Calcium waves sustained by calcium influx through mechanically activated channels in the cell membrane

Zbigniew Peradzyński * ,Bogdan Kaźmierczak, Sławomir Białecki**,**

, Joanna Napiórkowska*

* Warsaw Military University of Technology (earlier in Faculty of Mathematics, Informatics and Mechanics, University of Warsaw),
**Institute of Fundamental Technological Research.

Łódź 11 October 2023

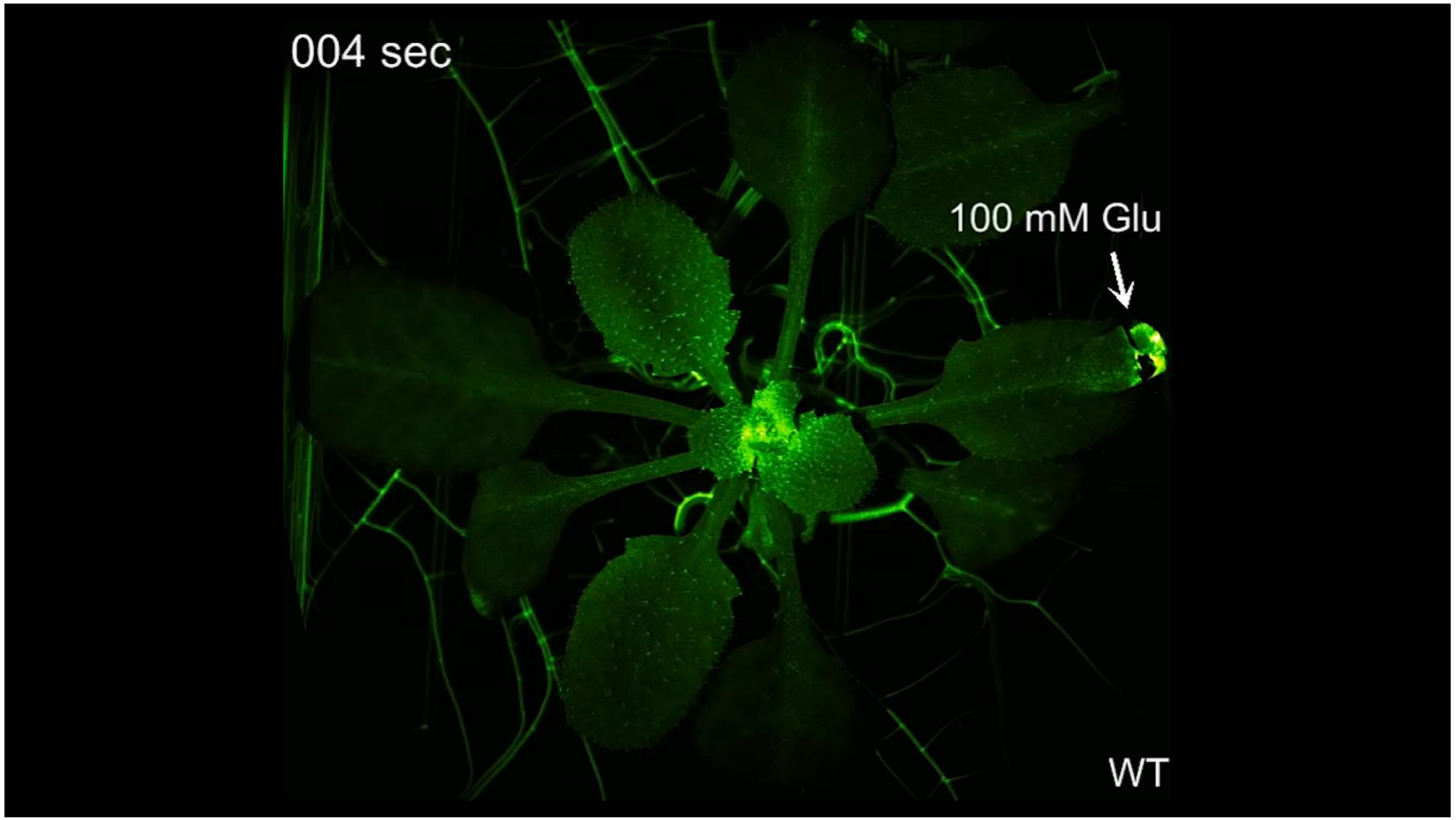
Provocative question:

Can plants be aware of the danger?

Please see the video:
https://www.youtube.com/watch?app=desktop&&v=7-3yFcZSyvo

„”Supplying glutamate directly to the tip of one leaf creates a strong wave of calcium across the entire plant, visualized by fluorescent light. This video is part of research by UW–Madison botany professor Simon Gilroy that shows how waves of calcium crisscrossing a plant help it respond to attacks by preparing for future threats.
The work was published in Science in September of 2018”.

It turns out that plants or their parts can communicate with each other (e.g by sending sigals calcium waves), preparing thus for unpleasant consequences



By waves we mean travelling waves, special solutions: $\boldsymbol{u = U(x - ct)}$ to Reaction-Diff. equations (c-const)

- Waves are usually associated with the wave equation or with hyperbolic systems. However hyperbolic equations are almost nonexisting in biology. One predominantly encounters parabolic equations or semilinear parabolic systems – Reaction-Diffsion Systems.
- The travelling waves in R-D eqs are appearing as an interplay between the diffusion and nonlinearity.

Single reaction –diffusion equation

$$\frac{\partial}{\partial t}u = D\Delta u + F(u)$$

If u(t,x) – density of individuals, F(u) = ru(1-u/K), then one can speak of a simple model in population dynamics. The diffusive term reflects the fact that individuals are moving erratically. The reaction term F(u) is responsible for the birth and death processes.

Here travelling wave solutions are heteroclinic fronts. As F is monostable, because u=0 is unstable equilibrim, there are solutions for an arbitrary speed $\geq c_0$.

Bistable case; the wave speed is uniquely determined!

F(u) has two stable: u_1, u_3 and one unstable (u_2) equilibrium.

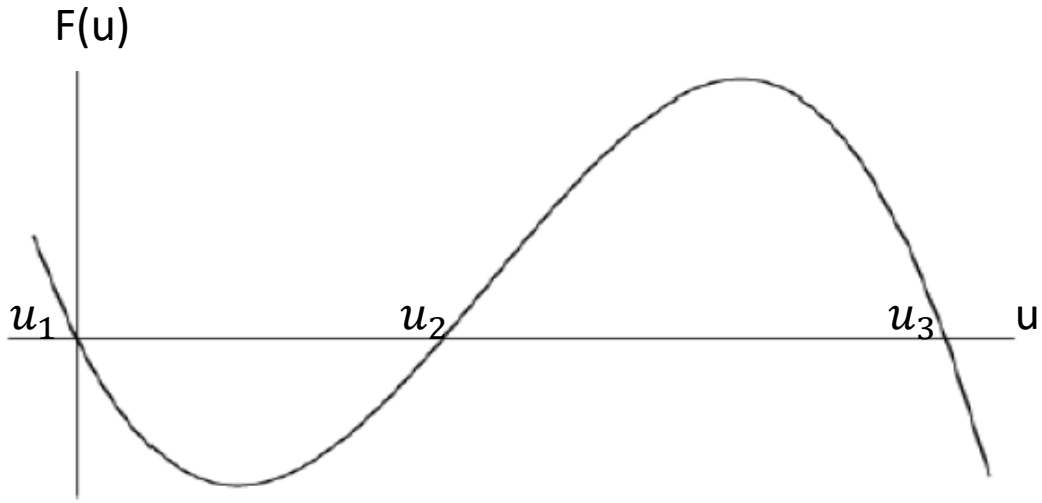


Fig. An example of a bistable source function:

$$F(u) = -A(u - u_1)(u - u_2)(u - u_3)$$

An example of a travelling front

The following bistable reaction diffusion equation with a cubic (**bistable)** source term

$$\frac{\partial}{\partial t}\boldsymbol{u} = \boldsymbol{D}\frac{\partial^2}{\partial x^2}\,\boldsymbol{u} - \boldsymbol{A}\,\boldsymbol{u}(\boldsymbol{u}-\boldsymbol{a})(\boldsymbol{u}-\mathbf{1})$$

has (D=1, A=1) following travelling front solutions

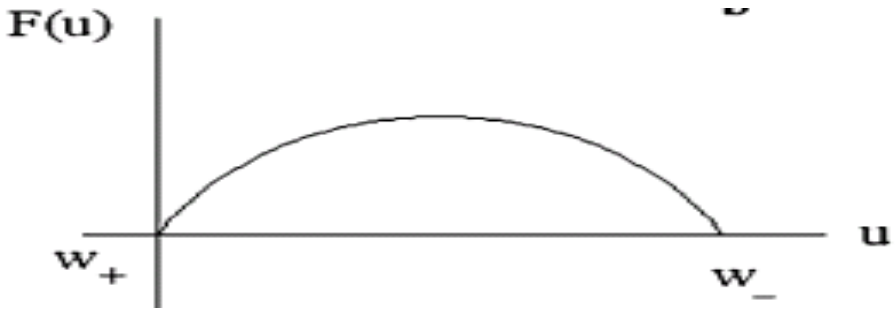
$$u = \frac{1}{1+\exp\left(\frac{\pm x - vt}{\sqrt{2}}\right)}$$

where $v = \sqrt{2}\,(\frac{1}{2} - a)$ defines the propagation speed.

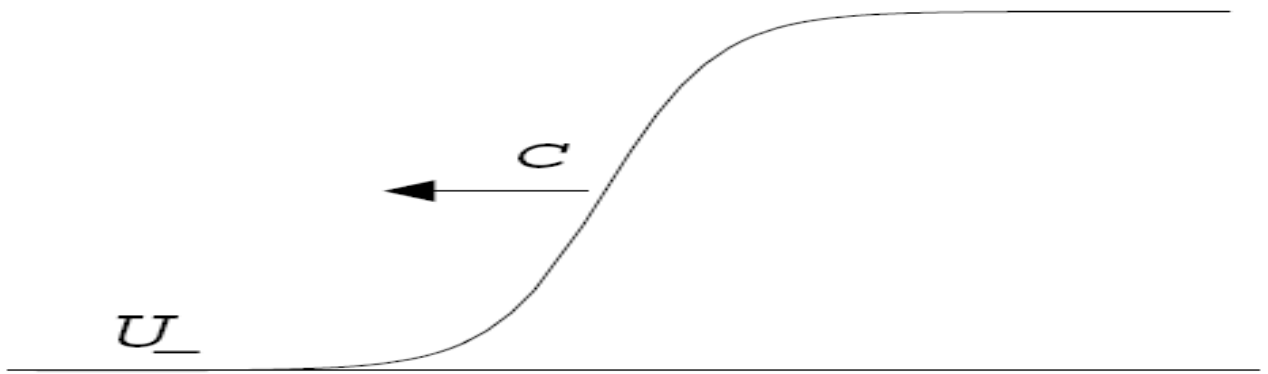
Monostable reaction term – waves can propagate with an arbitrary speed grater then some v_0. The minimal speed makes physical sense)

The case of $F(u)$= ru(1-u/K) is a good example of a monostable reaction term. It has two zeros:

Unstable state u=0 and stable state u=K



Just look at $u' = ru(1 - K/u)$



Theory based on single reaction diffusion equation predicts travelling waves in the form of heteroclinic fronts, joining two stable (in the bistable case) equilibria of the source term, whereas observed experimentally calcium waves are of homoclinic type. Thus, such simplified theory describes properly only the front part of the wave. To obtain the shape of a homoclinic, the additional equation for "recovery variable" is usually added.

In the proposed here theory for CICI waves this additional equation appears in a natural way.

Ecology, Population dynamics

Reaction Diffusion System (interacting species)

$$\frac{\partial}{\partial t}u_1 = D_1\frac{\partial^2}{\partial x^2}u_1 + ru_1(1 - A_1 \cdot u)$$
$$\frac{\partial}{\partial t}u_2 = D_2\frac{\partial^2}{\partial x^2}u_2 + ru_2(1 - A_2 \cdot u)$$

.....

$$\frac{\partial}{\partial t}u_n = D_n\frac{\partial^2}{\partial x^2}u_n + ru_n(1 - A_n \cdot u)$$

The matrix $A = (A_1, A_2, \dots, A_m)$ describes the interactions between the species. If the entries are positive we have the case of species competing for food.

MONOTONE SYSTEMS

Definition. The system

$$\frac{\partial}{\partial t}u_i = D_i \frac{\partial^2}{\partial x^2} u_i + F_i(u_1, \dots, u_n), \quad i = 1, \dots, n$$

is called monotone if $\frac{\partial F_i}{\partial u_j} > 0$ for $i \neq j, \quad i, j = 1, \dots, n$

is satisfied for all u. Such systems arise in numerous application in chemical kinetics and populations dynamics.

The maximum principle appears to be valid for monotone systems. Its applicability allows us to formulate the results on wave existence, stability and velocity similar to those for the scalar equation.

Comments on a multistable case

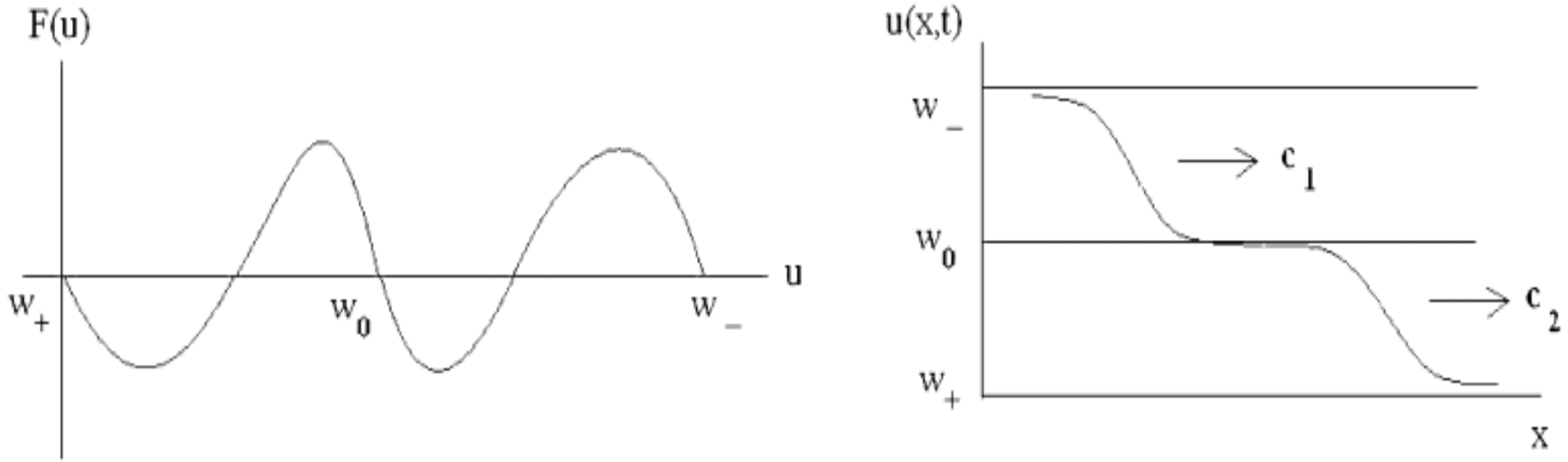


Fig. 2. Bistable nonlinearity with a stable intermediate zero w_0 (left). System of two waves, the speed c_2 of the lower wave is greater than the speed c_1 of the upper one (right).

Calcium waves were discovered in 1977 on medaka fish egg.

John C. Gilkey, Lionel f. Jaffe, Ellis B. Ridgway, and George T. Reynolds „*A FREE CALCIUM WAVE TRAVERSES THE ACTIVATING EGG OF THE MEDAKA, ORYZIAS LA TIPES*",, Journ. Cell Biology" Vol. 76, 1978

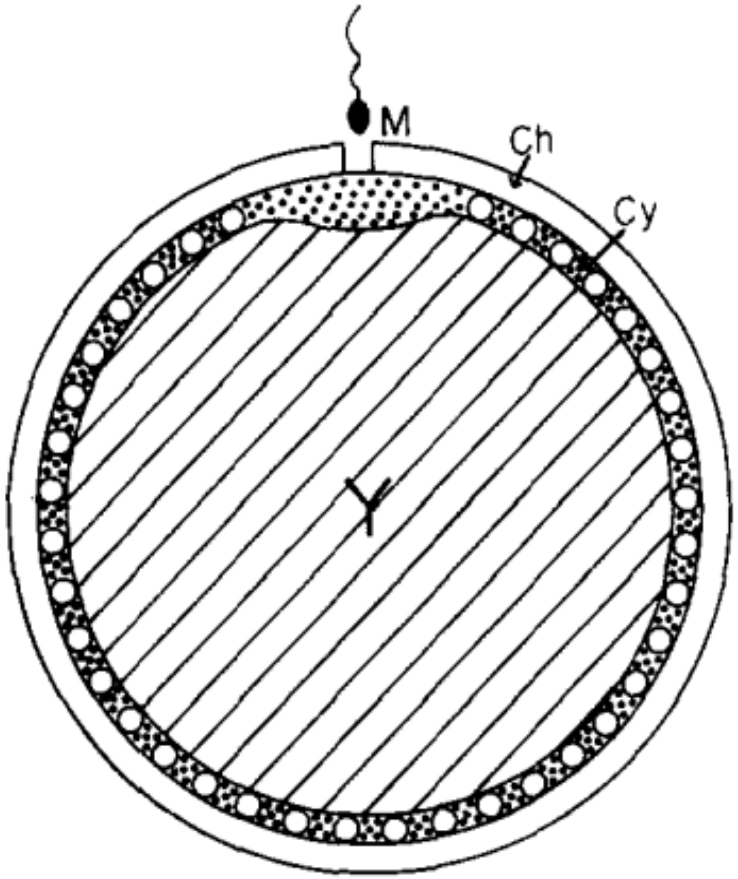
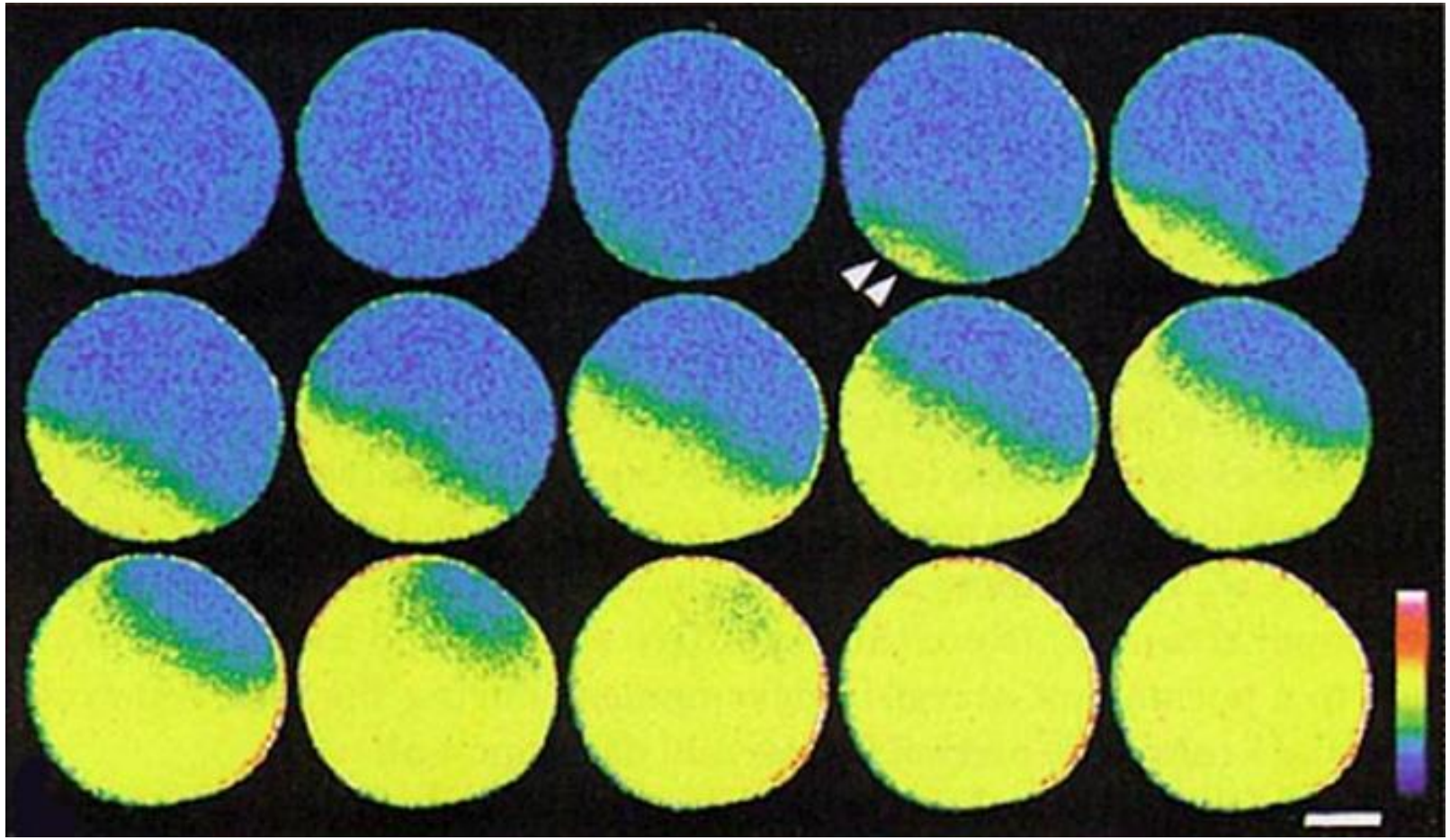
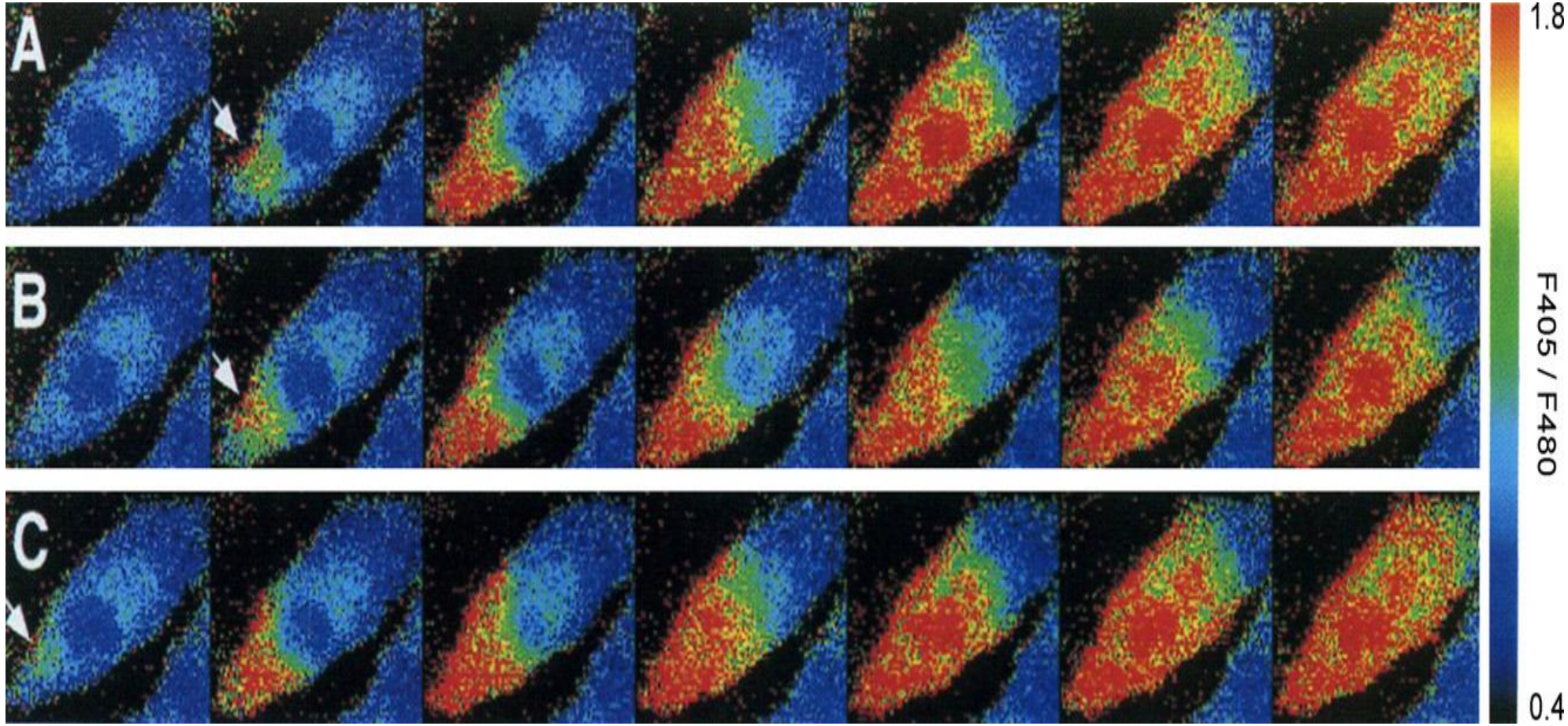


FIGURE 1 Diagram of unfertilized medaka egg (1.2-mm diameter). A sperm will cross the chorion (*Ch*) via the micropyle (*M*), enter the cytoplasm (*Cy*) and initiate a wave of cortical vesicle secretion. Vesicles are indicated by small circles. The bulk of the egg is occupied by a membrane-bounded yolk compartment (*Y*). The cytoplasmic thickness (0.03 mm) is exaggerated, and oil droplets are omitted for clarity.

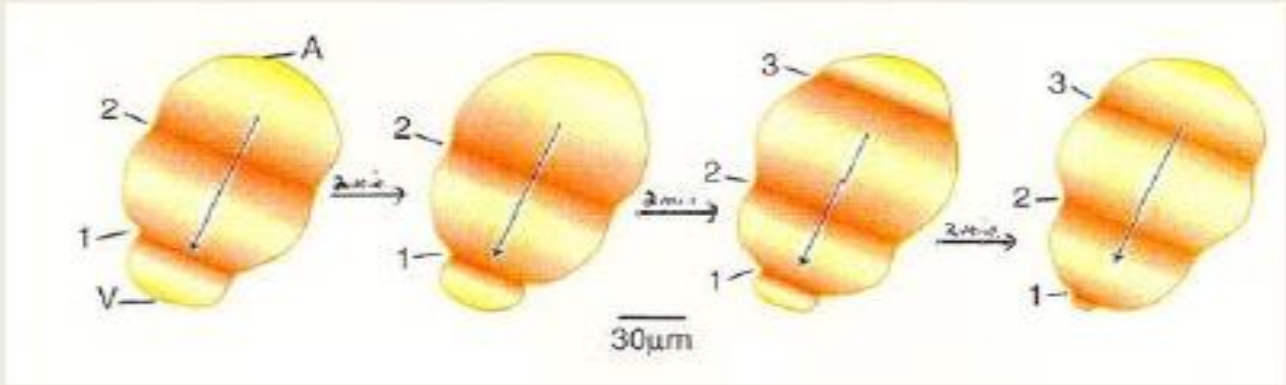
- Signals can be transmitted by various means – calcium concentration waves among the others. After the fertilization of an egg the wave sprading on its surface is generated, which changes the status of an egg. The second sperm can not enter the egg.



The calcium wave through moving amoebae. Speed 15 μm/s. (L. Jaffe)



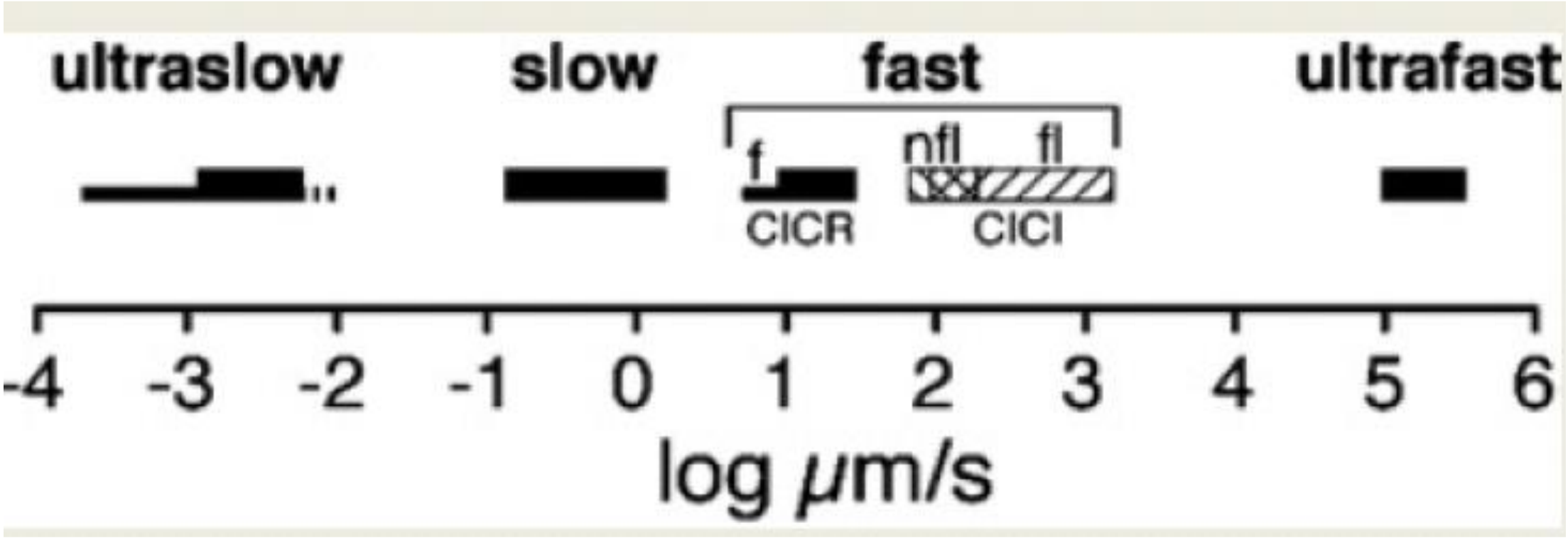
Deformation accompanying calcium waves on the surface of fertilized egg



From L. Jaffe

Calcium waves (first seen on the fertilizing medaka egg) turned out to be quite common. They can propagate both in individual cells and in tissues. The range of their speed: 1nm/s – 30 cm/s (nearly a billion fold) falling into four speed –based groups (after L. Jaffe)

In our lecture we will be interestet in CICI fast waves (see diagram below).



CICI WAVES

The mechanism of propagation of **CICR** waves is based on autocatalytic release of calcium from the internal stores (e.g. endoplasmic reticulum) located in the cells.

CICI waves. According to L. Jaffe this cannot explain the speed of the second group of „fast waves" . Their speed can be by two orders higher. Such waves are also observed in cells not having internal stores of calcium.

Thus: Stretch-activated ion channels in the membrane are responsible for the calcium delivery from the extracellular space.

CELL is extremally complex! (Nobel Prize 2013).

The cell membrane is equipped with

a) ion channels (MECHANICALLY, chemically or electrically controlled) through which ions are admitted into the cell interior.

b) There are pumps in the membrane - at least two types:

- ATP type - efficient at low Ca^{++} concentrations
- sodium-calcium exchangers; very efficient at high Ca^{++} concentrations.

Thanks to them, balance in the cell can be restored.

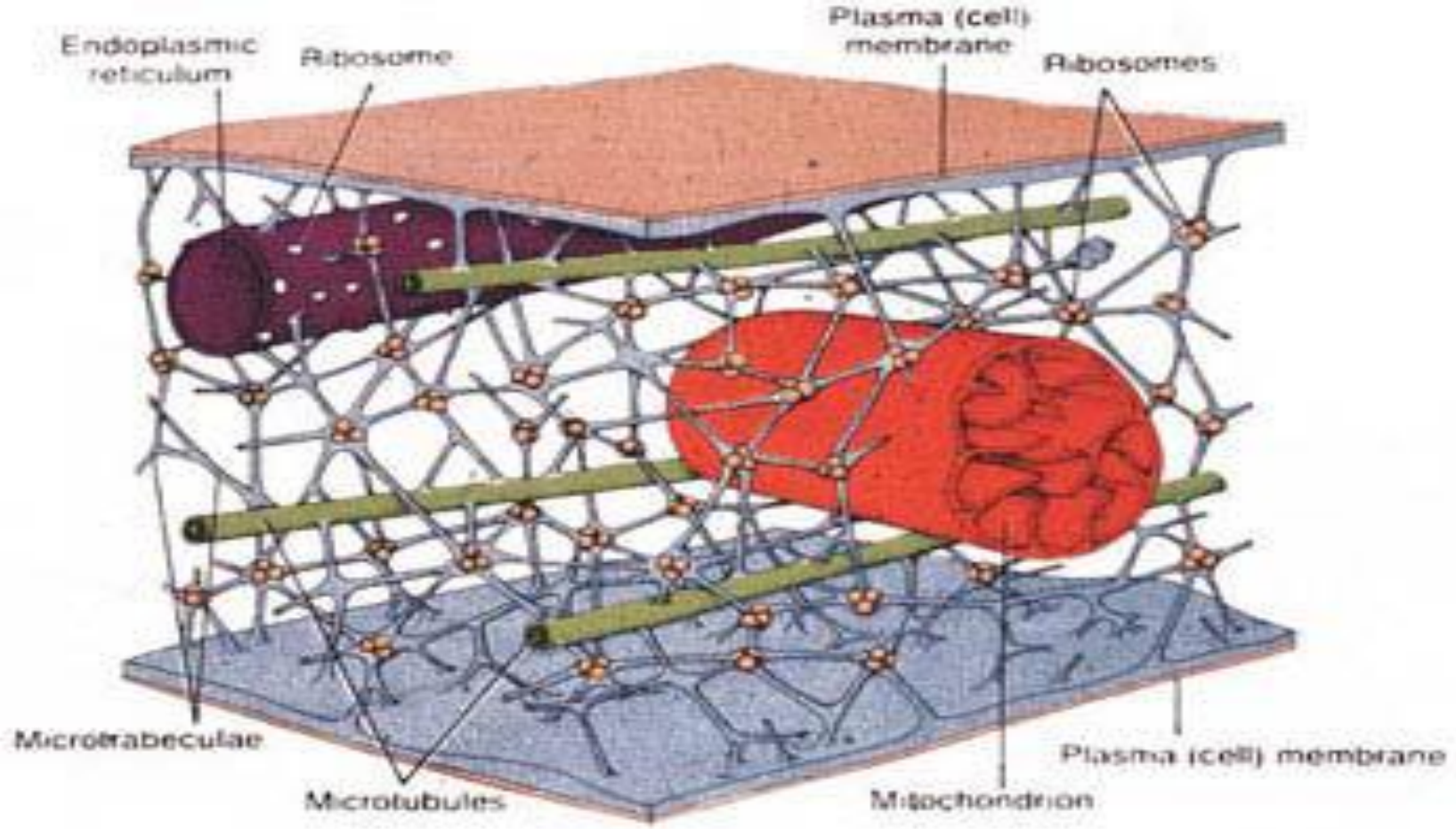
Mechanically operated ion channels (stretch activated) are opened when the membrane is stretched.

Inside the cel we have

1. Cytoplasm
2. Actin filaments
3. Internal stores of calcium (endoplasic reticulum)
4. Other important ingredients as: ion channels and ion pumps located in the cell membrane.

- As the Ca concentration increases, the filaments are increasingly connected by myosin bridges and the filament network contracts.
- The filaments also serve as routes along which various materials in bags (vesicles) are transported by appropriate motors. (F=2.7 pN). See for example : https://learn.genetics.utah.edu/content/cells/vesicles/

Model of a cell



(from the lecture by Kizylvova)

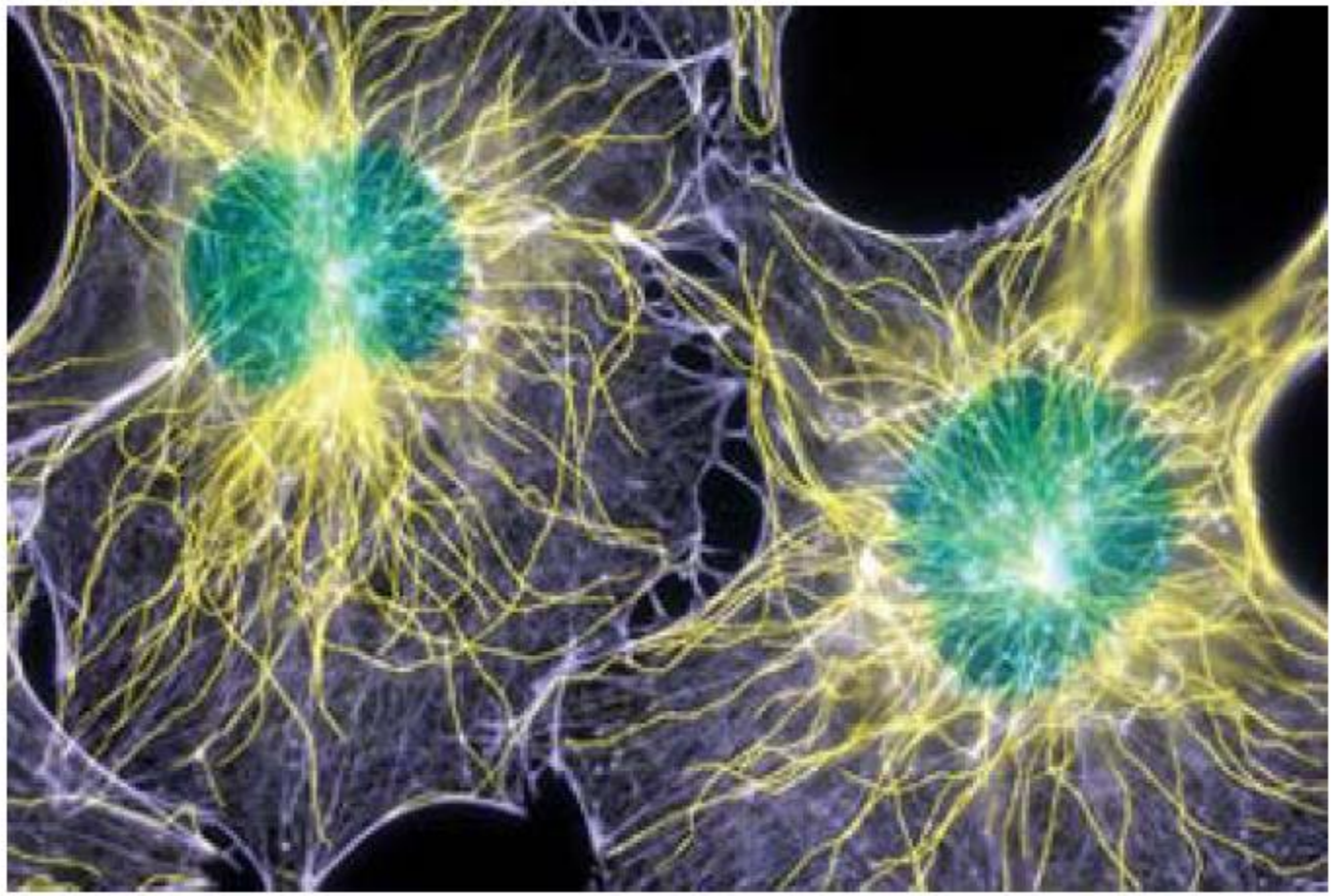
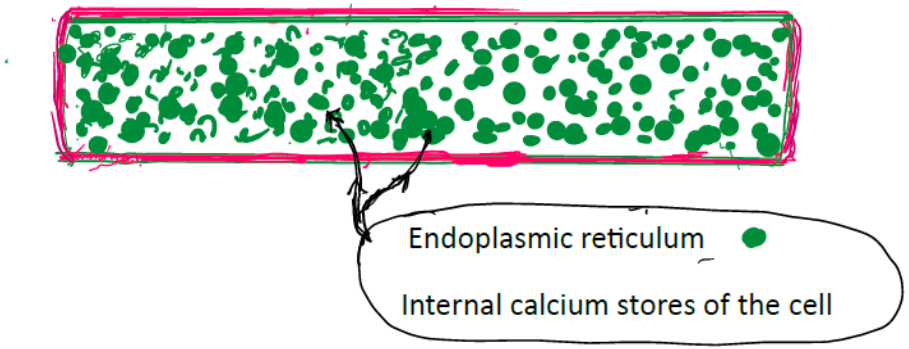


Figure 1: *Actin filaments (dark and thin) and microtubules (bright and thick) –*

Coming back to Ca waves

There are already well known and well researched CICR waves i.e. „Calcium Induced Calcium Released” waves (L. Jaffe) . The simplest theoretical description is based on single reaction diffusion equation with a bistable source term. For a small excess of calcium above the equilibrium concentration, calcium is absorbed into internal stores. After exceeding a certain threshold value (the second zero of the source function) calcium is released from the internal stores of the cell in an autocathalitic reaction, untill its concentration reaches the next equilibrium value (the third zero of source function).



Lionel Jaffe Hypothesis

According to L. Jaffe, the CICR mechanism cannot be responsible for high speed of CICI waves (see diagram).

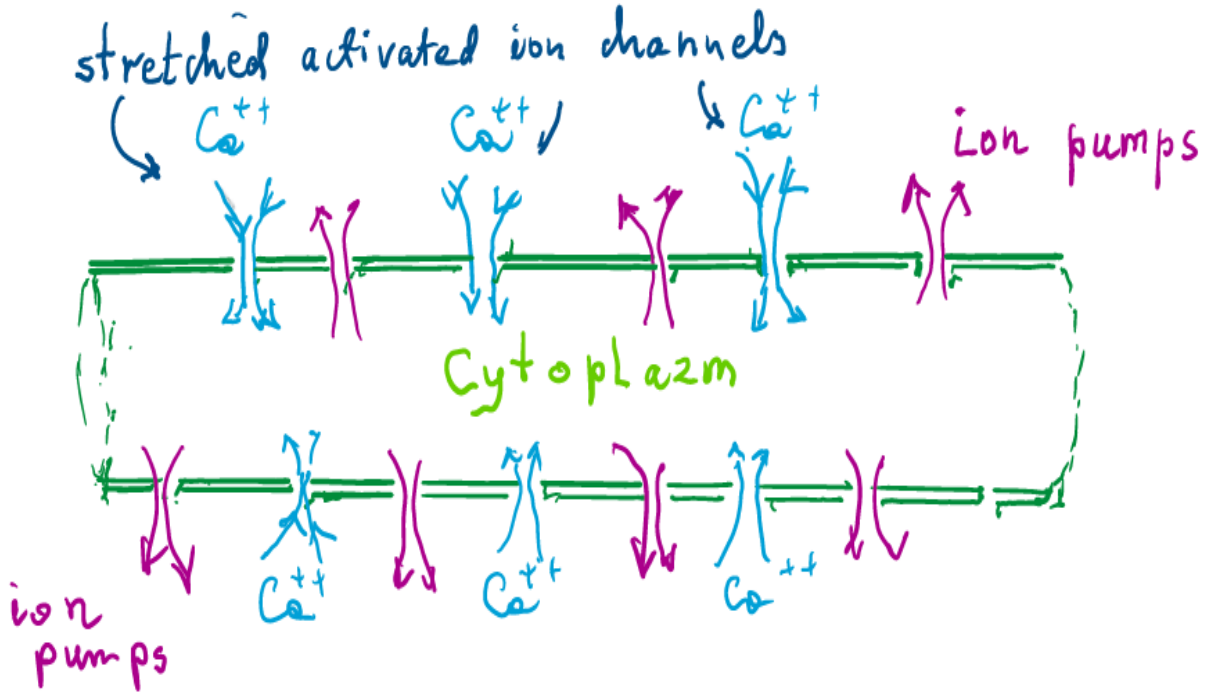
It is known that:

Stretching the membrane activates the ion channels and calcium can enter the cell from the extracellular space.

Hypothesis: when the calcium concentration grows the actin-myosin network is reorganized – the filament network contracts. Consequently, filaments are pulling the membrane. Mechanically stimulated channels are opened and calcium enters the cell. This mechanism (calcium induced calcium influx) supports the wave propagation.

Hypothetical CICI Waves – the subject of our modelling

- Accorfing to L. Jaffe in this case calcium from the extracellular space enters the cell through mechanicaly activated ion channels located in the cell membrane. In the extracellular space Ca^{++} concentration is by two orders higher than in the cell internal stores. The channels are opened when the membrane is stretched.



Calcium pumps

Calcium pumps are ion transporters found in the cell membrane. They are responsible for active transport of calcium out of the cell, keeping the intracellular calcium concentration 10 000 times lower than the extracellular. The plasma membrane Ca^{2+} ATPase and sodium-calcium calcium exchanger are the main regulators of intracellular Ca^{2+} concentration. The first type is efficient at low Ca concentration, whereas the second type is extremely efficient at higher concentrations.

They also seem to play the crucial role in supporting the CICI Waves!

Assumptions.

1. The contraction of the actomyosin network results in appearing of so called “traction forces”. However, the effect of contraction following the increase of calcium concentration appears with some delay –relaxation time is needed to form the myosin bridges

2. The calcium can enter from the intercellular space through the mechanically stimulated ion channels located in the cell membrane

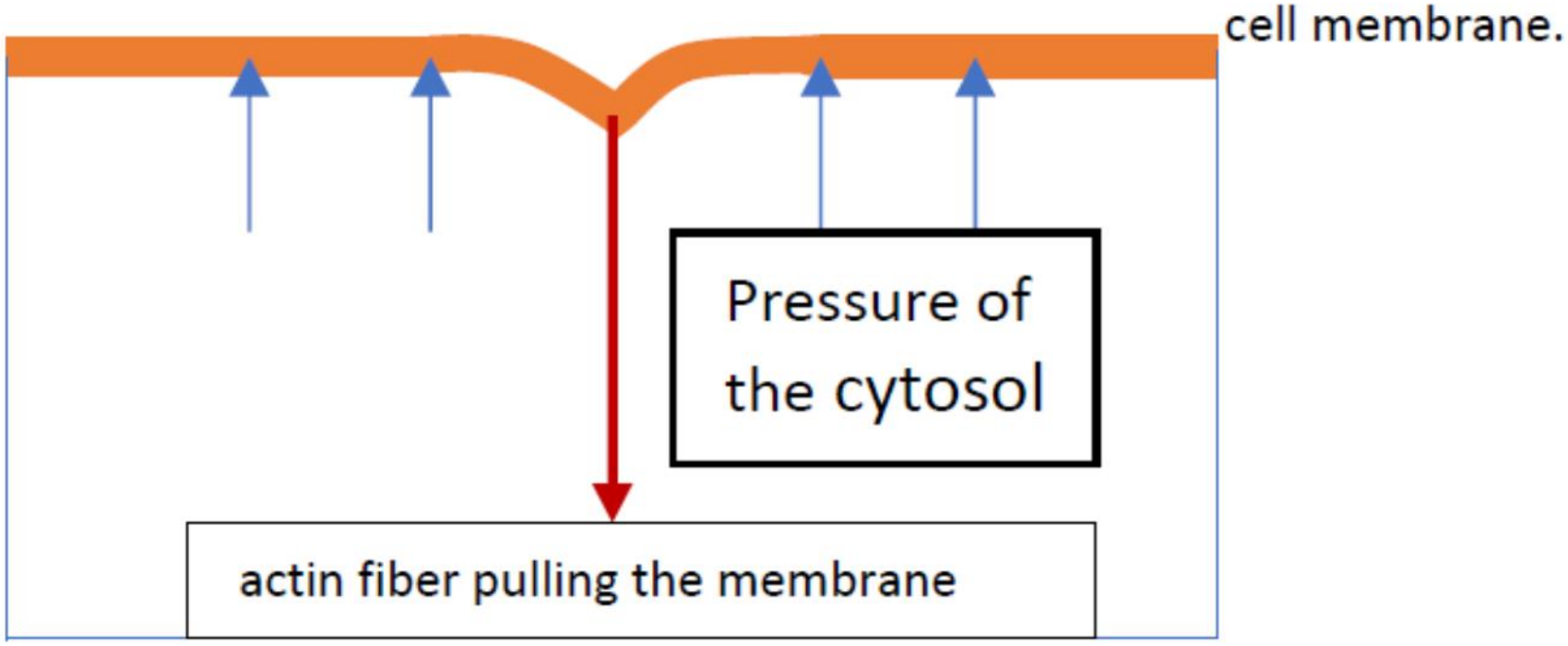
3. The mechanical stimulation of the membrane is caused by the actomyosin network - cortex. The fibers of the cortex as well as the rest of actomyosin network in the cell are subject to the contraction whenever the calcium concentration in the cell cytoplasm increases.

As the calcium concentration increases, the myosin filaments become more and more connected through the increasing number of myosin Bridges. This leads to the contraction of the filament network.

This contraction influences the shape of the cell. If we imagine the ideal cell of a cylindrical shape, then the cell radius will be reduced. Therefore, at first glance, we should not expect any stretching of the cell membrane.

This is however macroscopic view. Microscopically the membrane will be very unsmooth. Funnel-shaped depressions will appear under the influence of pulling forces, in places where the filaments are anchored. So in spite of this that the average radiuce gets smaller we will have the membrane stretching as its shape becames more complex.

When the wave passes, the cell radius shrinks. So how can we have stretching ? locally we expect the following picture



Suppose, the ion channels are openned whenever the membrane is streched. Then permanent stretch :

High calcium concentration over a long period of time would lead to the cell death. Therefore, a permanent state of stretch should not result in a continuous influx of calcium.

Experiment: oscillatory stretching leads to Ca^{++} influx proportional to the amplitude and oscillations frequency.

This suggests that the calcium influx should rather be related to the speed of membrane stretching !

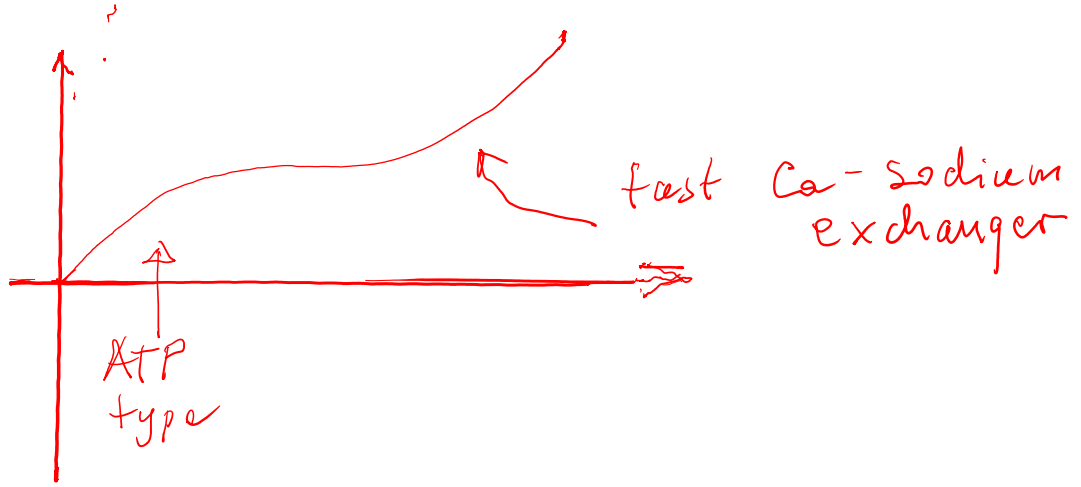
H.1. Therefore, if **n** is an internal unit vector normal to the cell membrane and **F** is the force acting on unit membrane area, then the calcium influx (flux per unit area) is proportional to the **positive part of the time derivative of the force** acting on the unit surface.

$$Ca^{++}\ influx \ \sim \ \left[\frac{\partial}{\partial t}(\boldsymbol{n}\cdot\boldsymbol{F})\right]_{+}$$

Positive part, because only stretching counts. One can show that otherwise the Ca concentration may become negative !

Taking into account the pumps p(c)

$p(c)$:



$$total\ Ca^{++}\ influx \ \sim \ \left[\frac{\partial}{\partial t}(\boldsymbol{n}\cdot\boldsymbol{F})\right]_{+} - p(u)\ \text{-}$$

This is the boundary condition for the Ca diffusion equation.

Now we arrived at the **MECHANICAL PROBLEM**:

Determine the forces acting on the membrane ; i.e. forces resulting from the actin filaments attached to it.

In principle two approaches seem to be possible:

a) **Calculate the distribution of forces on each filament of the contracting network due to the appearance of myosin bridges. In particular those anchored in the membrane. Then find the shape of deformed membrane.**

This seems hopelessly difficult !

Continuum mechanical approach ?

b) In mathematical biology (Murray, *Mathematical Biology*) , the cell is often treated as an elastic (or viscoelastic) body, and the forces associated with the contraction (traction forces) are expressed by the traction tensor. This description is very similar to termo-elasticity. Ca^{++} concentration plays the role of the temperature (in fact $-T$).

Applying this idea, we arrive at a system of three equations.

The system consists of

1. The equation of motion of the viscoelastic body, i.e cytoplasm with the filament network. The equation of motion (linear approximation) for the displacement vector $u(t,x)$ must be equipped with proper boundary conditions. Under the influence of traction forces the membrane is deflected. So basically, we should know the elasticity of the membrane. However, to estimate the forces acting on the membrane, one can assume that the membrane is stiff and not deformed. In such a case we have simple b-dry condition: $u(R) = 0$

Let us remind that if the initial position of a material point is x and it position changes to $\tilde{x}$ then $u(x) = \tilde{x} - x$.

2. Relaxation equation for the traction tensor $\widehat{T}$ with a given equilibrium form $\widehat{T}^*(c)$. We have $\widehat{T}(t,x) = \widehat{T}^*(c(t,x))$ for very slow changes of the concentration $c(t,x)$.

3. The diffusion equation for calcium concentration $c(t,x)$ and nonlinear boundary condition expressing the influx of calcium (by ion channels and ion pumps) caused by positive part of time derivative of traction forces acting on the membrane.

In fact, the diffusion of calcium in the cell is quite a complicated process because of the buffers - proteins that can attach and release calcium ions. This can be described by a system of equations for the diffusion reaction. If we use one equation as here, D should be treated as the effective diffusion coefficient.

Treating (idealized) cell as an Infinite cylinder we could try to solve:

(1) $\boldsymbol{\rho \frac{\partial^2}{\partial t^2} u - \nu_2 \Delta \dot{u} + (\nu_1 + \nu_2) \nabla \mathrm{div} \dot{u} = \mu \Delta u + (\mu + \lambda) \nabla div u + div \hat{T}(c)}$

with b-dry condition: $\boldsymbol{u}(t, R) = 0$

(2) $\frac{\partial}{\partial t} \hat{\boldsymbol{T}} = \beta [\hat{\boldsymbol{T}}^*(\boldsymbol{c}) - \hat{\boldsymbol{T}}],$ where $\hat{\boldsymbol{T}}^*(\boldsymbol{c})$ - known (e.g. linear)

(3) $\frac{\partial}{\partial t} c = D \Delta c$ inside the cell

$$D \frac{\partial}{\partial r} c(t, R, z) = Q \left[\frac{d}{dt} \sigma_{rr}(t, R, z) \right]^+ - p(u)$$ on the b-dry

suplied by initial conditions for u, T, c .

Comment. The first equation, the equation of motion can be simplified by omitting the dynamical term $\rho \frac{\partial^2}{\partial t^2} u$ and possibly the viscouse terms $\nu_2 \Delta \dot{u} + (\nu_1 + \nu_2) \nabla \mathrm{div} \dot{u}$.

Then one obtains an eliptic system for the displacement $u(t, x)$.

In principle it is possible to solve the above system numerically. For reasons discussed below, we decided on a slightly roundabout but simpler route.

In presented here equations we assumed the medium to be isotropic. However, the anisotropy, can be important as it can greatly influence the speed of waves. Indeed, the network structure - the way the filaments are connected, affects the transfer of forces acting on the membrane through the interconnected fibers.

Depending on the way the filament network is interconnected, calcium channels may be opened in places more or less distant from the front of the wave of increased calcium concentration. Thus, we should solve systems with different degree of anisotropy.

To avoid all these complications, we chose a slightly different modeling route.

Intermediate way, Here $\widehat{\boldsymbol{T}} = \tau \mathrm{I}$

Instead, we chose the intermediate solution. By solving the equations of mechanical equilibrium,

$$\boldsymbol{\mu}\, \Delta\, \boldsymbol{u} + (\boldsymbol{\mu} + \boldsymbol{\lambda}) \boldsymbol{\nabla} \boldsymbol{div} \boldsymbol{u} + \boldsymbol{div}\, \widehat{\boldsymbol{T}}(\boldsymbol{c}) = \mathbf{0}$$

assuming that the solution is independent of the axial variable, and for isotropic traction tensor $\widehat{\boldsymbol{T}} = \tau \mathbf{I}$ we can estimate the forces acting on the membrane as

$$\sigma_{rr}(t, R) = \frac{1}{\pi R^2} \int_0^R \tau(t, r) 2\pi r dr$$

Since the Ca influx is proportional to time derivative of σ_{rr}

$$\frac{\partial}{\partial t}\sigma_{rr}(t,R) = \frac{1}{\pi R^2}\int_0^R \frac{\partial}{\partial t}\tau(t,r)2\pi r dr$$

we have $\frac{\partial}{\partial t}\tau = \beta\,[\tau^*(c) - \tau]$, so

$$\frac{\partial}{\partial t}\sigma_{rr}(t,R) = \frac{\beta}{\pi R^2}\int_0^R [\tau^*(c) - \tau]\, 2\pi r dr$$

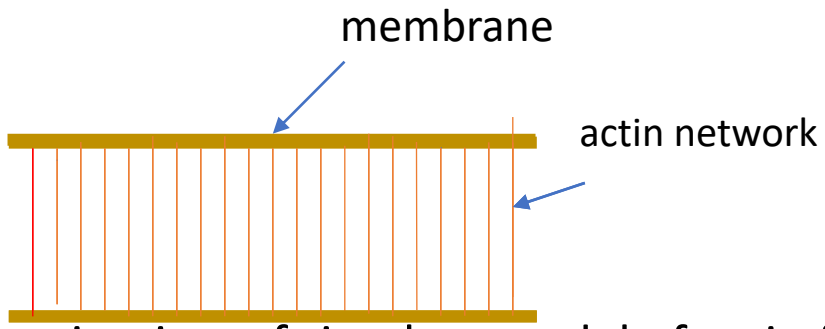
Smearing the force (interconnected filaments)

The previous step do not include transmition of force from one point to another by interconnected filaments. To take this into account we introduce a kind of smearing out of forces acting on the membrane through an averaging integral operator (convolution wit K_σ)

$$D\frac{\partial}{\partial r}c(t,R.z) = A\left\{K_\sigma * \left[\frac{2}{R^2}\int_0^R \left(\tau^*(c(t,r,z)) - \tau(t,r,z)\right) r dr\right]^+ - p(c)\right\}$$

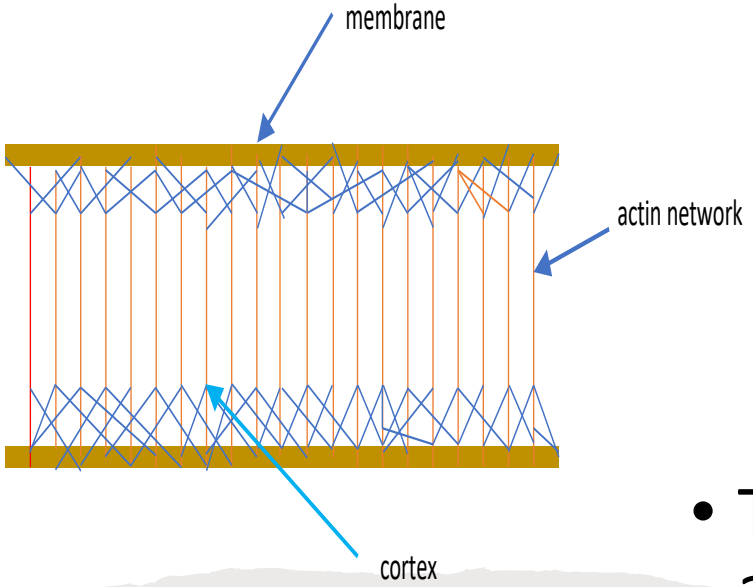
where in numerical simmulations we took $K_\sigma = \frac{1}{\sigma\sqrt{2\pi}}\exp(-\frac{z^2}{2\sigma^2})$.

This non-local mechanism embodies the idea of L. Jaffe



Schematic view of simplest model of actin fibers network in 2D. When Ca concentration increases the fibers contract pulling the membrane. This arrangment of fibers corresponds to completely anisotropic case (no myosin bridges between filaments). The force is not transfered between filaments – local mechanism.

$$K \sim \delta(x)$$



Nonlocal mechanism of propagation

- This mechanizm is nonlocal. The filaments are interconnected by myosin bridges. Their number grows with Ca concentration.
- The force that appears in one place is transferred by the tangled fibers to other neighboring ones. Thus the channels are openned ahead of the propagating wave of Ca^{++} concentration. This accelerates the wave propagation.

Numerical computations

All numerical computations were done for the diffusion coefficient **D**=1. The source term:

$[\boldsymbol{K}(\mathbf{0,25}\boldsymbol{u}+\mathbf{0.1}\boldsymbol{u}^{\mathbf{2}}-\boldsymbol{\tau})]_{+}-\boldsymbol{p}(\boldsymbol{u})$ where

$\boldsymbol{p}(\boldsymbol{u})=\boldsymbol{u}(\boldsymbol{u}^{\mathbf{2}}-\mathbf{1.15}\boldsymbol{u}+\mathbf{0.5})$

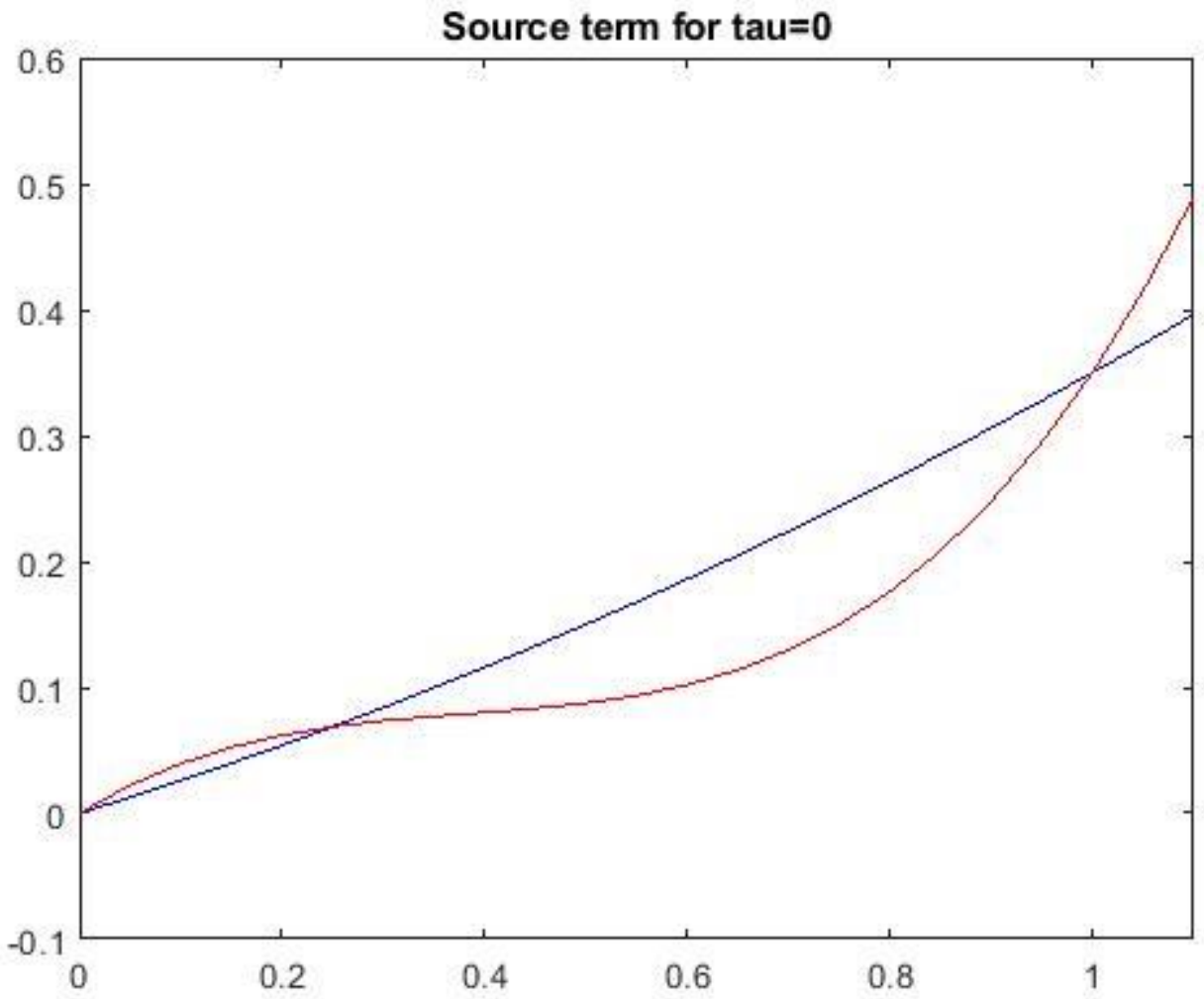
For K=id and $\tau \equiv 0$ the source term takes form

$$u(u-0{,}25)(u-1)$$

Eq. $\frac{\partial}{\partial t}u=\frac{\partial^2}{\partial x^2}\,u-u(u-0{,}25)(u-1)$ has heteroclinic solutions (travelling fronts) of the form

Source term for $\tau = 0$

For $\tau = 0$ we must have bistable case!



3D NUMERICAL SIMMULATIONS I

Assuming cylindical symmetry we solved numerically the system :

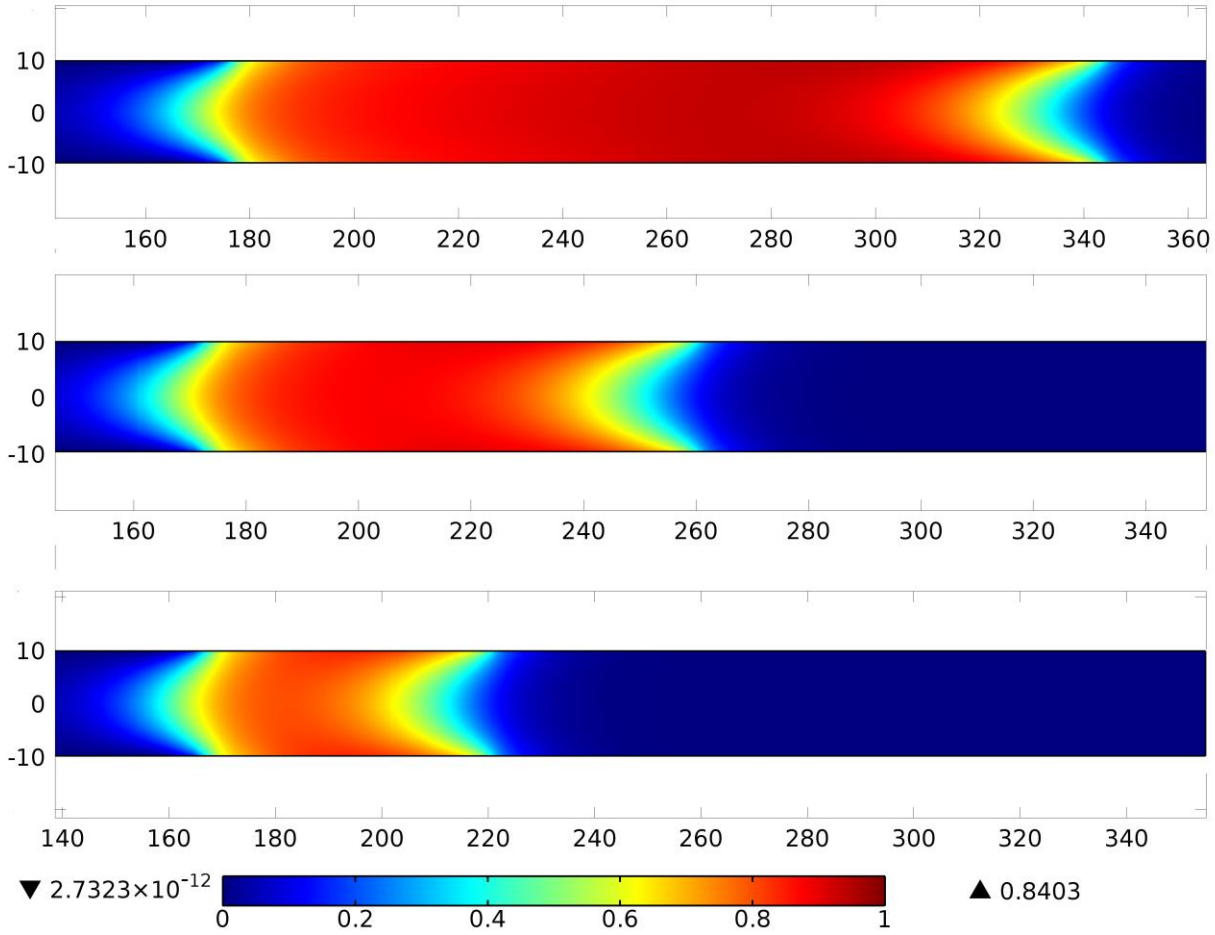
$$\frac{\partial}{\partial t} c = D \Delta c \quad \text{in } \Omega ,$$

$$D\, n \cdot \nabla \mathbf{c} = A\{\left[K_\sigma \frac{\partial}{\partial \mathbf{t}} \boldsymbol{\tau}\right]_+ - p(c)\} \qquad \text{on } \partial\Omega,$$

$$\frac{\partial}{\partial \mathbf{t}} \boldsymbol{\tau} = \boldsymbol{\beta}[\boldsymbol{\tau}^*(\mathbf{c}) - \boldsymbol{\tau}] \qquad \text{in } \Omega$$

Numerically determined travelling homoclinic waves (moving to the right)

Ca^{++} concentration (for different σ)



Numerical computations

All numerical computations were done for the diffusion coefficient **D**=1. The source term:

$[\boldsymbol{K}(\mathbf{0,25}\boldsymbol{u}+\mathbf{0.1}\boldsymbol{u}^{\mathbf{2}}-\boldsymbol{\tau})]_{+}-\boldsymbol{p}(\boldsymbol{u})$ where

$\boldsymbol{p}(\boldsymbol{u})=\boldsymbol{u}(\boldsymbol{u}^{\mathbf{2}}-\mathbf{1.15}\boldsymbol{u}+\mathbf{0.5})$

For K=id and $\tau \equiv 0$ the source term takes form

$$u(u-0{,}25)(u-1)$$

Eq. $\frac{\partial}{\partial t}u=\frac{\partial^2}{\partial x^2}\,u-u(u-0{,}25)(u-1)$ has heteroclinic solutions (travelling fronts) of the form

ONE DIMENSIONAL APPROXIMATION

Averaging our diffusion equation with respect to r :
and similarly, the equation for the traction, we arrive at the one dimensional problem

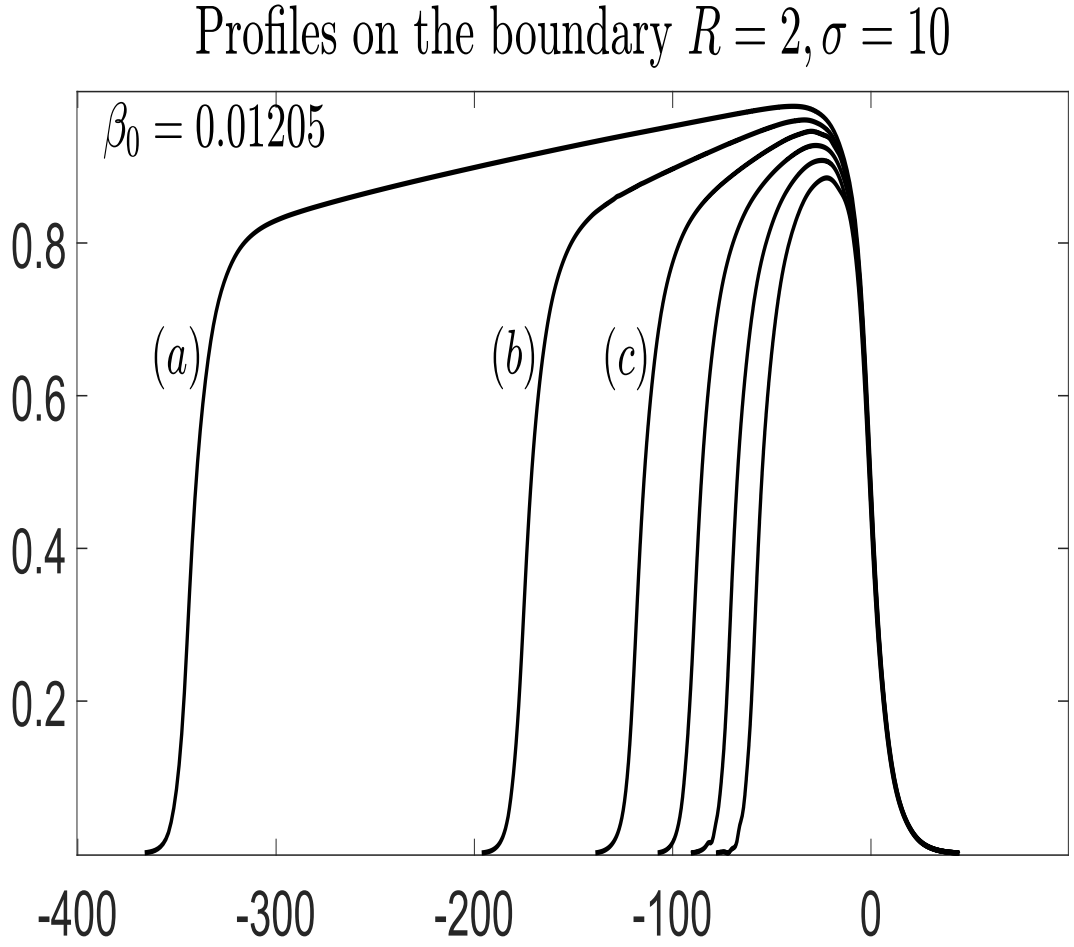
$$\frac{\partial}{\partial t}\boldsymbol{u} = \boldsymbol{D}\frac{\partial^2}{\partial x^2}\,\boldsymbol{u} + \frac{2A}{R}\,\boldsymbol{\beta}\mathbf{K_2} * [\boldsymbol{\tau}^*(\mathbf{u}) - \boldsymbol{\tau}] - \boldsymbol{p}(\boldsymbol{u})$$

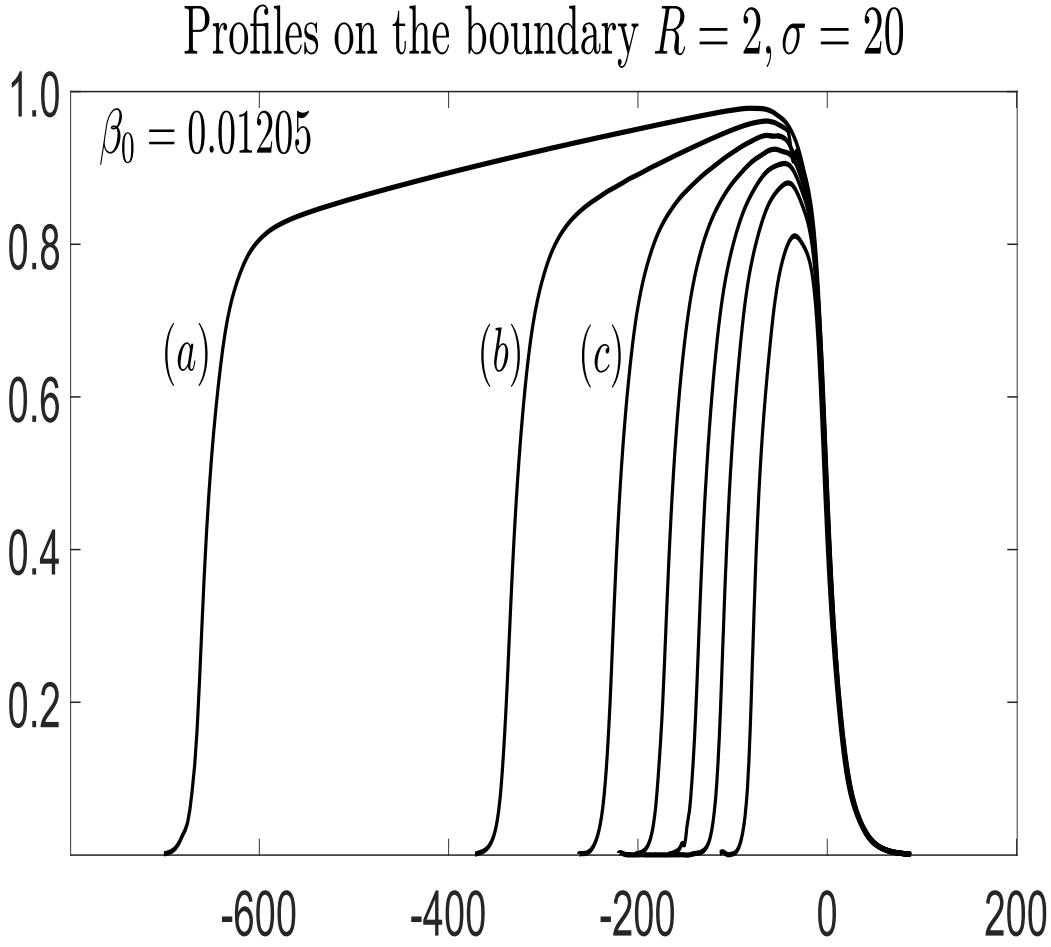
$$\frac{\partial}{\partial \mathbf{t}}\boldsymbol{\tau} = \boldsymbol{\beta}[\boldsymbol{\tau}^*(\mathbf{u}) - \boldsymbol{\tau}]$$

where

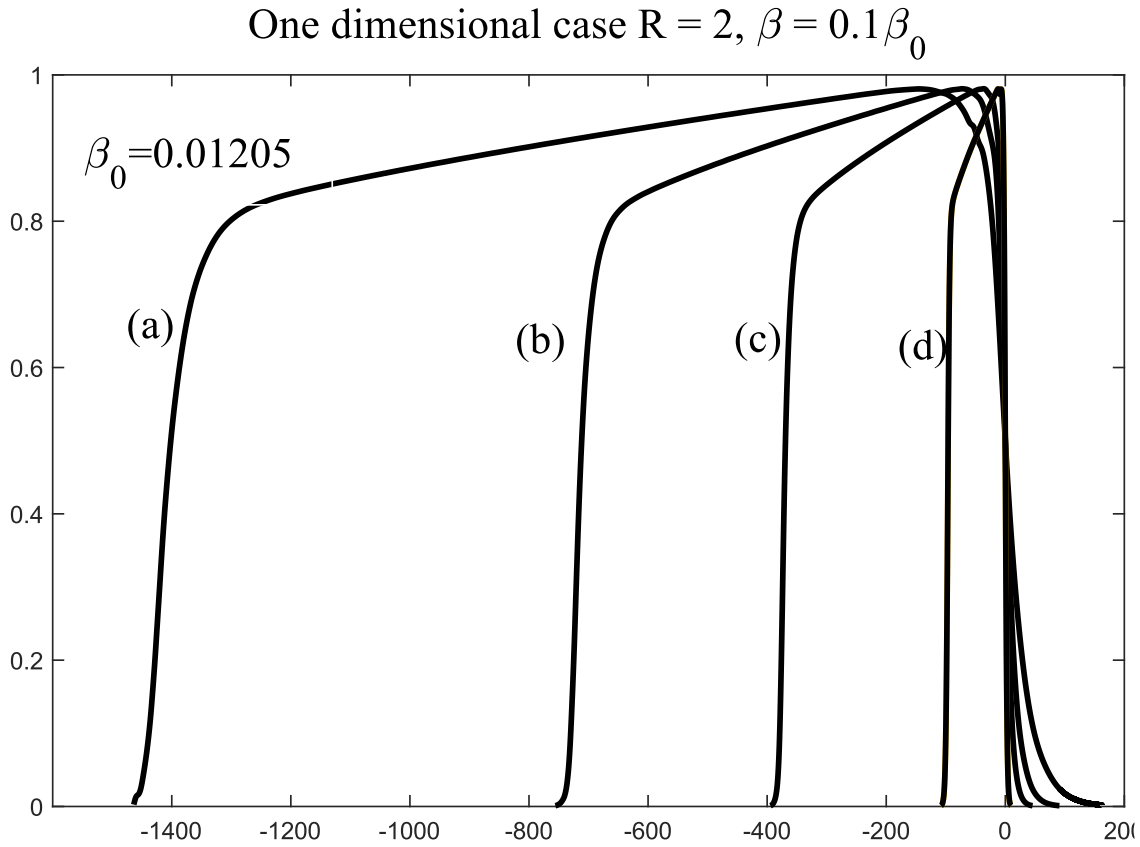
$$u(t,x) = \frac{1}{\pi R^2}\int_0^R 2\pi r\, c(t,x,r)dr$$

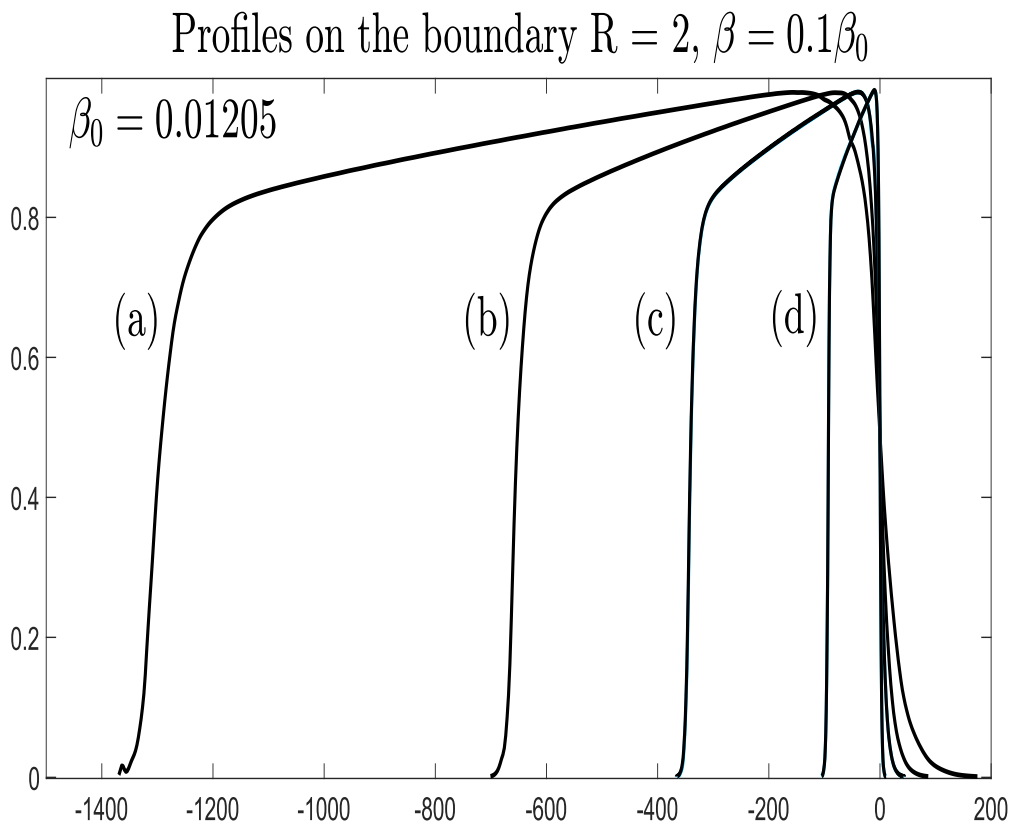
Waves profiles at r=R, (R=2) for different β: (a) β=0,1β_0, (b) β=0,2β_0, (c) β=0,3β_0 etc. where the reference β is $\beta_0 = 0,01205$. On the left for σ=10. On the right for σ=20.





On the left: wave profiles and wave velocities in 1-D simulations for A=1, and (a) σ=40, (b) σ=20, (c) σ=10, (d) σ=0 and for β=0.001205 (=0.1 β_0). On the right: 3D simulations for A=1, R=2, and β=0,001205 and the same values of σ. Propagation velocities with respect to the heteroclinic case ($v_0 = \sqrt{2}/4$) are: (a)13.7,(b) 6.96, (c) 3.63 , (d) 0.978





Fitzhugh –Nagumo type of approximation

The influence of the variance σ of K_σ on the wave velocity.

Expanding :

$\mathbf{K_2} * \boldsymbol{\tau}^*(\mathbf{u})$ we arrive to easier, local system of equations

$$\frac{\partial}{\partial t}\boldsymbol{w} = \frac{\partial^2}{\partial z^2}\left(\boldsymbol{D}\boldsymbol{w} + \frac{\boldsymbol{A}}{\boldsymbol{R}}\boldsymbol{\sigma}^2\,\boldsymbol{\tau}^*(\boldsymbol{w})\right) + \frac{\boldsymbol{2A}}{\boldsymbol{R}}\{[\boldsymbol{\tau}^*(\boldsymbol{w}) - \boldsymbol{\tau}]^+ - \boldsymbol{p}(\boldsymbol{w})\}$$

$$\frac{\partial}{\partial t}\boldsymbol{\tau} = \boldsymbol{\beta}[\boldsymbol{\tau}^*(\boldsymbol{w}) - \boldsymbol{\tau}]$$

with larger diffusivity. The wave velocity is $\sim\sqrt{diffusivity}$

F-N model is simple and gives good wave speed.

This F-N model we studied (with J. Napiokowska) for a particular shape of the source term step like $\boldsymbol{\tau^*(w)}$ and linear $\boldsymbol{p(w)}$.

- In this case the existence of homoclinic waves is proven for some range of $\beta < \beta_0$,
- For $\beta > \beta_0$ there are no homoclinic waves.
- There are two solutions for given $\beta < \beta_0$. Narrow one unstable and wider which is stable.

Conclusions

1. It seems that the idea of F. Jaffe works

a) Wave velocity grows as σ . σ – range of mechanical interactions due to actin-myosin fiber network.

b) The concentration of Ca in extracellular space is 100 times bigger than in endoplasmic reticulum, so flux through ion channel can be quite high. Again, wave velocity grows as $\sqrt{Source}$

2. 1-D approximation seems to work quite well ! It well reproduces the 3-D simulations.

REFERENCES

[1] L.F. Jaffe, "Stretch-activated calcium channels relay fast calcium waves propagated by calcium-induced calcium inux", Biol. Cell 99, 175{184 (2007).

[2] J.C. Gilkey, L.F. Jaffe, E.B. Ridgway, G.T. Reynolds GT, "A free calcium wave traverses the activating egg of the Medaka, Oryzias latipes", J. Cell Biol. 76, 448-466 (1978).

[3]Z. Peradzynski, B. Kaźmierczak, S. Białecki, Modelling fast CICI Waves – to be published.

[4] Murray JD. Mathematical Biology, Springer, Berlin, 2nd edition, 1993.

[5] W.S. Nishitani, Molecular mechanisms involved in cell response to mechanical forces, phd dissertation, University of Illinois at Urbana-Champaign, 2011.

[6] K. Okeyo, et al., "Actomyosin contractility spatiotemporally regulates actin network dynamics in migrating cells", J. Biomech. 42(15), 2540-8 (2009).

[7] Z. Peradzynski, "Diffusion of calcium in biological tissues and accompanying mechanochemical effects", Arch. Mech. 62, 423-440 (2010).

[8] B. Kaźmierczak, Z. Peradzyński, Calcium waves with fast buffers and mechanical effects, J. Math. Biol., DOI 10.1007/s00285-009-0323-2, 2010.

Thank you for your attention

and

the organizers for the invitation.