MRI Master Class 2009/2010:
Numerical Bifurcation Analysis of Dynamical Systems
WEEK 13, Mar 30 and Apr 01: Willy Govaerts (Gent)
"Mathematical evolution models in the life sciences"

Summary

We consider two famous examples from life sciences where dynamical systems theory and numerical methods have important applications. In each case we discuss the modeling, the dynamical (numerical) study and the consequences for the model.

1.The Morris-Lecar model

The first neural model was that of the giant axon of the squid and it was obtained by Alan Hodgkin and Andrew Huxley in 1949-1952. They received the Nobel Prize in Physiology and Medicine in 1963.

We concentrate on the Morris-Lecar neuron. The Morris-Lecar equations grew out of an experimental study of the excitability of the giant muscle fiber of the huge Pacific barnacle, balanus nubilis (named by Charles Darwin, who probably meant to call it balanus nobilis), cf. *C. Morris and H. Lecar, Voltage oscillations in the barnacle giant muscle fiber, Biophys. J. 35 (1981) 193-213.*

Its complicated dynamical properties will be studied, in particular spiking and bursting. It is generally believed that these phenomena are the basic mechanisms of muscle and neural cells; in particular all information processing in the nervous systems of animals and humans is based on them.

We deal with:

1. Modeling issues: description of the underlying physical concepts, e.g. the Nernst potential, experiments done to build the model, e.g. voltage clamp, use of sigmoid functions for threshold phenomena, elimination of a variable by a quasi steady state assumption, the use of bifurcations for calibration.

2. Study of the model: a complete analysis in a two-parameter unfolding, i.e. a parameter plane is divided into regions with the same qualitative behaviour. The regions are bounded by curves of codimension-1

bifurcations that meet in codimension-2 points.

3. Special aspects:

   - Type I and Type II excitability are linked to Hopf bifurcations and homoclinic bifurcations, respectively.
   - Neural bursting is linked to slow-fast dynamical systems.

2.The Tyson-Novak model for budding yeast.

The basic mechanism of the cell cycle was discovered by Paul Nurse in 1976. He received the Nobel Prize in Physiology and Medicine in 2001.

We concentrate on the Tyson-Novak dynamical systems model for the cell cycle of budding yeast, cf. *J.J. Tyson and B. Novak, Regulation of the eukaryotic cell cycle: molecular antagonism, hysteresis, and irreversible transitions. J. Theor. Biol. 210 (2001) 249-263.* In spite of having 8 state variables and about 36 parameters, it is one of the simplest models and it has a rich bifurcation behaviour.

We deal with:

1. Modeling issues: stoichiometric equations, interaction of opposing proteins (cyclins and APC's), law of mass action, Michaelis-Menten kinetics voor phosphorylation and dephosphorylatrion, constant relative growth, constant relative degradation, Hill functions, quasi-steady state assumption, regulatory networks.

2. Study of the model: equilibria, periodic orbits, homoclinic orbits and their bifurcations, merging of periodic orbits, relation to the processes in the cell.

3. Special aspects:

   - A slow manifold in a slow-fast system.
   - Insensitivity to initial conditions (the funnel effect).
   - Computation of the cell cycle as a boundary value problem that can be solved by the fixed point iteration of a map.