Spatio-temporal dynamics of glycolysis (experiment and model)

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Content

- Introduction

- Experiment

- Model and experimental data
- Theoretical studying of model

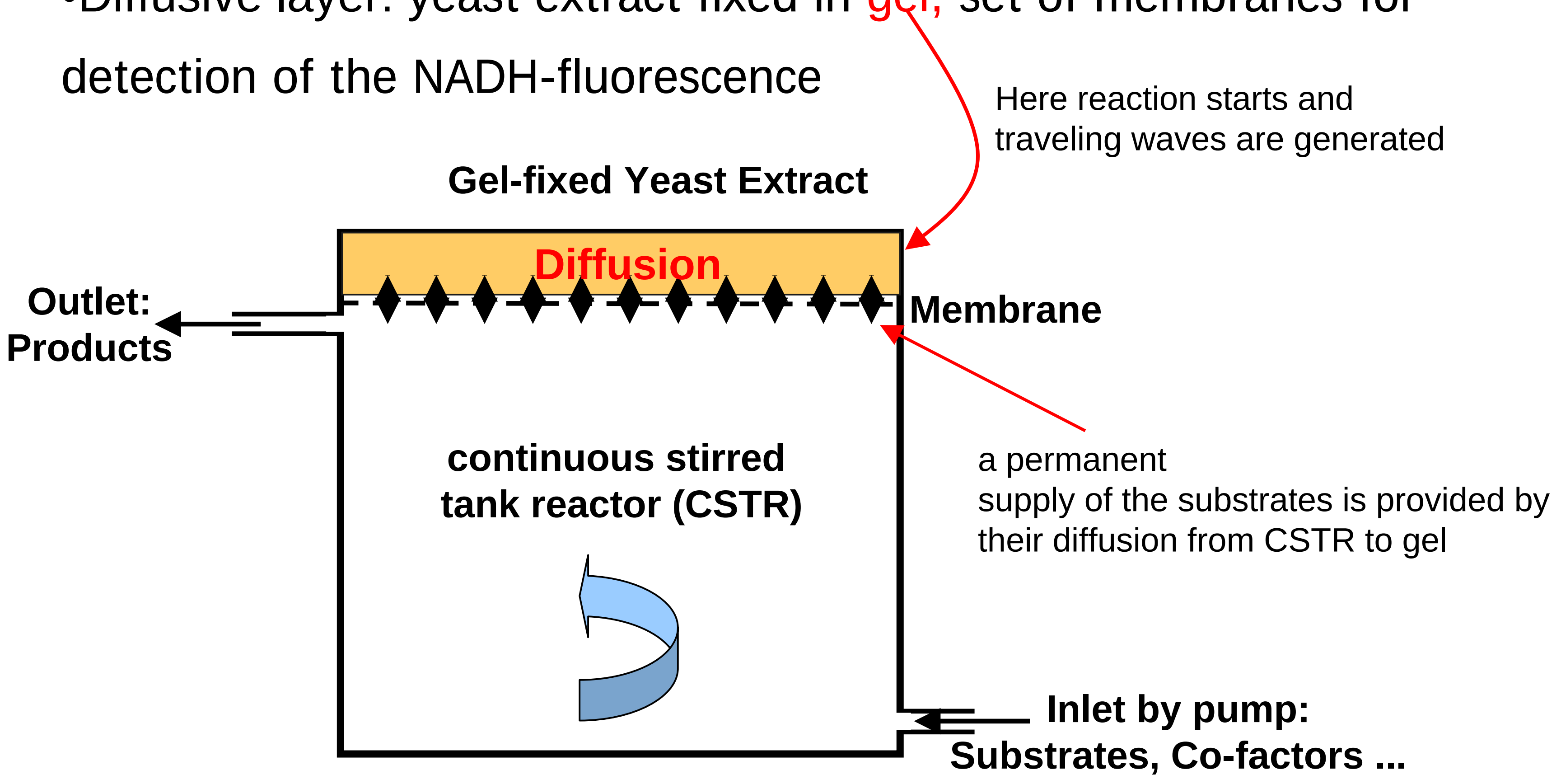
- Conclusions

Experiment. Open spatial reactor

(all experiments were obtained by Bagyan S. and Mair T.)

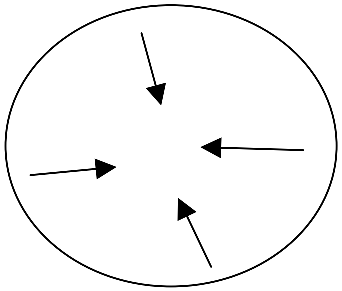
•OSR: diffusive layer with content of CSTR

•Diffusive layer: yeast extract fixed in gel, set of membranes for detection of the NADH-fluorescence



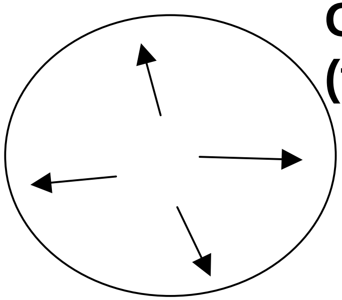
Experiment. Cross-sections (obtained by Bagyan S.)

Inward waves (top view)

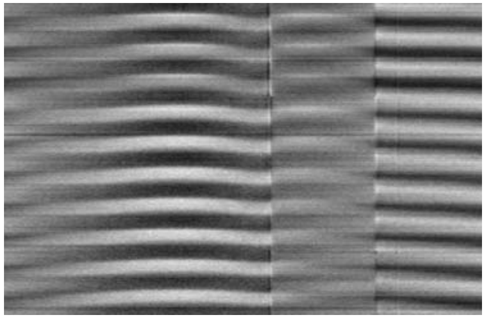


cross-sections
In the middle of gel

Outward waves (top view)

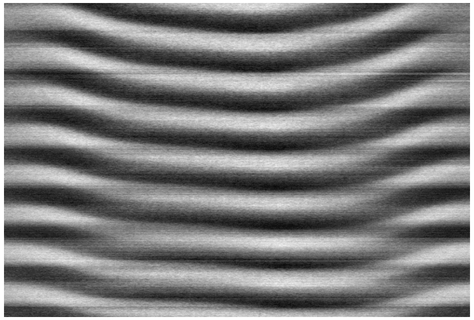


Time,min



space,mm

Time,min



space,mm

- Traveling substrate waves are generated after 10 min.
- A spontaneous change of the direction of wave propagation is observed after about 100 min.

Model (Selkov's model)

$$\frac{\partial x}{\partial \tau} = v - xy^2 + D_1 \frac{\partial^2 x}{\partial r^2},$$

$$\frac{\partial y}{\partial \tau} = xy^2 - wy + D_2 \frac{\partial^2 y}{\partial r^2}.$$

x -substrate (ATP), supplied by a certain source *v* is irreversibly converted to the product *y*(ADP). The product irreversibly removes form reaction with rate parameter *w*.

The boundary conditions were zero fluxes:

$$\frac{\partial x}{\partial r}(0,\tau) = \frac{\partial x}{\partial r}(1,\tau) = 0, \frac{\partial y}{\partial r}(0,\tau) = \frac{\partial y}{\partial r}(1,\tau) = 0$$

The initial conditions were small deviation form stationary values of variables: $\bar{x} = w^2 / v, \bar{y} = v / w$

Results

We assumed that the direction of wave propagation:

•is determined by a non-homogeneous substrate inflow to the gel

•we model it by a parabola which defined as

$$v(r) = v_0 + 4(v_b - v_0)(r - 0.5)^2$$

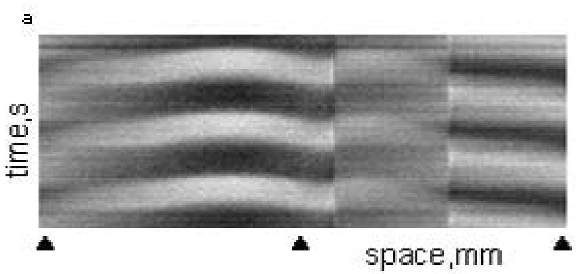
define the value of influx in extremum and at the borders

Space variable

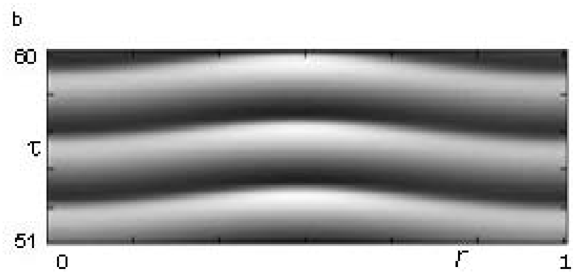
For this numerical simulations v_b and v_0 were chosen in such a way that shift of phases of all oscillators in initial time was very small!

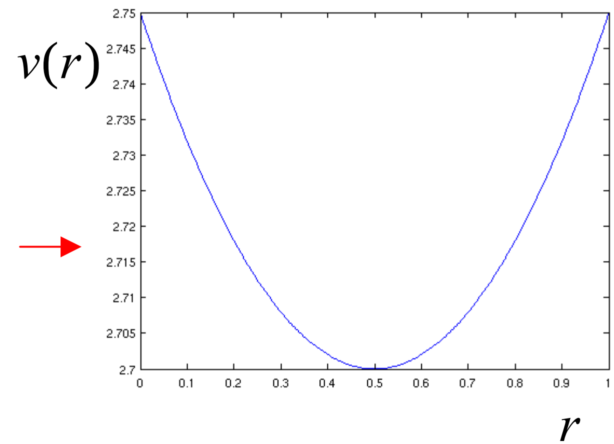
Results

Experimental data.
Inward waves

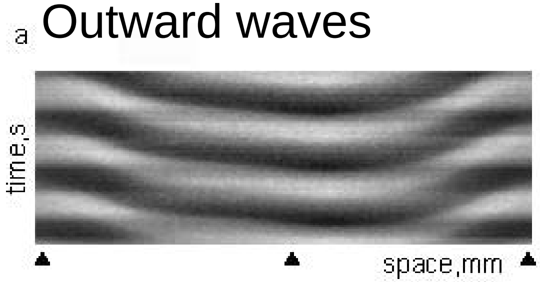


Numerical simulations
Inward waves

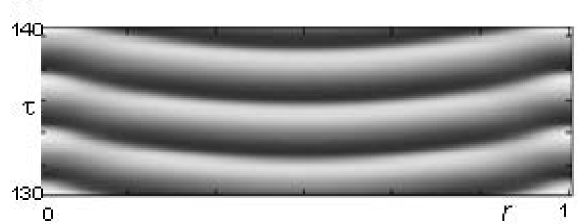


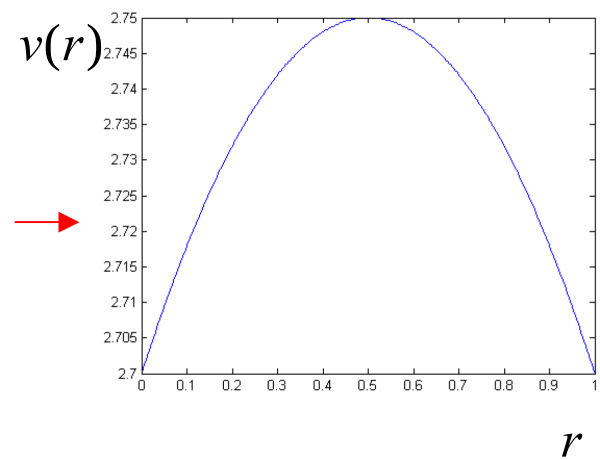


Experimental data.
Outward waves



Numerical simulations
Outward waves





How waves can change the direction of their propagation?

Come back to Selkov local model

Rewrite the original Selkov system into new variables

$u = v - wy$ - total flux

$z = x + y$ - whole concentration of metabolites in the reaction

and sum two equations:

$$\frac{dz}{dt} = u \qquad (1)$$

$$\frac{du}{dt} = -w(u - v) - w^{-2}(wz + u - v)(u - v)^2$$

The steady state of the system

$$\begin{cases} u_0 = 0, \\ z_0 = \dfrac{w^2}{v} + \dfrac{v}{w}. \end{cases}$$

In this state the total flux (u_0) is equal zero and total concentration of all reagents is equal z_0

Let us introduce new variable

$$\xi = z - z_0$$

And after short transformations we can obtain new system:

$$\frac{d\xi}{dt} = u,$$

the compensation of an unbounded growth

$$\frac{du}{dt} = 2\lambda\left(1 + c_1 u - c_2 u^2\right)u - \left[\Omega\left(1 - v^{-1}u\right)\right]^2 \xi,$$

asymmetry in the limit cycle

Where $\lambda = \left(w - v^2 w^{-2}\right)/2$

$$c_1 = \left(3vw^{-2} - wv^{-1}\right)/2\lambda$$

$$c_2 = w^{-2}/2\lambda$$

$$\Omega = \frac{v}{\sqrt{w}}$$ → frequency of oscillations

In the case if λ is a small parameter a linear approximation of the system reduces it to the equation of harmonic oscillations.

Theoretical studying. Local system.

To find an approximate analytical solution of, we use the averaging method (Van der Pol–Krylov–Bogolyubov scheme). Namely, we consider the representation of the solution in the form of simple harmonic function with variable amplitude and phase:

$$\xi(t) = A(t)\cos\left(\Omega t - \phi(t)\right) + \xi_0(A),$$ -the shift of the limite cycle center

$$u(t) = -\Omega A(t)\sin\left(\Omega t - \phi(t)\right).$$

We get the following equations for the amplitude and phase:

$$\frac{dA}{dt} = \lambda A\left(1 - k_1 \frac{3c_2}{4}\Omega^2 A^2\right),$$

$$\frac{d\phi}{dt} = -k_2 \frac{\Omega^3}{8v^2} A^2.$$

-all term as $u^2\xi_0, u\xi_0$ are neglected

! $k_1 = c_2/c_1 \quad k_2 = 2c_1/vc_2$

Theoretical studying. Distributed system.

Let us write distributed system for amplitude and phases:

$$\frac{\partial A}{\partial t} = \lambda A\left(1 - k_1 \frac{3c_2}{4}\omega^2 A^2\right) + \frac{D}{2}\left(\frac{\partial^2 A}{\partial r^2} - A\left(\frac{\partial \phi}{\partial r}\right)^2\right),$$

$$\frac{\partial \phi}{\partial t} = -k_2 \frac{\omega^3}{8v^2} A^2 + \frac{D}{2}\left(\frac{\partial^2 \phi}{\partial r^2} + \frac{2}{A}\frac{\partial A}{\partial r}\frac{\partial \phi}{\partial r}\right).$$

$$v(r) = a + 4(b-a)(r-0.5)^2,$$

$$v_0 = 2.8, v_b = 2.73$$

$$\lambda = \left(w - v(r)^2 w^{-2}\right)/2$$

$$k_2 = 2c_1 / v(r) c_2$$

$$\Omega = \frac{v(r)}{\sqrt{w}}$$

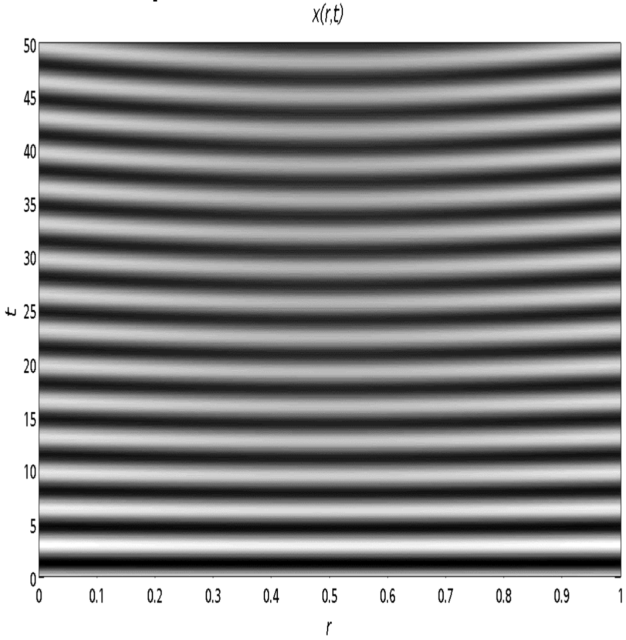
For initial conditions we have considered three cases:

1) uniform initial conditions
2) maximum in phase distribution corresponds to maxima of *v*
3) phase distribution in opposition to influx distribution

Theoretical studying. Distributed system.

Having these solutions, one can transfer back to the initial concentration variables as $x = w^2 v^{-1} + w^{-1} u + z \quad y = w^{-1} v - w^{-1} u$

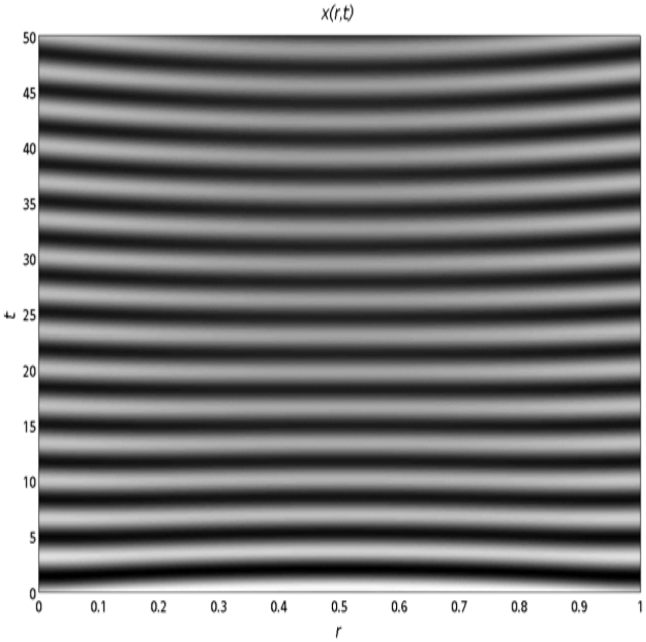
Uniform initial conditions and maximum in phase distribution corresponds to maxima of *v*



$$A(r,t) = 1 \quad \phi(r,t) = 1$$

,

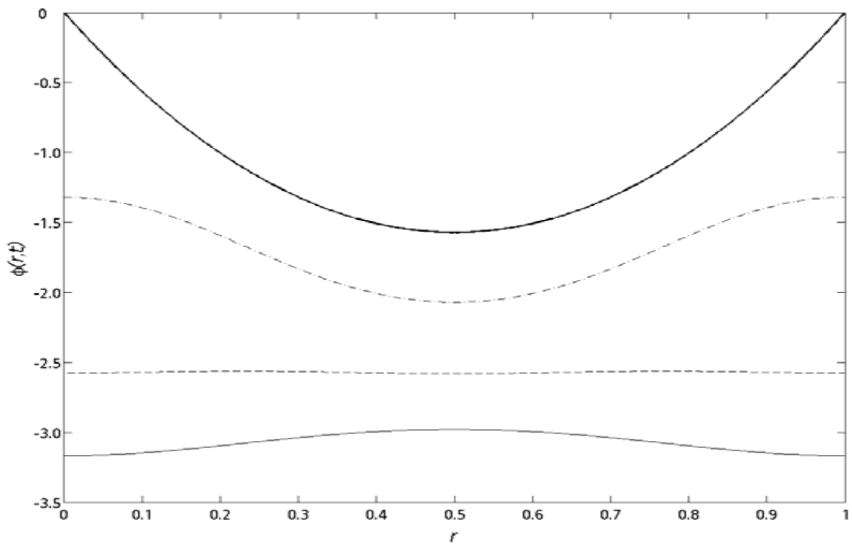
phase distribution in opposition to the influx distribution



$$A(r,t) = 1 \quad \phi(r,0) = 2\pi r\left(r-1\right)$$

Theoretical studying. Distributed system.

Flip of the phase curve.



. Neglect the diffusion and consider the origin of the wave reversal for fixed distribution of influx. As solution of AP equations we obtain:

$$\phi(r,t) = \phi_0(r) - k_2(r)\frac{\Omega(r)^3}{8v(r)^2}\int_0^t A^2(r,t)dt$$

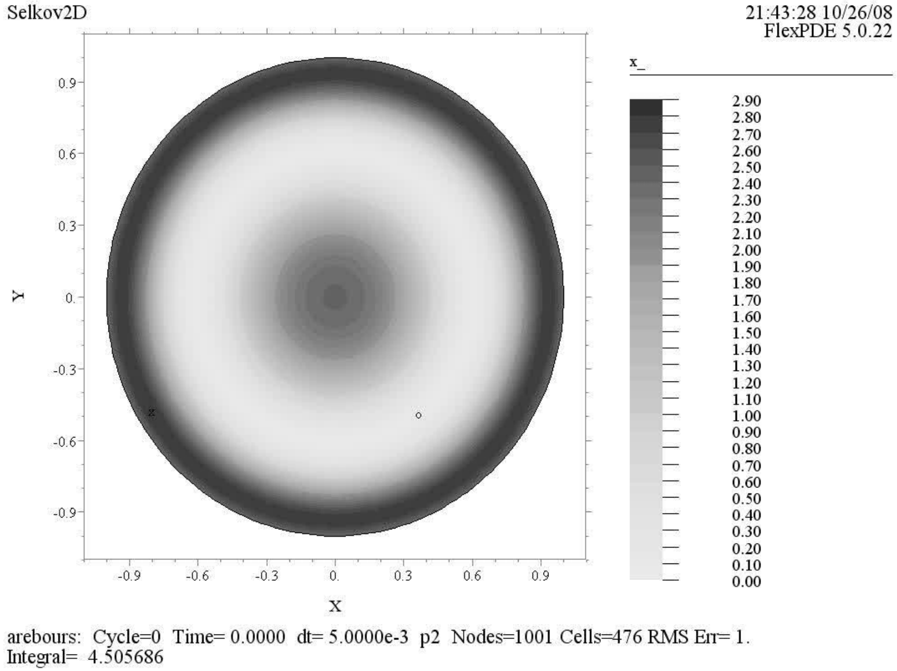
. The space distribution is presented at the following time steps:
0 (bold solid line), 10 (dash-dotted line), 34 (dashed line), 49 (thin solid line).

Dependence of the wave behavior on *D*

The study of the dependence of the solutions on the coefficient's range $D = 0 - 10^{-1}$

shows that the dynamical behaviour has slightly dependence on this parameter!

Two-dimensional model. Results



Initial conditions

$$x_0 = w^2 v^{-1} + w^{-1} u + A_0 \cos(\phi_0)$$

$$y_0 = w^{-1} v + w^{-1} + \Omega A_0 \sin(\phi_0)$$

$$\phi_0 = 2\pi(r^2 - 1)$$

Conclusions and outlook

These and rest results are published here:

- 1. Lavrova AI**,** Postnikov EB Schimansky-Geier L., Phase reversal in the Selkov model with inhomogeneous influx, Phys. Rev. E. **79,** 057102 (2009)
- 2. Lavrova AI, Bagyan S., Mair T., Hauser M., Schimansky-Geier L., Modeling of glycolytic wave propagation in an open spatial reactor with inhomogeneous substrate influx, BioSystems, **97**, 127 (2009)

I hope that next devoted to Selkov model will be published...

1. Lavrova AI**,** Postnikov EB The inner autoparametric resonance: new insight on an old topic, (in preparation)

- 2. Postnikov E, Verisokin A , Verveyko D., Lavrova A**,** Self-sustained oscillations and waves with a feedback determined only by boundary conditions, Phys. Rev. E. , (under review)
- 3. Lavrova AI, Warnke C., Postnikov B., Mair T., Hauser M., Schimansky-Geier L., Temperature gradients and glycolytic waves (in preparation)