Dynamical Systems with Python - Workshop 1: An Introduction to Dynamic Modelling - Building a Model

We start with reactions in time and end with dynamics in time and space.

1. Michaelis Menten (MM) and Hill kinetics in vitro (closed system). MM is nonlinear but monotonous. Hill with $n>1$ is nonlinear with a qualitative transition, the inflection point. Predict $n=1$ -> $n=4$ sigmoidal changes in open flow. Open flow and nonlinearity are the basic ingredients of every complex living systems. Concept: mathematical treatment of nonlinear functions.

2. Forward inhibition induces a new feature in open flow setting, namely, instability. The lower and the upper state of the sigmoidal Hill function can now overlap and co-exist in the same situation. Example: ATP kinetics of the PFK1 reaction. This allows switching between states by external regulatory processes. Concept: numerical simulations of the bifurcation diagram and "potential".

3. Extensions: Additional feedback inhibition leads to spontaneous oscillations and self-organised temporal order. Processes can switch autonomously and repeatedly. Adding features can increase the complexity of self organisation, the idea of a hierarchy. Concept: self-organised rhythms in living systems.

4. Spatial recordings add new dimensions. In spatial models, a grid is needed to describe what happens at each location. Diffusion is the simplest processes to mediate spatial coupling: a material flow happens whenever there is a concentration gradient between neighbouring grid points. Diffusion itself is passive and attempts to homogenise. But combined with nonlinear kinetics it creates patterns that (self-)organise concentrations in time and space. Incredibly rich dynamics is possible in space. Transitions can be normal or abnormal. Perturbation experiments may help to figure out mechanisms.

Nonlinear Enzyme Kinetics:

1. Hill equation with special case n=1
2. Brief analysis of functions
3. Rate landscape

Focus: physical chemistry

Bistability:

1. Reaction scheme(s)
2. Time Series: two fates
3. Bifurcation diagram
4. Steady State and Potential Analysis
5. Waddington Potential Landscape

Focus: Programming

Oscillations:

1. Reaction scheme(s)
2. Time Series: SS or LC
3. Bifurcation diagram:
4. State Space Analysis
5. Animated oscillations

Focus: systems theory

Spatiotemporal Waves:

1. Diffusion only Animation
2. Reaction CICR 2V model
3. CICR in a 2D reaction-diffusion medium: spontaneous & with stimulation

Focus: connection with experiment

Some Experimental Findings:

Cardiac spiral waves: https://www.teledynevisionsolutions.com/en-gb/learn/learning-center/scientific-imaging/whole-tissue-calcium-imaging/

Calcium waves in hippocampus slices: https://journals.physiology.org/doi/full/10.1152/jn.1998.79.2.1045

Calcium waves in development (gastrulation) https://www.pnas.org/doi/10.1073/pnas.96.1.157#supplementary-materials

Video: Calcium waves in epithelial cells: