Spatial Structure and Stability

Rüdiger Thul

Hahn Meitner Institute, Berlin

Martin Falcke

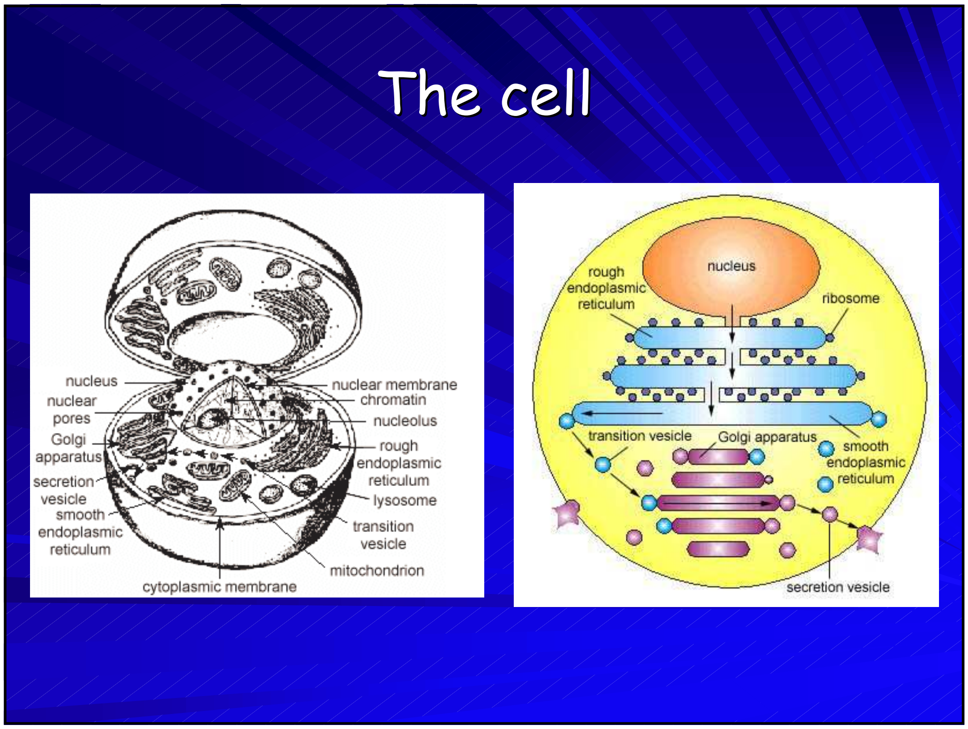
KITP, 08/20/03

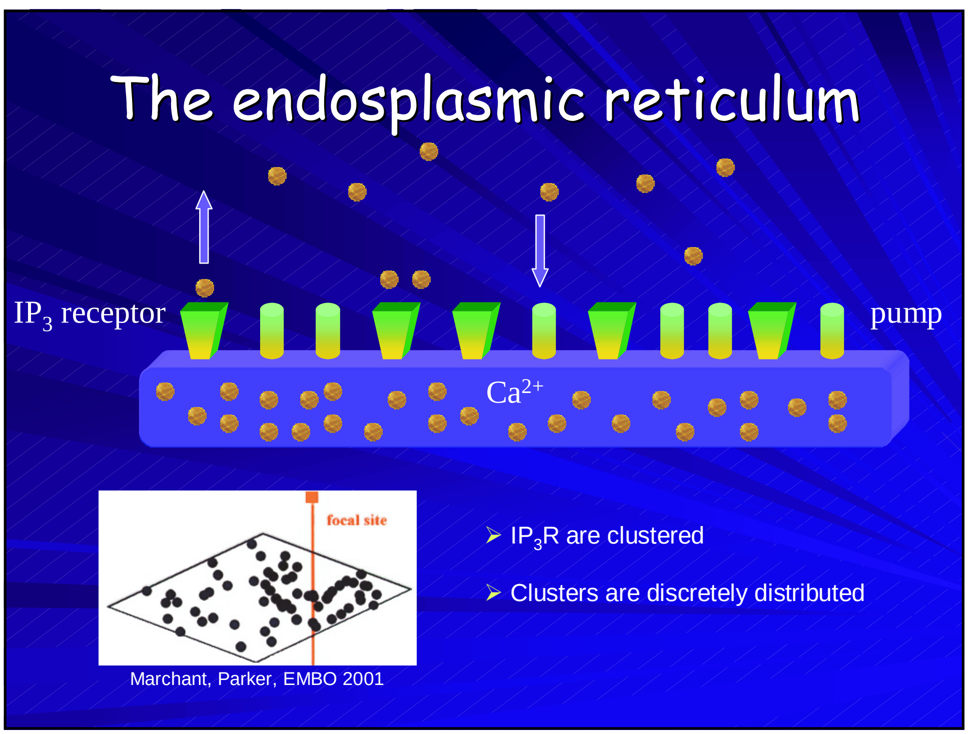
Spatial Structure and Stability

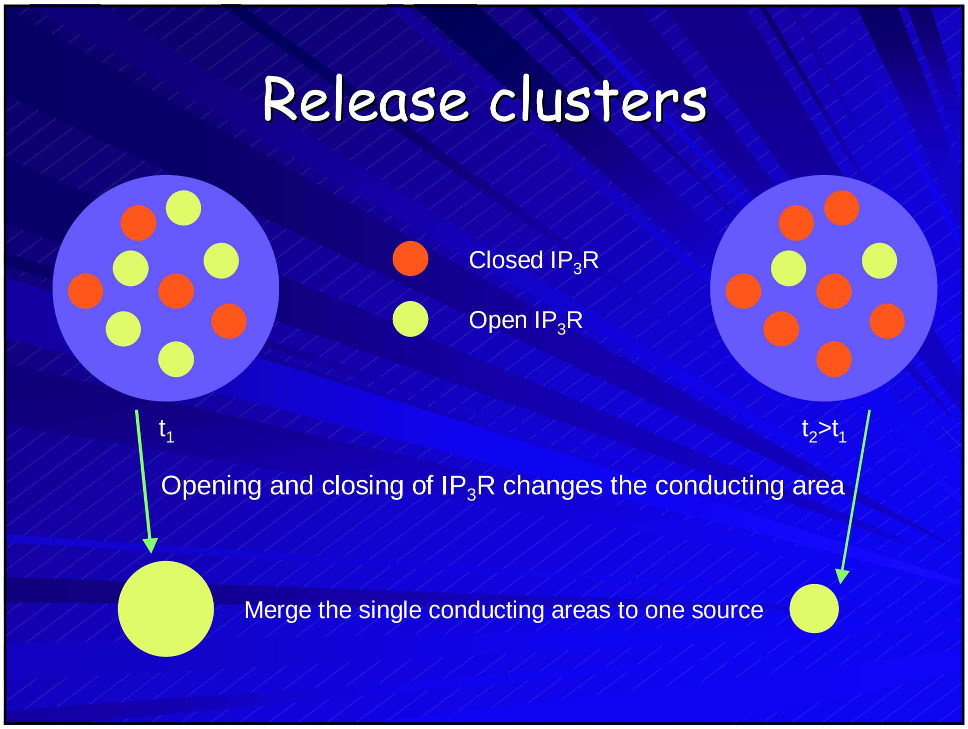
Motivation

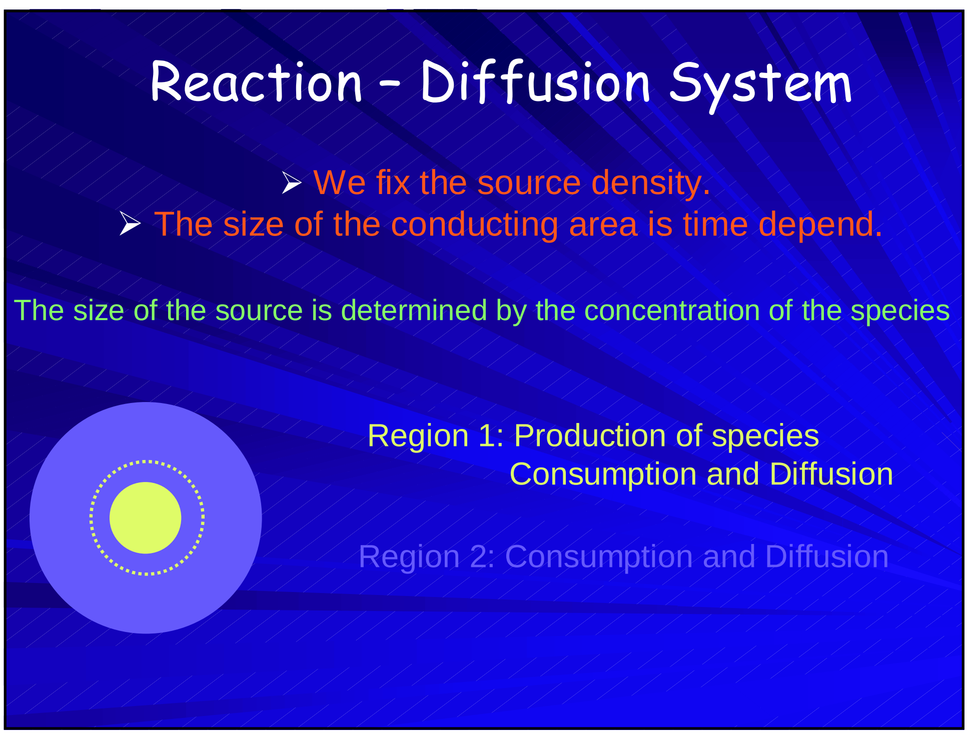
The Model

Biological Applications


The cell
nucleus
nuclear pores
Golgi apparatus
secretion vesicle
smooth endoplasmic reticulum
nuclear membrane
chromatin
nucleolus
rough endoplasmic reticulum
lysosome
transition vesicle
mitochondrion
cytoplasmic membrane
nucleus
rough endoplasmic reticulum
ribosome
transition vesicle
Golgi apparatus
smooth endoplasmic reticulum
secretion vesicle


The endosplasmic reticulum
IP3 receptor
pump
Ca2+
focal site
Marchant, Parker, EMBO 2001
IP3R are clustered
Clusters are discretely distributed


Release clusters
Closed IP_3R
Open IP_3R
t_1
$t_2>t_1$
Opening and closing of IP_3R changes the conducting area
Merge the single conducting areas to one source


Reaction – Diffusion System
➢ We fix the source density.
➢ The size of the conducting area is time depend.
The size of the source is determined by the concentration of the species
Region 1: Production of species
Consumption and Diffusion
Region 2: Consumption and Diffusion

Reaction - Diffusion System

RD Dynamics $\dot{c} = D\nabla^2 c + f_1(c)\Theta\,(a-r) + f_2(c)\Theta\,(r-a)$

Gate Dynamics $\dot{h}_i = g_i(c, h_1, \ldots, h_n)\,, \quad i = 1, \ldots, n$

Radius $a = f(c, h_1, \ldots, h_n)$

RD Dynamics decouples from gating dynamics

⇨ PDE for c

Gating dynamics enter via boundary conditions (c = C^1)

Stationary points

ODE for c can be solved (analytically) in each region

$$0 = D\nabla^2 c + f_1(c)\Theta\,(a-r) + f_2(c)\Theta\,(r-a)$$

⇨ Coefficients of the solution in the two regions: $A_1(a), B_1(a), A_2(a), B_2(a)$

With c known solve $0 = g_i(c, h_1, \ldots, h_n)\,, \quad i = 1, \ldots, n$

⇨ $h_1(a), h_2(a), \ldots, h_n(a)$

Inserting the above solutions in $a = f(c, h_1, \ldots, h_n)$

⇨ Implicit equation for a: $a = f(a)$

Linear stability analysis

Decoupled PDE for y:=δc can be solved separately in each region

$$\dot{y} = D\nabla^2 y + \left\{ f_1'(c_{st})\Theta(a_{st} - r) + f_2'(c_{st})\Theta(r - a_{st}) \right\} y + \left\{ f_1(c_{st}) - f_2(c_{st}) \right\} \delta(a_{st} - r)\delta a\,(y, z_i)$$

Matching conditions entail

$$y_1(a_{st}) = y_2(a_{st})$$

$$\frac{\partial}{\partial r} \left\{ y_2(r) - y_1(r) \right\}_{a_{st}} = \left\{ f_1(c_{st}) - f_2(c_{st}) \right\} \delta a\,(y, z_i)$$

Computing the eigenvalues:
Evaluation of the zeros of the determinant originating from the matching conditions

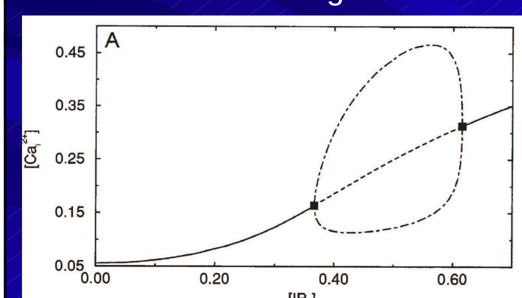
Two component system:

$$\frac{\partial}{\partial r} \left\{ y_2(r) - y_1(r) \right\}_{a_{st}} = \eta y_1(a_{st})$$

$$k_2 a_{st} + k_1 a_{st} \coth(k_1 a_{st}) - \eta = 0$$

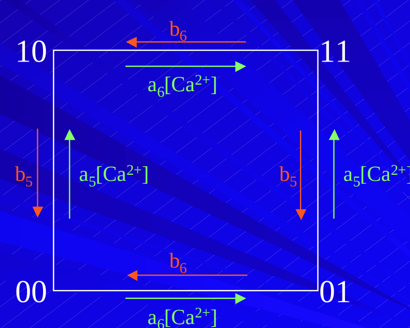
De Young - Keizer model

Bifurcation diagramm



Gating dynamics has 8 dimensions

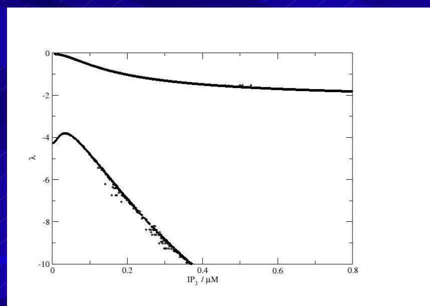
Lumped state approximation

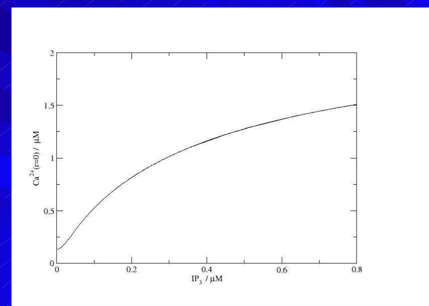


Investigating lumped DeYK

Original parameters except rescaling of channel flux to discrete sources

$$k_c^{dis} = k_c^{cont} R^3 / a_0^3$$





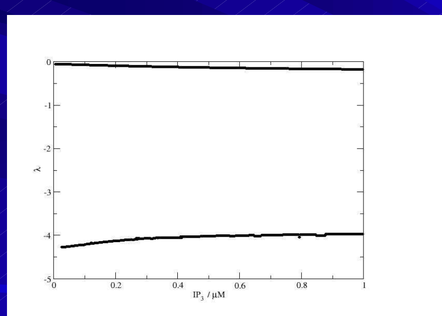
Linearly stable

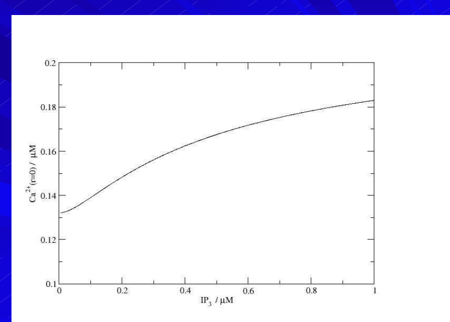
Ca^{2+} concentrations are higher

Investigating lumped DeYK

Original parameters except rescaling of channel flux to discrete sources

k_c 100 times smaller than before

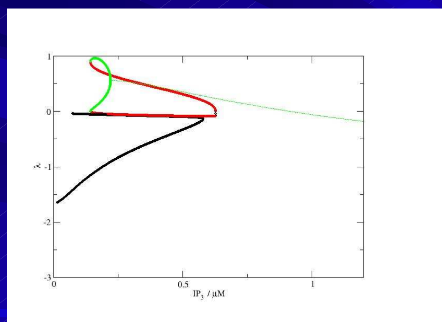


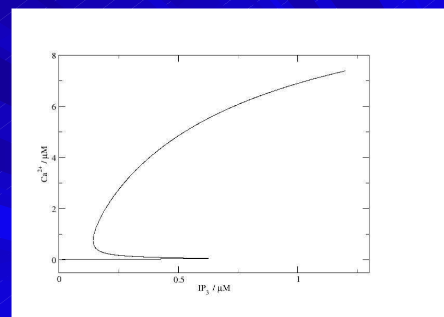


Linearly stable

Investigating lumped DeYK

Rescaling of parameters to achieve more realistic Ca^{2+} concentrations

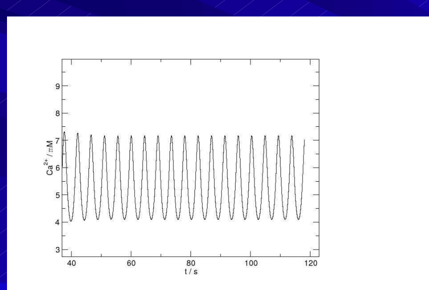


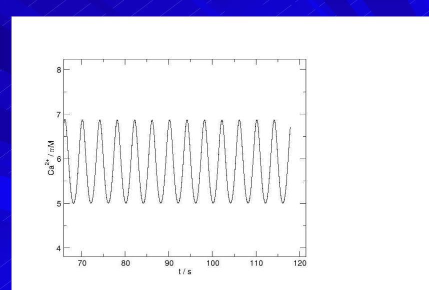


Two saddle node bifurcations

Numerical Integration of the lumped DeYK

Rescaling of parameters to achieve more realistic Ca^{2+} concentrations





IP_3=0.6 µM

IP_3=0.7 µM

Summary

- Introduction of a new model with fixed source density and a time dependent size of the conducting area
- Applicable when the conducting area is one order of magnitude larger than the active elements
- Decoupling between the RD dynamics and the gating dynamics
- DeYK parameters result in a linearly stable system
- More realistic parameters show saddle node bifurcations