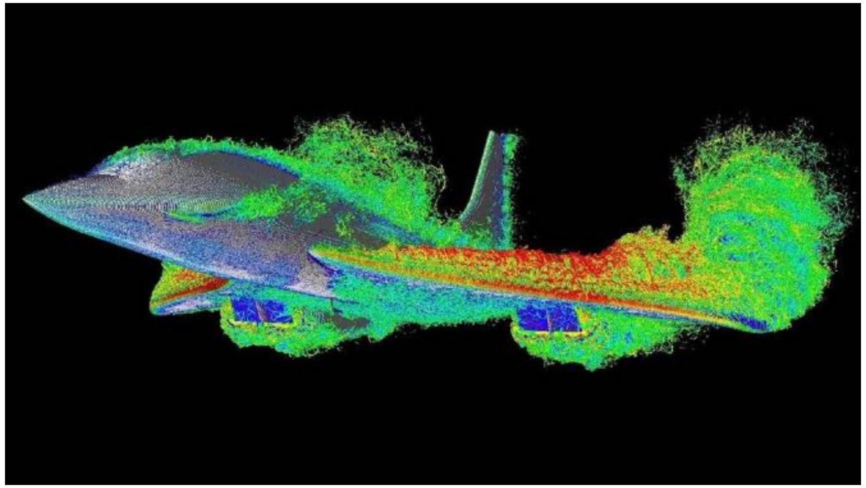
cellular metabolism
and cell-cell interactions

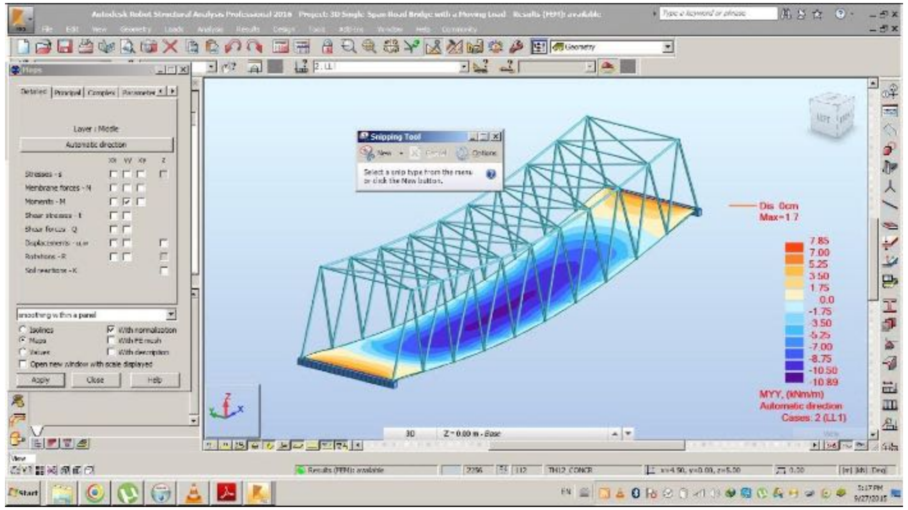
flying birds and
neighbour-neighbour interactions (rules)

Models in science and engineering

Mechanical engineering

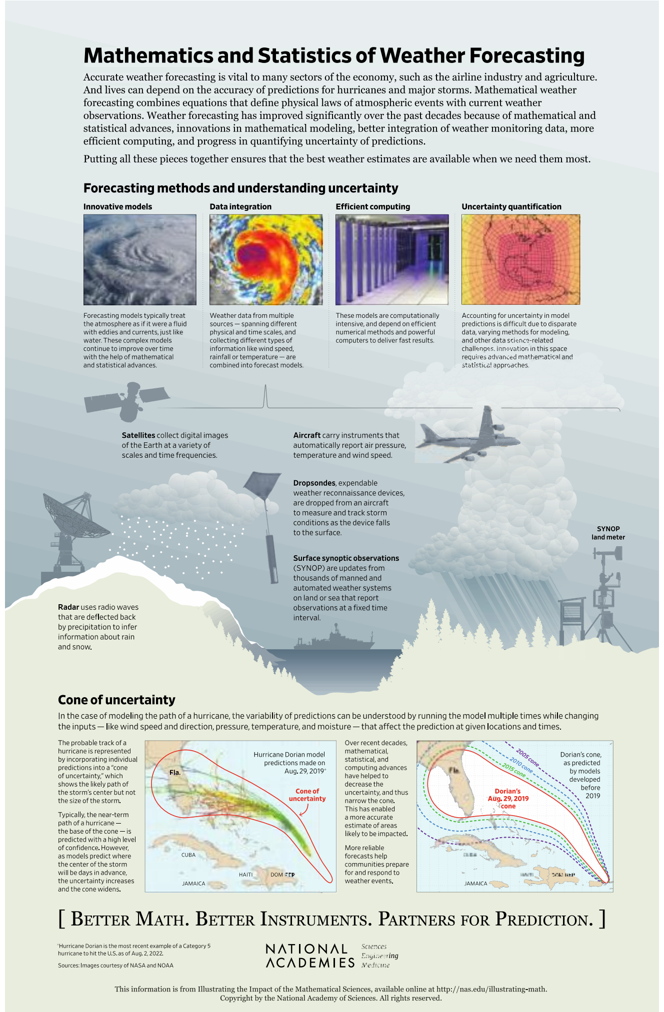


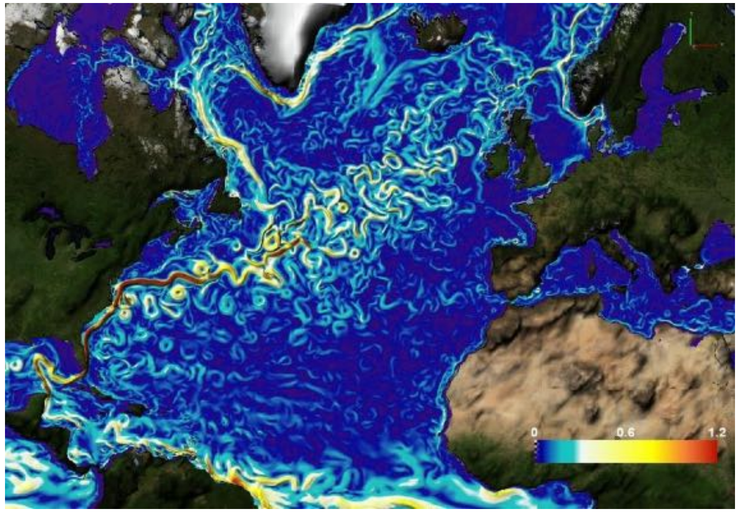


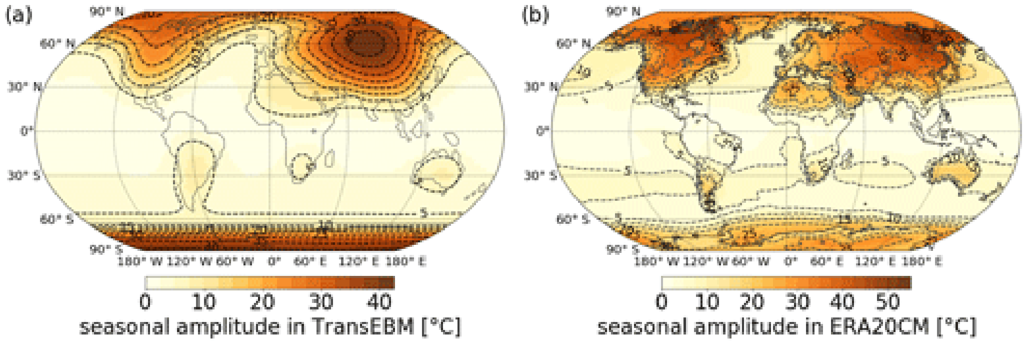


Models in science and engineering

Weather forecasting, ocean currents, temperature distribution earth



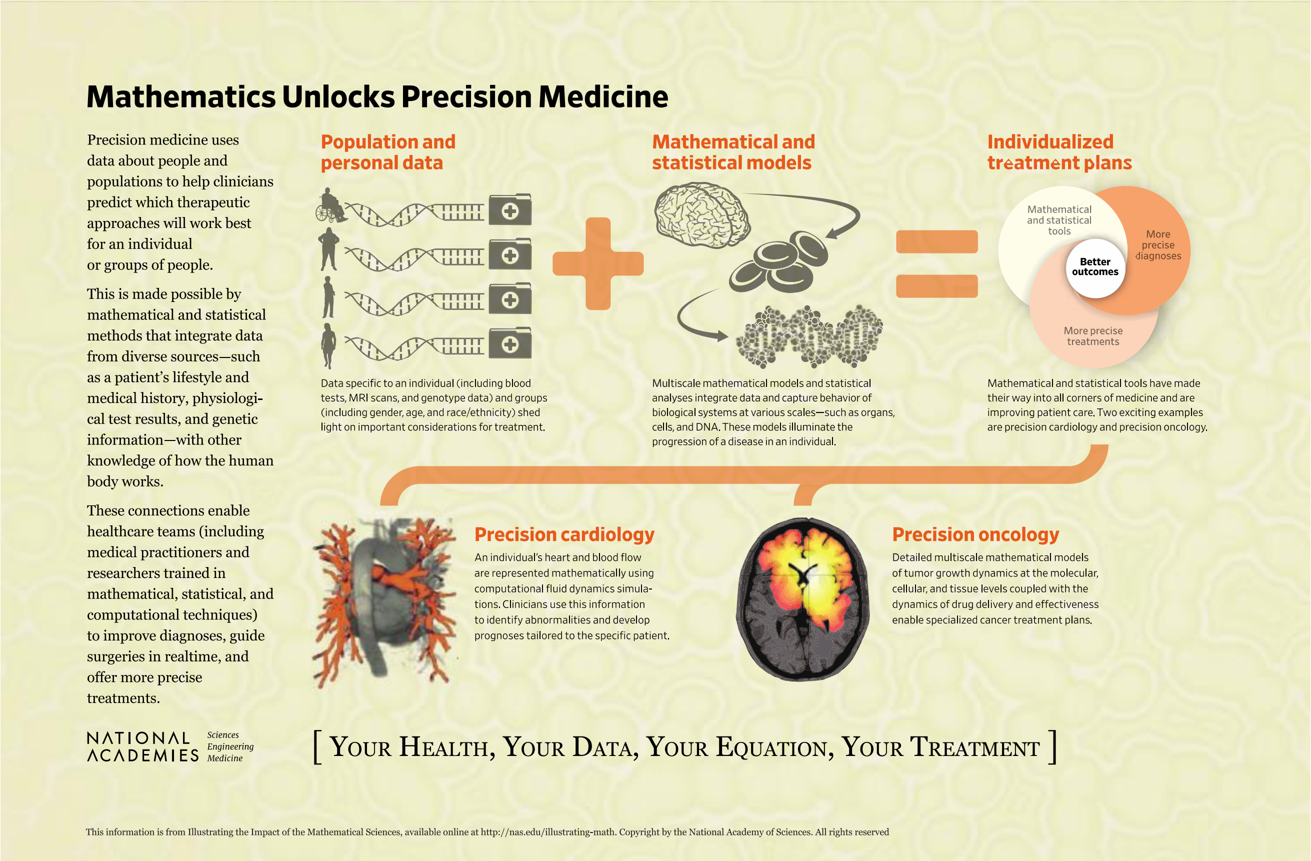


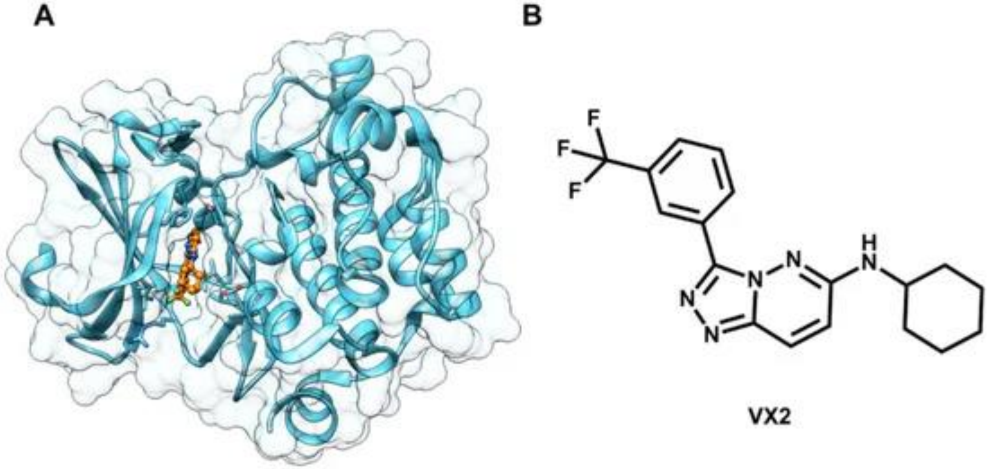


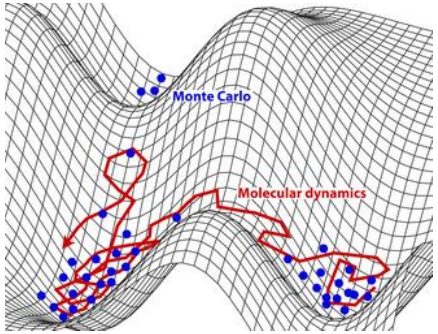
https://gmd.copernicus.org/articles/14/2843/2021/

Models in science and engineering

Medicine

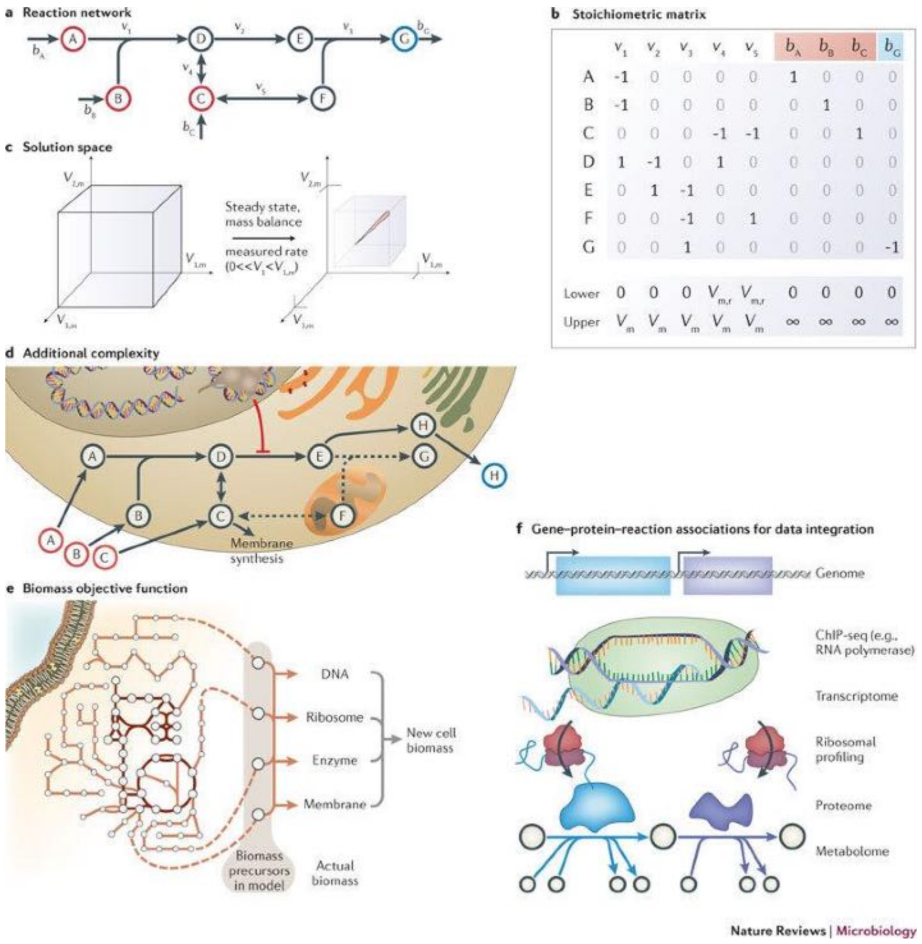






Models in science and engineering

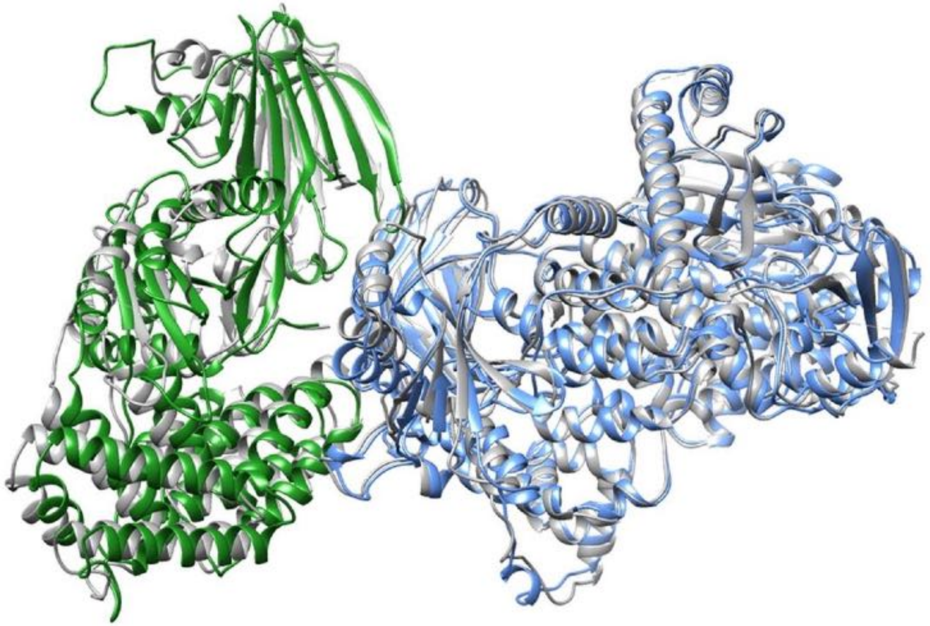
Metabolic engineering and biotechnology



genome-scale stoichiometric models

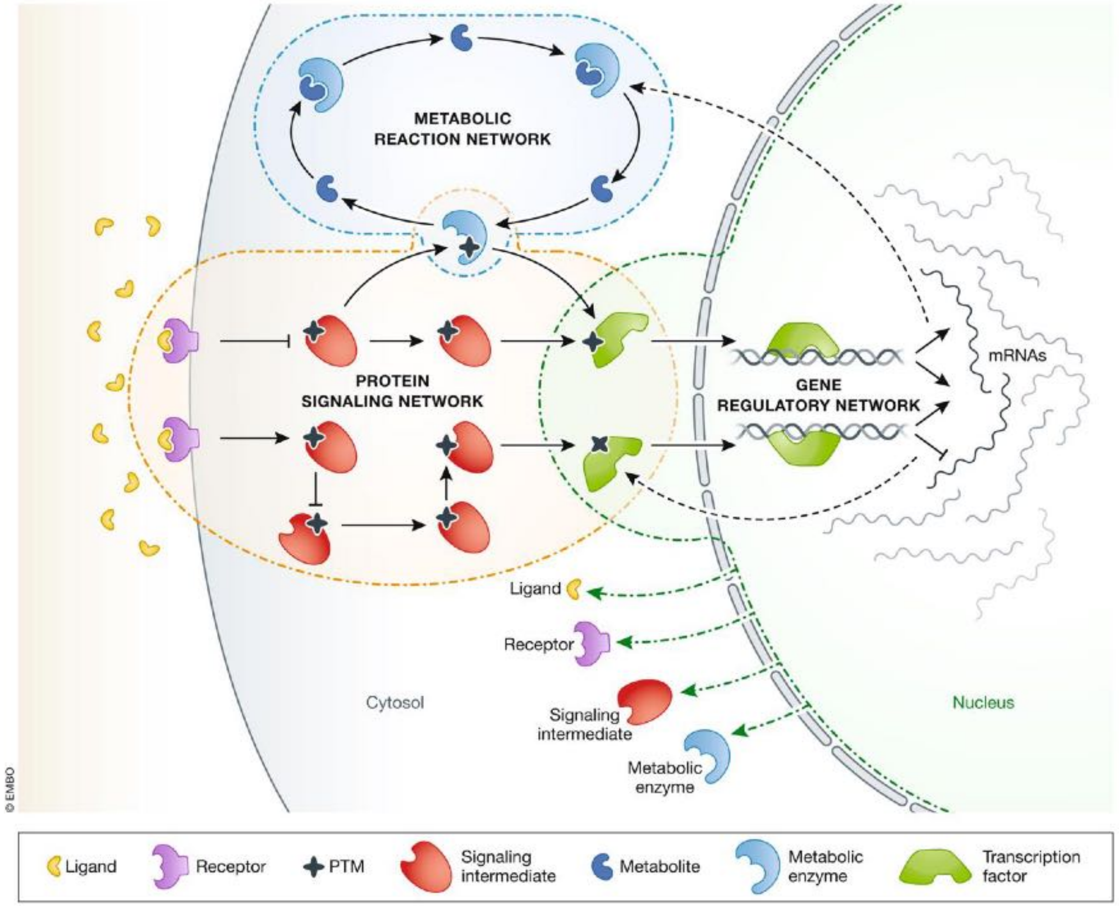
Models in science and engineering

Alphafold and ChatGPT; data-extensive trained neural networks, regression



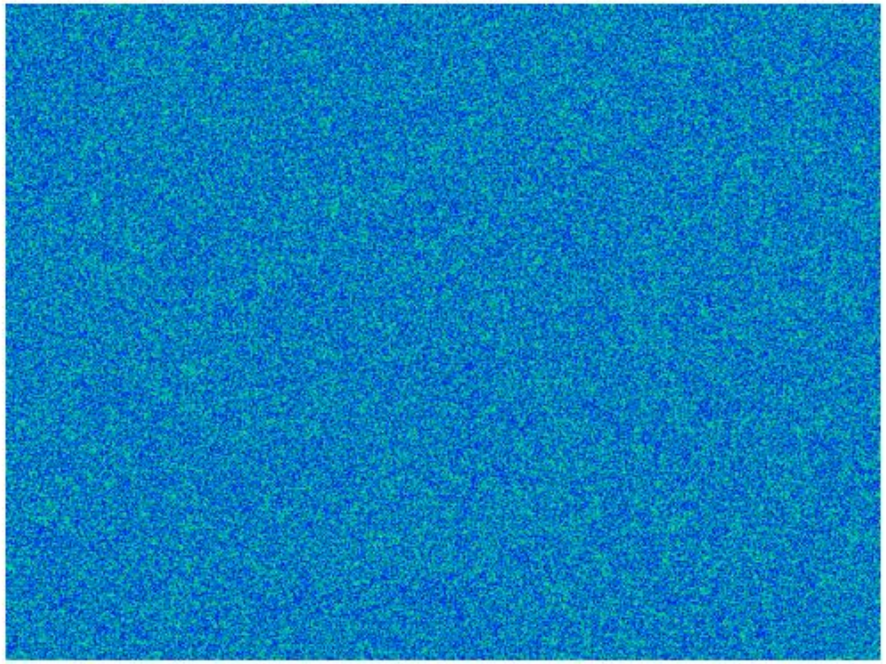
Models in science and engineering

Cell biology, biochemistry and drug target identification



Models in science and engineering

Cell biology, biochemistry and drug target identification



different types of models (we will consider all of them in this course)

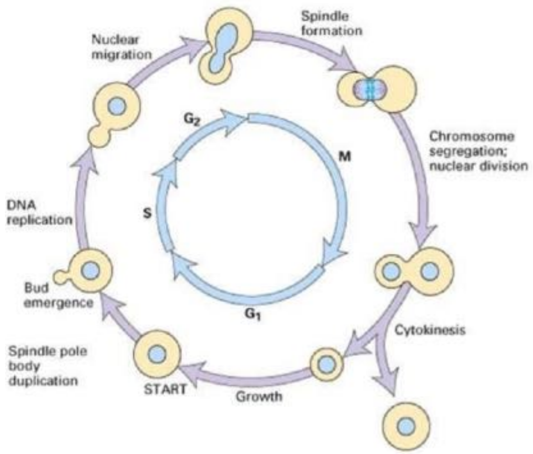
- Equation-based models
  - causal mechanistic models of systems
    - given the properties of the parts of a system
  - phenomenological models
    - given a crude description of a phenomenon generated by a system
  - empirical models
    - given data

- “Equation-free” models
  - neural networks (can approximate any mathematical equation)
    - heavily reliant on the existence of the right set and sufficient data (still rare)

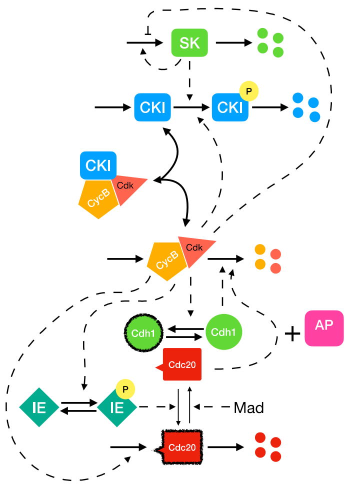
Dynamic models – we will make many of them

Biological process

A.

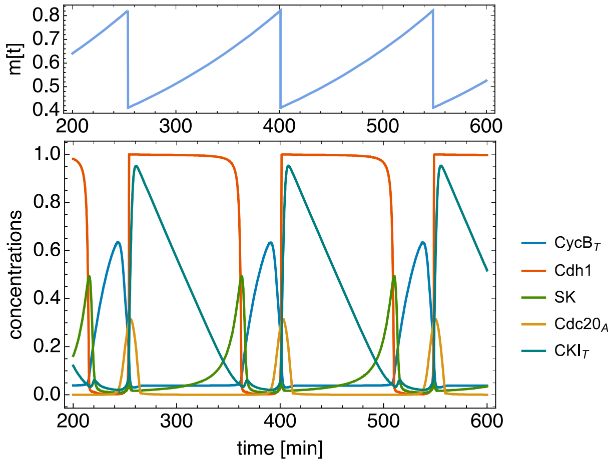


B.

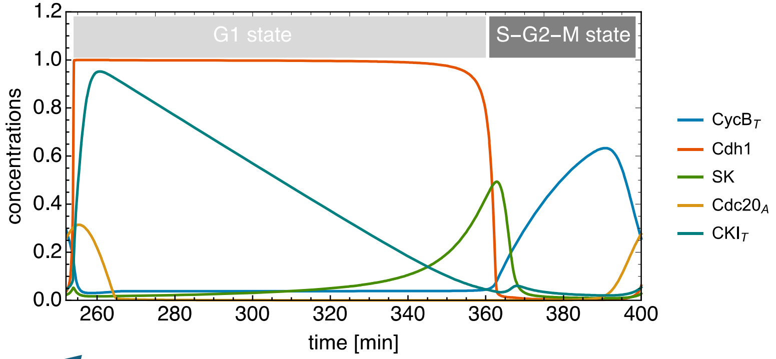


proposed molecular mechanism

C.

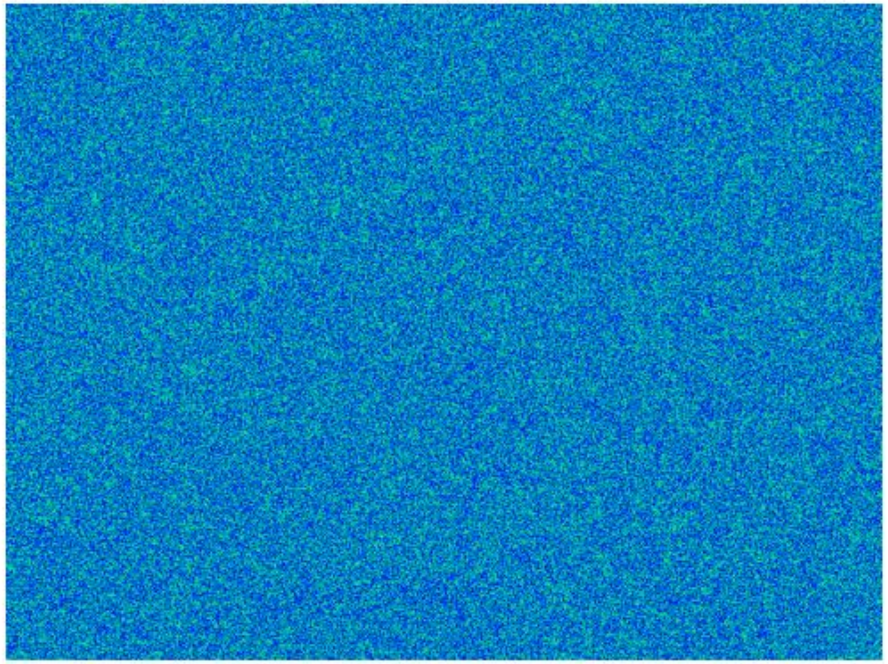


D.



outcome of mechanistic model

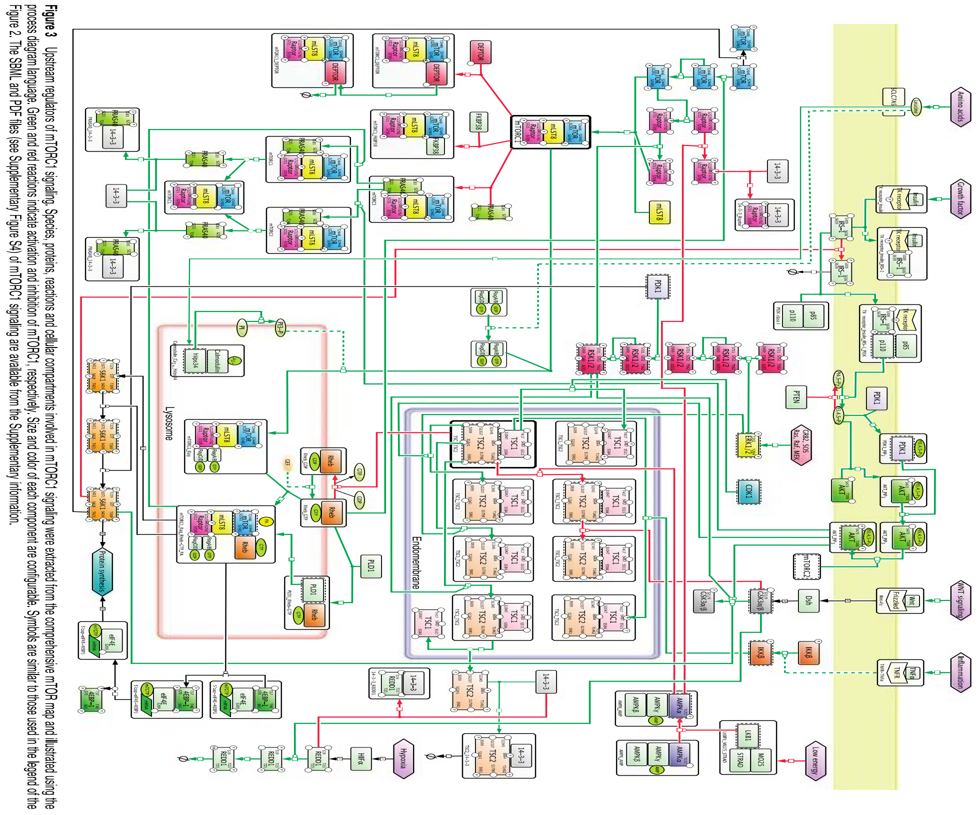
different simulation formalisms of models



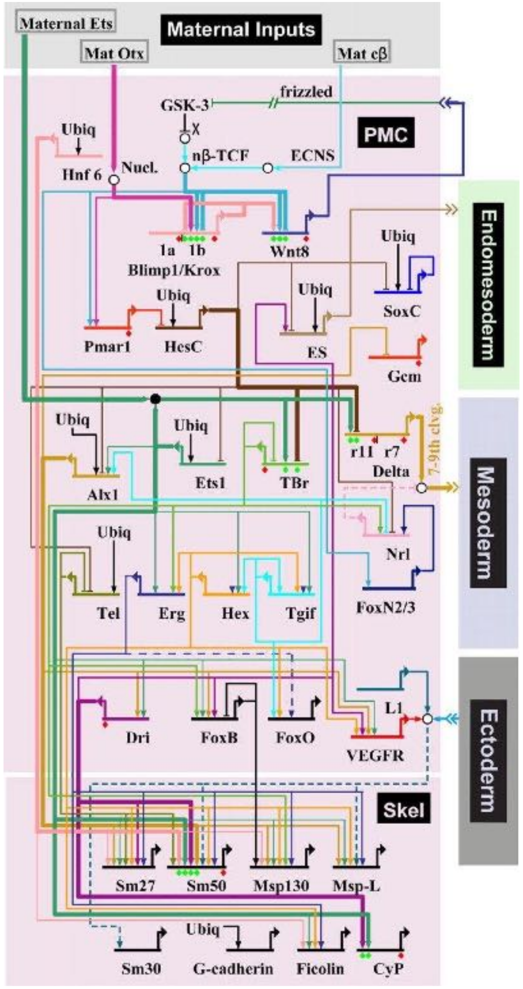
- deterministic model
  - as function of time
  - as function of time and space
- non-deterministic (stochastic) models
  - as function of time
  - as function of time and space
- these modelling formalisms are used in biology, engineering, physics, sociology, oceanography, you name it.
- The mathematics and modelling formalisms are discipline independent

reduction and explanation

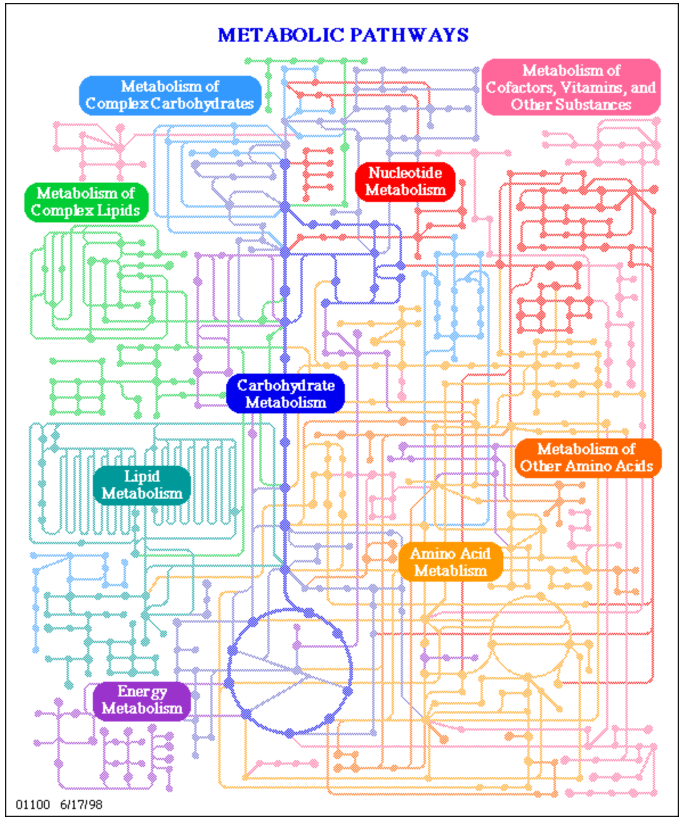
molecular complexity and a need for simplification



signalling



genetic networks



metabolic networks

Approach – scientific method

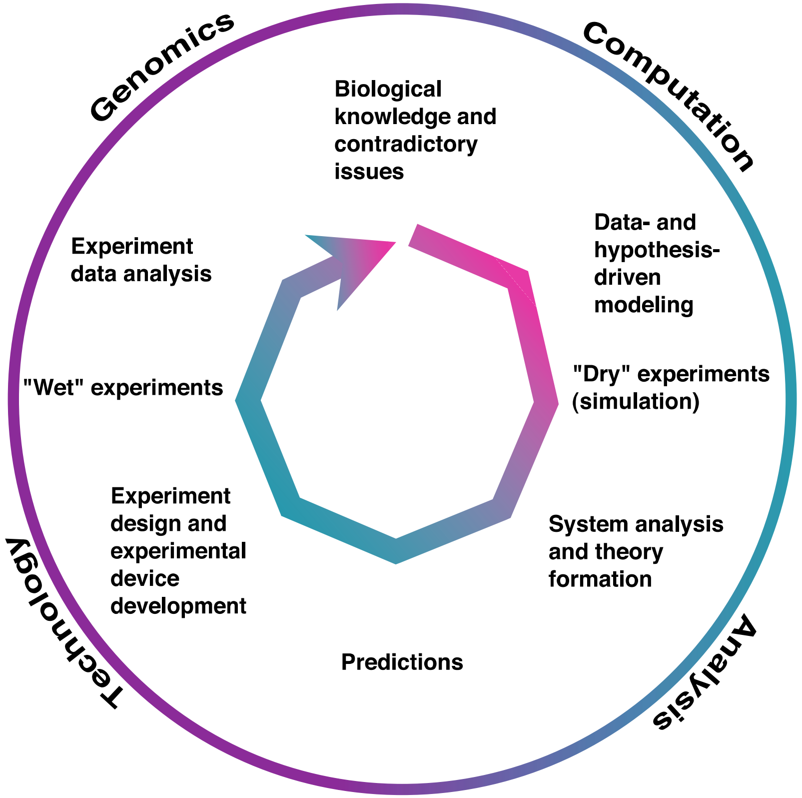


Fig. 1. Hypothesis-driven research in systems biology. A cycle of research begins with the selection of contradictory issues of biological significance and the creation of a model representing the phenomenon. Models can be created either automatically or manually. The model represents a computable set of assumptions and hypotheses that need to be tested or supported experimentally. Computational "dry" experiments, such as simulation, on models reveal computational adequacy of the assumptions and hypotheses embedded in each model. Inadequate models would expose inconsistencies with established experimental facts, and thus need to be rejected or modified. Models that pass this test become subjects of a thorough system analysis where a number of predictions may be made. A set of predictions that can distinguish a correct model among competing models is selected for "wet" experiments. Successful experiments are those that eliminate inadequate models. Models that survive this cycle are deemed to be consistent with existing experimental evidence. While this is an idealized process of systems biology research, the hope is that advancement of research in computational science, analytical methods, technologies for measurements, and genomics will gradually transform biological research to fit this cycle for a more systematic and hypothesis-driven science.

the next approx. 2 weeks