International Conference

Instabilities and Control of Excitable Networks:

from macro- to nano-systems

Proceedings

Supporters and Sponsors

May 25-30, 2012
Dolgoprudny, Russia

www.icenet2012.net

Proceedings of the International Conference

Instabilities and Control of Excitable Networks:

From Macro- to Nano-Systems

Dolgoprudny, Russia

May 25-30, 2012

УДК 001:004.7:007.5:519.1:573:576.3:65.
БКК 28.071+28.91+32.97

Instabilities and Control of Excitable Networks / Moscow: MAKS-Pess, 2012, 133 p.

The present book contains the proceedings of the International Conference “Instabilities and Control of Excitable Networks: From Macro- to Nano-Systems” (ICENet-2012) hosted by Moscow Institute of Physics and Technology in Dolgoprudny, Russia, on 25-30 May, 2012. The conference was devoted to the problems of complex excitable network dynamics in physiology, biomedicine, physics, chemistry and social systems.

Неустойчивости в возбудимых сетях и возможности управления ими / Москва: МАКС-Пресс, 2012. — 133 с.

В сборник вошли труды участников международной конференции “Instabilities and Control in Excitable Networks: From Macro- to Nano-Systems” (Неустойчивости в возбудимых сетях и возможности управления ими: от макро- к нано-системам), проходившей в Московском физико-техническом институте (г. Долгопрудный, Россия) в период с 25 по 30 мая 2012. Конференция была посвящена изучению сложного возбудимого динамического поведения систем, организованных по сетевому принципу, в физиологии, биомедицине, физике, химии и социальной сфере.

Organizing Committee

K.I. Agladze — co-chairman

G.Th. Guria — co-chairman

A.A. Muraviev

D.V. Goldshtein

A.M. Pertsov

K.E. Zlobina — scientific secretary

A.R. Gagarina — secretary

Acknowledgments

Moscow Institute of Physics and Technology

National Research Centre for Haematology

Russian Foundation for Basic Research

Conference Management System

Moscow Center of Technology Transfer

Skolkovo Innovation Center

Preface

International Conference
"Instabilities and Control of Excitable Networks:
From Macro- to Nano-Systems"

was held in Dolgoprudny, Russia in May 25-30 and devoted to the problems of complex excitable network dynamics in physiology, biomedicine, physics, chemistry and social systems. The main topics were:

- Instabilities in far-from-equilibrium excitable network dynamics;
- Pattern formation in network-organized systems;
- Control of threshold and kinetic cascade avalanche-like phenomena;
- Conceptual items and their application to natural and social systems.

The main goal of the conference was to advance interdisciplinary research and develop new cross-disciplinary links in Russia and abroad. The Conference was attended by a few vibrant groups of researchers at different stages of their academic careers. The participating scholars have studied problems related to self-organization in various systems, engineering of excitable biological tissues and control of excitable networks. We believe that this conference was foster new contacts and an exchange of exciting ideas. Presented in this issue collection of the papers to some degree reflects the present state of art in the area.

Sincerely Yours,
Co-Chairs,
Konstantin Agladze
and
Georgy Guria

Contents

N.N. Agladze, N.I. Doronina, K.I. Agladze
Cardiac tissue engineering with the aid of polyhydroxybutyrate membranes and nanofibers 1

V.N. Biktashev, D. Barkley, I.V. Biktasheva, G.V. Bordyugov, H. Dierckx, A.J. Foulkes, S.W. Morgan, G. Plank, N.A. Sarvazyan, O. Selsil, H. Verschelde
Asymptotic dynamics and control of spiral and scroll waves 8

O.A. Dudchenko, G.Th. Guria
Self-Sustained Peristaltic Transport in Biological Systems: A Theoretical Study 19

W. Ebeling, A.P. Chetverikov, M.G. Velarde
Solitonic excitations and control in nonlinear chains and networks 28

E.V. Gasnikova
One way to generate Lyapunov function for the chemical kinetic equations 40

M.A. Herrero
Mathematical Models in Social Dynamics 43

A.E. Kaplan, S.N. Volkov
"Locsitons" in self-interacting atomic nanolattices 53

A.V. Khalyavkin
From macro- to nano-systems and back in search of the primary cause and control of aging 69

A.S. Kholodov, S.S. Simakov, Y.N. Soe, T.M. Gamilov
Computational Model of Blood Flow Optimization in Lower Extremities during Intensive Exercise 77

A.V. Leonidov, E.L. Rumyantsev
Russian interbank networks: main characteristics and stability with respect to contagion 83

V.A. Malyshev, A.A. Zamyatin
Mathematics for some classes of networks 90

A.A. Polezhaev, M.Yu. Borina
Spatial-Temporal Patterns Arising in Active Media in the Vicinity of the Wave Bifurcation 104

A.S. Rukhlenko, K.E. Zlobina, G.Th. Guria
Threshold activation of blood coagulation cascade in intensive flow and formation of fibre-like fibrin polymer networks 113

Asymptotic dynamics and control of spiral and scroll waves

V. N. Biktashev[1,2,*], D. Barkley[3], I. V. Biktasheva[1], G. V. Bordyugov[1,4], H. Dierckx[1,5], A. J. Foulkes[1,6], S. W. Morgan[1], G. Plank[7], N. A. Sarvazyan[8], O. Selsil[1] and H. Verschelde[5]

[1]*University of Liverpool, UK*
[2]*University of Exeter, UK*
[3]*Warwick University, UK*
[4]*Humboldt University, Berlin, Germany*
[5]*Ghent University, Belgium*
[6]*Manchester University, UK*
[7]*Graz University, Austria*
[8]*George Washington University, Washington DC, USA*
[*]*e-mail address: v.n.biktashev@exeter.ac.uk*

1 Introduction

Spiral waves in two spatial dimensions (2D), and scroll waves in three dimensions (3D), are regimes of self-organization observed in physical, chemical and biological dissipative systems, where wave propagation is supported by a source of energy stored in the medium [1–9]. A spiral wave is a remarkably stable solution: it only reacts to perturbations if they are sufficiently close to its "core". The result of that is that when only relatively small perturbations are concerned, dynamics of spiral waves is phenomenologically similar to that of "particles", despite the fact that a spiral wave is in no way a localized object, but tends to fill up all the available medium. This macroscopic "wave-particle duality" [10] extends to three dimensions: scroll waves can be described as "string-like" objects [11].

This article is a retelling of a conference presentation which reviewed a few selected papers, dedicated to exploring this particle- and string-like dynamics and possibilities of exploiting it for the purposes of their control. A particular importance of control may be in cardiac tissue, where spiral and scroll waves underlie dangerous arrhythmias.

2 An outline of the theory

Here we briefly overview the key results of the asymptotic theory of spiral wave dynamics, more details of which can be found *e.g.* in [10, 12, 13] This theory centers on reaction-diffusion systems,

$$\partial_t \mathbf{u} = \mathbf{f}(\mathbf{u}) + \mathbf{D}\nabla^2\mathbf{u} + \varepsilon\mathbf{h}, \quad \mathbf{u},\mathbf{f},\mathbf{h} \in \mathbb{R}^\ell,\ \mathbf{D} \in \mathbb{R}^{\ell\times\ell},\ \ell \geq 2.$$

Here ℓ is the number of reacting components, $\mathbf{u} = \mathbf{u}(\vec{r},t)$ is the column-vector of reagent concentrations, $\vec{r} \in \mathbb{R}^2$ or $\mathbb{R}^3$ is the position vector in the physical space, $\mathbf{D}$ is the matrix of diffusion coefficients, $\mathbf{f}$ is the column-vector describing the reaction rates, and $\varepsilon\mathbf{h} = \varepsilon\mathbf{h}(\mathbf{u},\nabla\mathbf{u},\vec{r},t)$, $\varepsilon \ll 1$, is a small perturbation. The rationale of considering $\varepsilon\mathbf{h}$ separately from $\mathbf{f}$ is that at $\varepsilon = 0$, the system has a symmetry with respect to translations and

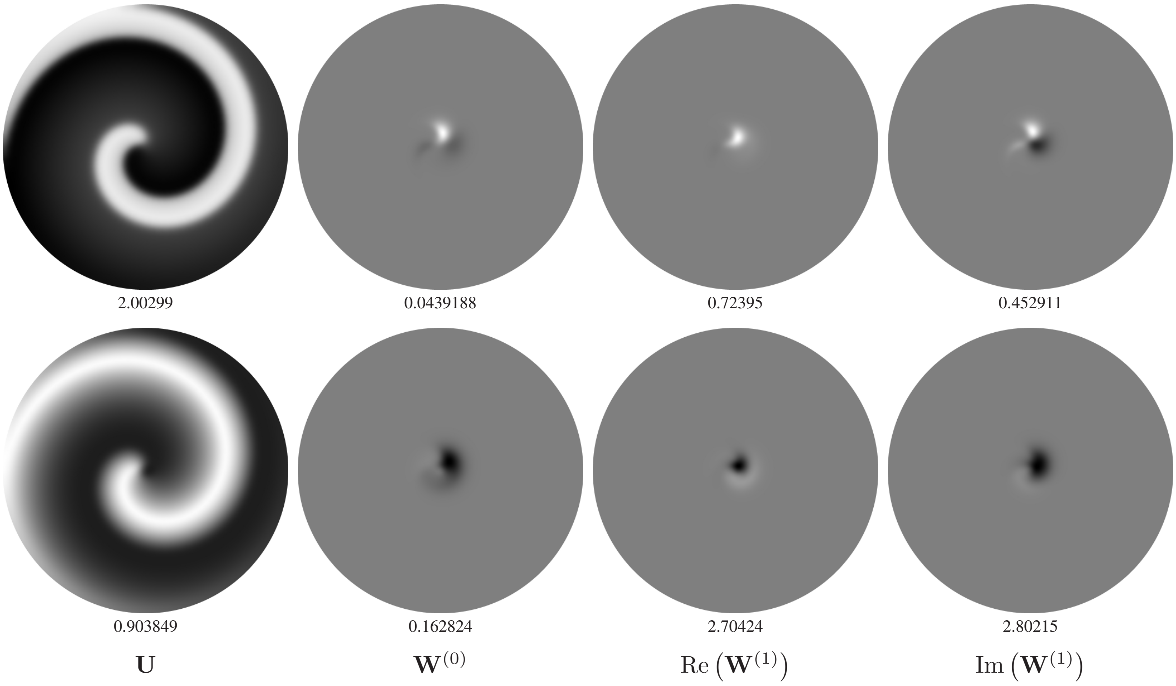


Figure 1: Response functions for FitzHugh-Nagumo system [14].

rotations of the $\vec{r}$ space and translations in time t, so $\varepsilon\mathbf{h}$ is a generic symmetry-breaking perturbation.

We assume existence of steadily rotating spiral wave solutions at $\varepsilon = 0$:

$$\mathbf{u}(\vec{r},t) = \mathbf{U}(\rho(\vec{r}-\vec{R}), \vartheta(\vec{r}-\vec{R}) + \omega t - \Phi),$$

where $\vec{r} = (x,y)$, $\rho(\cdot)$ and $\vartheta(\cdot)$ are polar coordinates, $\vec{R} = (X,Y) = \text{const}$, $\Phi = \text{const}$, and ω is an eigenvalue, *i.e.* there are only discrete values of ω possible for any given reaction diffusion system; typically just one (up to the sign). This is not always the case with spiral waves: in some systems they "meander", that is rotate unsteadily; this case is not considered here.

If ε is nonzero but small enough, the spiral drifts: solution remains approximately as above, but with $\vec{R}$ and Φ no longer constant but changing with time, $\mathrm{d}\vec{R}/\mathrm{d}t = \mathscr{O}(\varepsilon)$, $\mathrm{d}\Phi/\mathrm{d}t = \mathscr{O}(\varepsilon)$.

The velocity of the drift caused by the perturbation is given by

$$\dot{R} = \varepsilon \int\limits_{\phi-\pi}^{\phi+\pi} \mathrm{e}^{-\mathrm{i}\xi} \left\langle \mathbf{W}, \tilde{\mathbf{h}}(\mathbf{U};\rho,\theta,\xi) \right\rangle \frac{\mathrm{d}\xi}{2\pi} + \mathscr{O}(\varepsilon^2),$$

where (ρ,θ) are corotating polar coordinates, ϕ and ξ measure the rotation phase, $\phi = \omega t - \Phi(t)$, and the angular brackets denote an inner product in the functional space, that is an integral of the form

$$\langle \mathbf{w}, \mathbf{v} \rangle = \int\limits_{\mathbb{R}^2} \mathbf{w}^+(\vec{r})\, \mathbf{v}(\vec{r})\, \mathrm{d}^2\vec{r} = \oint \int\limits_0^\infty \mathbf{w}^+(\rho,\theta)\, \mathbf{v}(\rho,\theta) \rho \, \mathrm{d}\rho \, \mathrm{d}\theta.$$

These expressions use the so called response function $\mathbf{W}(\rho,\theta) = \mathbf{W}^{(1)}(\rho,\theta) \in \mathbb{C}$: eigenfunction of the adjoint linearized operator, corresponding to eigenvalue $\mathrm{i}\omega$. More precisely, this is "translational" eigenfunction as it describes drift (translation) of spiral centre $\vec{R}$

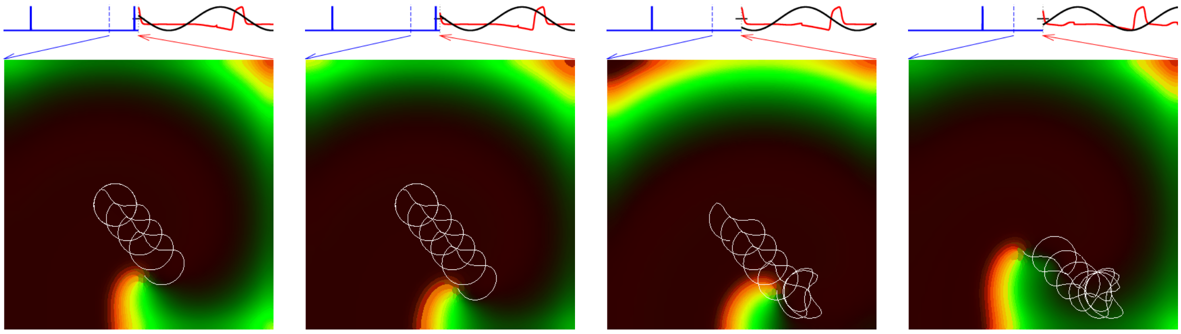


Figure 2: Resonant drift and resonant repulsion of a spiral wave in FitzHugh-Nagumo system. Graphs on top: the record of the action potential in the top right corner, vs the sinusoidal representing the clock that controls periodic stimulation. Change of relative position of action potential with respect to the clock means change of the direction of the drift. [13, 15]

through space; there is also "rotational" eigenfunction $\mathbf{W}^{(0)}(\rho,\theta)$, which describes the drift of the spiral's fiducial rotation phase Φ; this is of a lesser interest in this review. Figure 1 illustrates the spiral wave solution and the response functions in a popular simple model of excitable media, the FitzHugh-Nagumo system. The pictures represent density plots of the corresponding solutions at a selected moment of time; they rotate clockwise as time progresses. The crucial feature of the response functions is that they quickly approach zero beyond the "core" area near to the rotation centre. This is the mathematical basis for the "particle-like" behaviour of spiral waves: the response functions show how an instantaneous and infinitesimal perturbation of a particular component will affect the spiral wave position, so the grey area outside the core means that any perturbation there will have virtually no long-term effect of the spiral, whereas perturbation into the lighter or darker areas within the core can cause a shift of the spiral wave rotation centre.

The simplest sort of spiral wave drift is a "resonant drift" of spirals, theoretically predicted by Davydov *et al.* [16] and first experimentally observed by Agladze *et al.* [17]. It occurs in response to perturbation explicitly depending on time, $\mathbf{h}=\mathbf{h}(\mathbf{u},t)$, so violating the time shift symmetry. This dependence on time is periodic, with a period equal to the period of the spiral wave, thus "resonant". The idea is illustrated in figure 2. The perturbation has a form of periodic pulses; the clock that controls these pulses is represented by the sinusoidal curve on top of the pictures. The result of one pulse is a displacement of the scroll by a certain distance in the direction, depending on the orientation of the spiral wave at the moment of the pulse delivery. The subsequent pulses are delivered with the period equal to the period of the spiral, hence they fall at the same orientation of the spiral and cause its displacements in the same direction again and again. The direction of this drift thus depends on the relative phase of the stimulation clock and the spiral wave phase, which is represented by the action potential, recorded at the top right corner, also shown on top of the pictures. However, the period of the spiral wave changes as its core approaches the boundary of the medium. Hence the phase relationship between the spiral and the stimulation changes, as can be seen by the change of the relative position of the action potential and the stimulation clock. Change of the phase difference means change of the direction of the drift, which will continue until the spiral moves far enough from the boundary, so the resonance restores and the drift proceeds at a straight line away from the boundary. This appears as a "repulsion" of the spiral from the boundary. An asymptotic description of this resonant repulsion mechanism can be found in [12, 15]. Since spiral waves underlie cardiac arrhythmias, their elimination by forcing them to drift to an inexcitable boundary can be a viable anti-arrhythmic strategy. In this

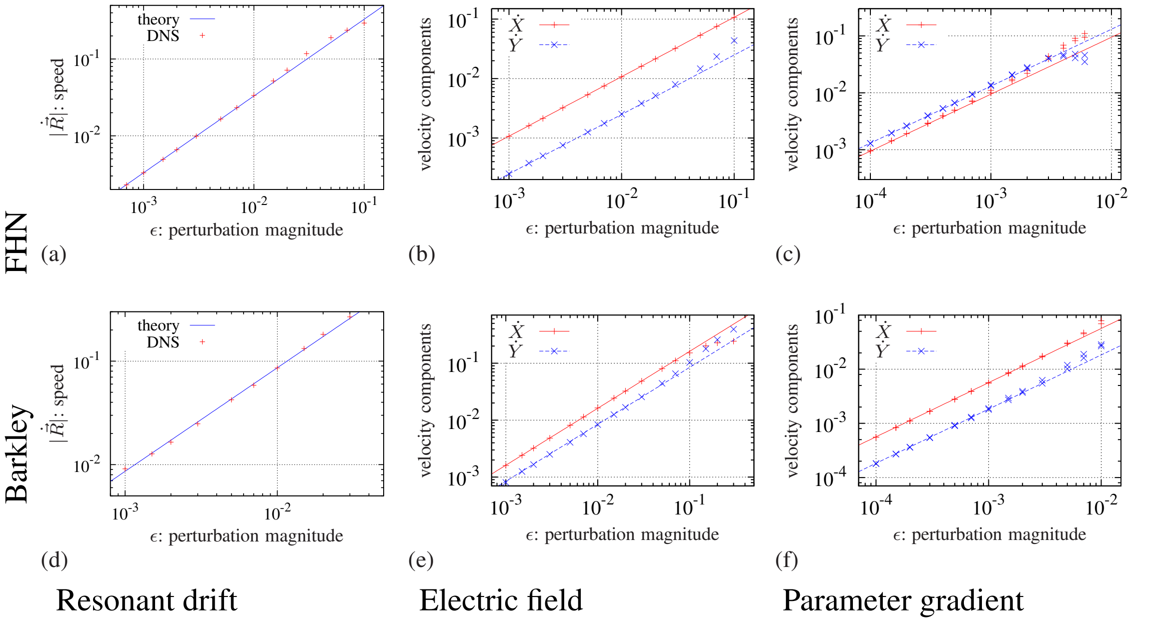


Figure 4: Drift speed: asymptotics (“theory”) vs direct numerical simulations (“DNS”) [13].

context, the resonant repulsion is an undesirable effect. It can, however, be easily overcome by using a feed-back, to synchronize the stimulation with the rotation of the spiral wave and thus ensure the resonance [12, 18].

Another well known sort of drift happens when the perturbation violates the spatial translation symmetry, $\mathbf{h} = \mathbf{h}(\mathbf{u}, \vec{r})$. This means, that the right-hand sides of the reaction-diffusion system depend on space coordinates, or, in physical language, the medium is spatially inhomogeneous. Within the perturbation theory, this results in an oscillating perturbation, applied by the spiral wave “onto itself”, as it rotates through points of the medium with different properties, so the perturbation is periodic and always resonant. This sort of drift is illustrated in figure 3, where the blue component of the colour represents one of the parameters of the reaction kinetics, so the right and left halves of the medium are slightly different in their properties, which causes the spiral to drift.

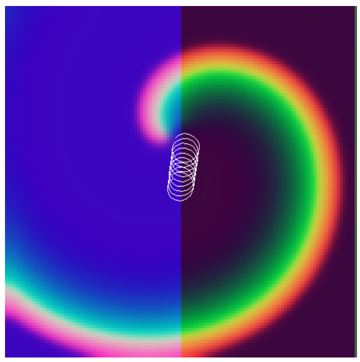


Figure 3: Drift of a spiral wave caused by stepwise parametric inhomogeneity in FitzHugh-Nagumo system [12, 13, 19].

The speed and direction of the drift caused by a stepwise inhomogeneity, as in figure 3, depend on the position of the spiral’s instant rotation centre relative to the step. If the inhomogeneity is in the form of a slight linear gradient speading over a long distance, then the spiral can drift with the same speed in the same direction throughout that distance. A yet another sort of perturbation that can cause drift is the one that breaks the rotational symmetry of the problem: $\mathbf{h} = \mathbf{h}(\mathbf{u}, \nabla\mathbf{u})$. For instance, if the molecules of the reacting species are electrically charged and an external electric field is applied, then $\mathbf{h} = \mathbf{A}\nabla\mathbf{u}$ where diagonal matrix $\mathbf{A}$ represents electrophoretic mobilities of the reagents.

Knowing the response functions, the velocities of these types of drift: resonant, electrophoretic and inhomogeneity-induced, can be predicted. Figure 4 compares these predictions with direct numerical simulations, for the FitzHugh-Nagumo system, and for the Barkley system, which is a very popular variation of the FitzHugh-Nagumo, particularly convenient for conceptual simulations.

Theoretical predictions based on the response functions showed that the dependence of the inhomogeneity-induced drift on the relative location of the spiral wave and inhomogeneity sometimes may be not straightforward: attraction at some distances may change to repulsion at other distances. For the case of a localized inhomogeneity, this may lead to the situation that there is a stable distance between the spiral and the inhomogeneity, so a spiral wave starting from a wide range of initial conditions launches into a circular "orbital motion" around the inhomogeneity, as shown in figure 5.

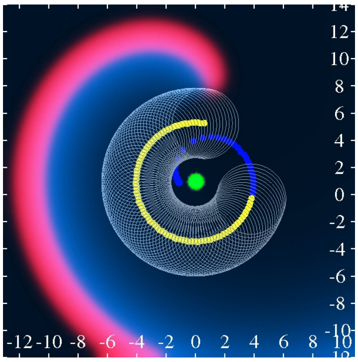


Figure 5: Orbital movement of a spiral wave in Barkley system around a localized inhomogeneity [20].

In the figure, the circular green spot in the middle represents the inhomogeneity, *i.e.* the site where the parameters of the reaction kinetics slightly differ. The spiral wave is depicted by the red/blue colour palette, with red component representing the "excitation" variable of the Barkley system and the blue component representing the "recovery" variable. The thin white line depicts the trajectory of the tip of that spiral wave, which is defined as an intersection of selected isolines of the two components. This trajectory was averaged over every period of rotation, and the corresponding instant rotation centres are represented by blue (earlier time moments) and yellow (later time moments) small circles. At the selected parameters, the inhomogeneity is repelling at small distances and attracting at larger distances. Correspondingly, the spiral wave that started near the local inhomogeneity, departs away from it, but only until it reaches the distance beyond which the repulsion changes to attraction. The spiral then continues to drift along the circle of the radius at which the radial component of the drift force generated by the inhomogeneity vanishes. The radius and the velocity of this orbital drift are in good agreement with predictions based on the response functions.

3 Application in 2D: drift of spirals in an ischaemic border zone

In the asymptotic theory described above, the drift velocity $\dot{\vec{R}}$ linearly depends on the perturbation $\mathbf{h}$. This immediately implies that when several different types of perturbations are applied simultaneously, their effects add up. Thus we have a superposition principle: a superposition of various perturbations

$$\varepsilon\mathbf{h} = \sum_j \varepsilon_j \mathbf{h}_j,$$

has additive effect on the drift velocity

$$\dot{R} \approx \sum_j \varepsilon_j \gamma_j,$$

where the "specific forces" are

$$\gamma_j = \int\limits_{\phi-\pi}^{\phi+\pi} \mathrm{e}^{-\mathrm{i}\xi} \left\langle \mathbf{W}, \tilde{\mathbf{h}}_j \right\rangle \frac{\mathrm{d}\xi}{2\pi}.$$

This has been used to explain some phenomena observed in a computational model, describing experiments with cultures of cardiac cells, which in turn mimic events that happen at a boundary of an ischemic zone that gradually recovers during reperfusion ([21], see figure 6). In the experiments and in the simulations, a certain combination of variations in

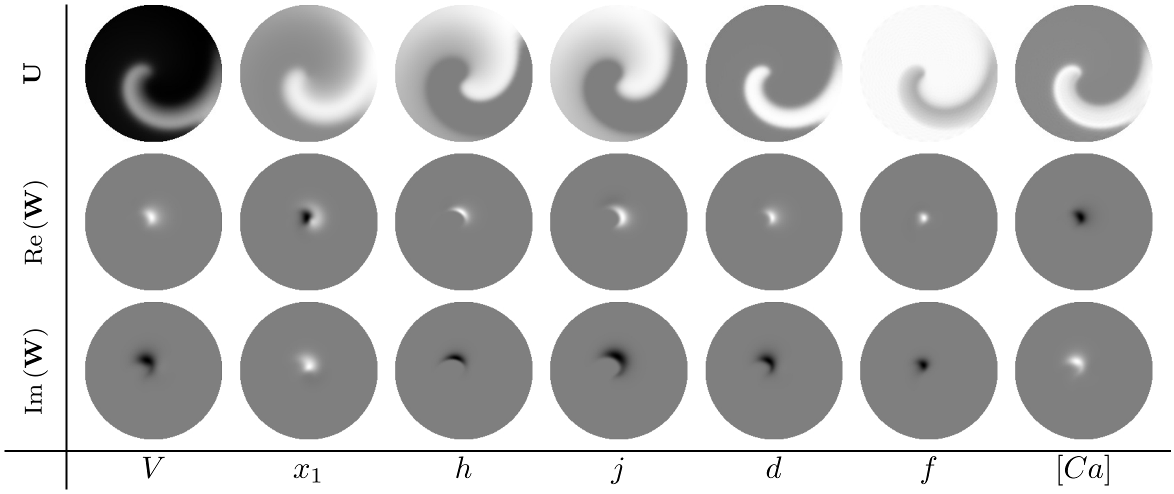


Figure 7: Translation response functions for Beeler-Reuter-Pumir model [22].

cell excitability/automaticity and in strength of their electric coupling with each other created conditions in which spontaneous activity of individual cells created propagating waves which broke up creating microscopic-scale spiral wave activity. One notable feature of these spiral waves was their drift, which would often temporarily stop, or "pin" at local heterogeneities. This feature was essential for the arrhythmogeneity of the ischemic border zone, as the pinned spiral waves had the chance to be not dragged together with the border zone, but survive its passage, after which they develop into macroscopic scale re-entrant waves.

The asymptotic theory has been applied to analyse and explain these phenomena. Figure 7 illustrates the response functions calculated for the particular ionic model of cardiac excitability that was used in the simulations of [21]. The figure shows the spiral wave solution and the components of the translational response function, in the same format as in figure 1, only this model has $\ell = 7$ components. As before, a prominent feature is the localization of all the components of the response function, which justifies the particle-like description of spiral waves in this system.

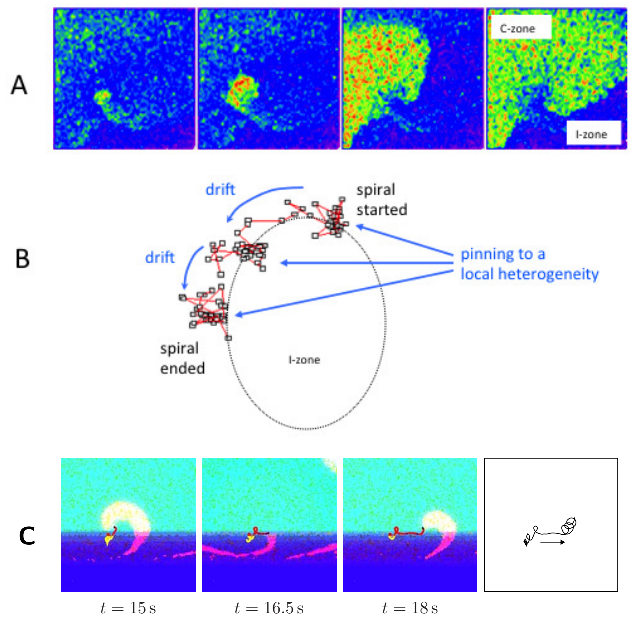


Figure 6: Start/stop drift of spiral wave in (A,B) a culture of neonathal rat cells, (C) in simulations using Pumir's modification of Beeler-Reuter model [21].

Indeed, comparison of the predictions of the asymptotic theory with standard numerical simulations, such as electrophoretic drift, showed a good agreement. In simulations more specific for the electrophysiological setting described above, one deals with a combination of perturbations: localized heterogeneities, smooth gradients of excitability and of cell-to-cell coupling strength, *i.e.* diffusion coefficient. In realistic simulations, the strength of these perturbations is not necessarily small enough for quantitative correspondence, still the asymptotic theory has been able to explain, on the qualitative level, some of the observed phenomena.

Figure 8 presents comparison of asymptotic theory with direct numerical simulation. Panel (a) is a fragment of simulation where the drifting spiral wave (the trajectory of the tip is shown by a thin white line) is temporarily stopped at a dark spot and then resumed the drift afterwards. A small puzzle was that the experimental data suggested that such temporary stopping could happen both near spots of higher excitability, as well as spots of lower excitability, whereas asymptotic theory predicts that if a localized perturbation of one sign is attracting then a perturbation of the opposite sign must be repelling.

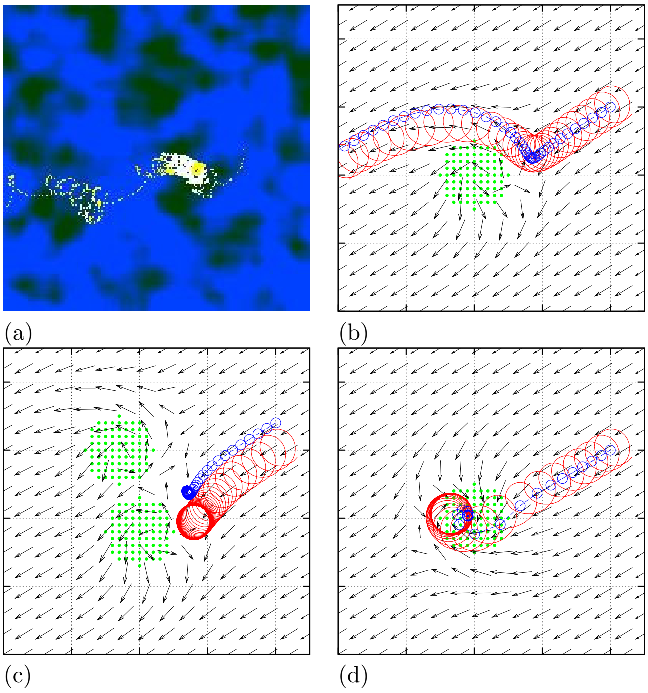


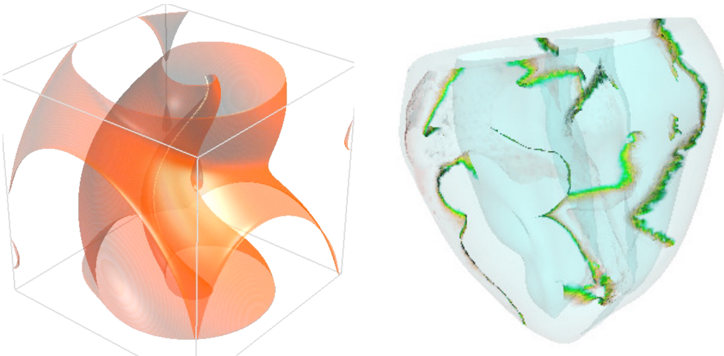
Figure 8: Pinning of drifting spiral wave to local heterogeneity.

A hypothetical explanation that repulsion may change to attraction at different distances (see discussion of "orbital motion" above), did not work for this case as the response functions in this system did not show the sign-changing character required for that. Figure 8(b) describes a hypothetical mechanism of temporary pinning at a repulsive inhomogeneity, which is consistent with the present system. In this case, the spiral drift slows down near an unstable equilibrium point, where the drift forces due to localized inhomogeneity and due to the smooth gradients equilibrate each other. Panel (c) illustrates another possibility, where two repelling circular local inhomogeneities are arranged in such a way that a stable equilibrium between now three forces exists, where the spiral can pin indefinitely (or in reality, until the smooth gradients move away due to reperfusion). Panel (d) shows for comparison the more straightforward case of pinning to an attracting heterogeneity. In panels (b–d), green dots in the middle represent the local heterogeneities, the red cyloidal line is the trajectory of the tip in the numerical simulations, the small black arrows are the direction field of the drift according to the asymptotic theory and blue open circles are the trajectories of the drift calculated based on the asymptotic theory.

4 Applications in 3D: resonant drift of scrolls and filament tension

The asymptotic theory of spiral waves in 2D can be extended to scroll waves in 3D. The instantaneous rotation center of a spiral wave becomes the filament of a scroll in 3D. So equations of motion for the spiral position $\vec{R}(t)$ and phase $\Phi(t)$ are transformed to equations of motions of the scroll wave filament $\vec{R}(\sigma,t)$ and the corresponding phase distribution $\Phi(\sigma,t)$, where σ is a coordinate along the filament. Thus we have new degrees of freedom in 3D: the filament can be curved, and the phase may vary along the filament.

Variation of scroll phase along its filament is called twist. Remember that the direction of the resonant drift of a spiral wave depends on the phase of that spiral. So if resonant forcing is applied to a twisted scroll, then "spiral waves" in different cross-sections of this scroll will have different phases and drift in different directions. This will lead to formation of a scroll with a filament of a helical shape, illustrated in figure 9(a). The picture shows a snapshot of a wavefront, defined as an isosurface of the excitation variable, more precisely its part where the recovery variable is less than a certain constant, so only the front of the excitation wave is shown but not the back. Note that as a result, the scroll as a whole does not drift anywhere, as its different parts tend to go into different directions.



(a) (b)

Figure 9: Twisted scroll with helical filament caused by resonant stimulation, (a) in Barkley system, (b) in the rabbit ventricle anatomical model with modified Beeler-Reuter kinetics [23].

The twist of the scroll in figure 9(a) was created artificially by using appropriate initial and boundary conditions. In cardiac tissue, twist may occur spontaneously due to inherent inhomogeneities of the electrophysiology of cells and anisotropy of the structure of tissue. This may result in a failure of the resonant forcing to eliminate scrolls in heart tissue. A snapshot of a simulation of resonant forcing of a fibrillatory activity in an anatomically realistic model of heart ventricles is shown in figure 9(b). Unlike panel (a), here are shown only parts of the wavefronts that are close to the filament. Technically, the wavefront is defined as an isosurface of the variable representing transmembrane voltage, which is usually understood as the excitation variable. One of the other 6 variables was chosen as the recovery variable that is often used to distinguish wave fronts from wave backs. Here the selection of the voltage isosurface pieces for visualization was done by selecting only intermediate (neither the front, nor the back) values of the recovery variable. So we may assume that depicted are the “lines of singularity”, which correspond to the tips of the spiral waves in 2D, and which rotate around the scroll filaments. Besides, we can see variations of the phase of the filament, as change of orientation of the visualized stripe of the front surface. Twist of the filament correlates with its helical shape.

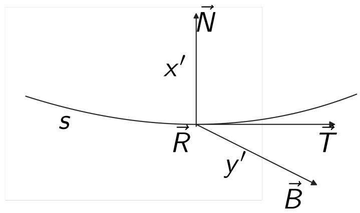


Figure 10: Frenet-Serret frame at a point of the scroll filament.

Dynamics of the filament position can be interesting in itself even without effects of twist or resonant forcing. The asymptotic motion equation can be written in terms of the Frenet-Serret frame, see figure 10, where $\vec{T}$ is the tangent vector, $\vec{N}$ is the principal normal vector and $\vec{B}$ is the binormal vector at a point of the filament with coordinate σ along the filament.

Then in the lowest order, the filament equation of motion is [26]

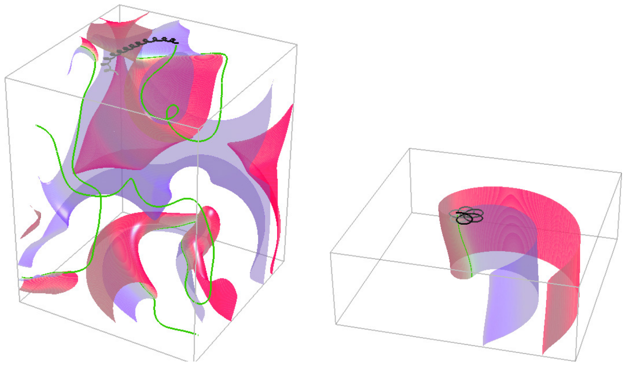
$$(\vec{N}+\mathrm{i}\vec{B})\cdot\dot{\vec{R}} = (b_2+\mathrm{i}c_3)\kappa \tag{1}$$

where $\kappa = |\partial_s\vec{T}|$ is the filament curvature, s is the arclength coordinate, so $\mathrm{d}s = |\partial_\sigma\vec{R}|\,\mathrm{d}\sigma$, and the coefficients b_2 and c_3 can be calculated using the response function. A simple property of this equation of motion is that, neglecting boundary effects, the total length of the filament satisfies

$$\frac{\mathrm{d}}{\mathrm{d}t}\int \mathrm{d}s = -\int b_2\kappa^2\,\mathrm{d}s,$$

that is, if the coefficient $b_2 > 0$, then the filament shrinks unless it is straight; and if $b_2 < 0$, then it will lengthen, and the straight filament is unstable. Thus this coefficient is sometimes called filament “tension”.

Instability of the straight filament, in a large enough volume of excitable medium, leads to constant lengthening through curving, and multiplication through break-up of scroll filaments, and can result in "scroll wave turbulence", see figure 11(a). The apparently chaotic character of this regime, and the "critical mass" phenomenon, in that a large enough volume is required for it, make it similar to cardiac fibrillation, hence a possibility that negative tension may play a role in some forms or stages of cardiac fibrillation.



(a) (b)

Figure 11: Effects of negative filament tension: (a) scroll wave turbulence in a big volume, (b) buckled scroll in a thin volume, Barkley system [24, 25].

Notably scroll wave turbulence occurs in 3D in the same equations which in 2D render perfectly stable spiral waves. Hence it is interesting, how transition from a stable 2D rotation to a 3D turbulence happens in thin sheets of excitable media, like some cardiac muscles, including human atria. Figure 11(b) illustrates one such regime, where the filament bends but only slightly, and a result of that bend is precession, showing up on the surface of the medium as a meandering spiral, whose tip describes a flower-like trajectory. A similar phenomenon was observed in a model of heart tissue [27]. This regime can be described using response functions, but higher-order asymptotics compared to those in equation (1) are required [25]. The key role in restabilizing a filament with negative tension belongs to a coefficient called "filament rigidity". There is an analogy here with mechanics of an elastic beam, so that the negative tension of the scroll filament corresponds to the compressive stress of the beam, the filament rigidity corresponds to the beam's stiffness, and the regime illustrated in figure 11(b) is similar to "Euler's buckling" of the beam.

The theory of arrhythmogenicity of retracting ischamic border zone, briefly described above, was 2D, as were the cell culture experiments on which it was based. However some real cardiac muscles, including human ventricles, are essentially 3D. The concept of filament tension is useful for consideration of possible 3D aspects, which cannot be studied in cell culture experiments, but can be simulated numerically. Two snapshots from such numerical experiments are shown in figure 12. The settings in these two experiments were exactly the same except for the value of an excitability parameter for the bulk of the recovered tissue above the retracting ischaemic boundary zone. On the left panel, the excitability is low, so that the filament tension is negative. After transition of the boundary zone, there is a scroll wave in the recovered tissue, *i.e.* in the cardiac muscle we would see a macroscopic re-entry. On the right panel, on the contrary, the excitability is higher and the filament tension is positive. As a result, since all the newly born scroll waves have filaments ending within the chaotic activ-

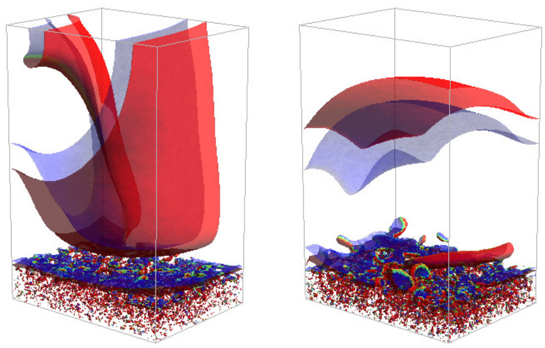


Figure 12: Effect of filament tension on arrhythmogeneity of retracting ischemic border zone. Left: negative tension. Right: positive tension [22].

ity of the moving boundary zone, these filaments are dragged down together with that zone by that tension. In the simulation in the right panel, after the passage of the boundary zone, the medium returns to the resting state, which would correspond to no re-entrant activity in the cardiac muscle.

5 Conclusion

Mathematically, the localization of the response functions of spiral waves is a special feature of the corresponding linearization operator, when the eigenfunctions of the operator and of its adjoint have very different properties and belong to different spaces. Physically this localization means that spiral waves behave like point objects, and scroll waves behave like string objects, despite their wave appearance. Asymptotic theory based on that is (within its limits) in good quantitative agreement with direct simulations. This asymptotic theory can successfully predict new qualitative phenomena (orbital motion, pinning to repelling inhomogeneity, scroll turbulence, buckling). This theory is applicable to cardiac excitation models and may have impact on clinically relevant problems.

Acknowledgements

Studies described in this mini-review have been supported through the years by: Welcome Trust grants 03881712, 045192, EPSRC grants GR/S75314/01, EP/S016391/1, EP/D500338/1, EP/D074789/1, EP/D074746/1, EP/I029664/1 (UK), Royal Society grant 2005/R4 (UK), NIH grants HL076722, HL095828 (USA), Austrian Science Fund FWF grant F3210-N18 and a travel grant of FWO-Flanders (Belgium). Experimental results shown in figure 6 were obtained in collaboration with A. Arutyunyan.

References

[1] A. M. Zhabotinsky and A. N. Zaikin. Spatial phenomena in the auto-oscillatory system. In E. E. Selkov, A. A. Zhabotinsky, and S. E. Shnol, editors, *Oscillatory processes in biological and chemical systems*, page 279. Nauka, Pushchino, 1971.

[2] M. A. Allessie, F. I. M. Bonke, and F. J. G. Schopman. Circus movement in rabbit atrial muscle as a mechanism of tachycardia. *Circ. Res.*, 33:54–62, 1973.

[3] F. Alcantara and M. Monk. Signal propagation during aggregation in the slime mold *Dictyostelium Discoideum*. *J. Gen. Microbiol.*, 85:321–334, 1974.

[4] N. A. Gorelova and J. Bures. Spiral waves of spreading depression in the isolated chicken retina. *J. Neurobiol.*, 14:353–363, 1983.

[5] B. F. Madore and W. L. Freedman. Self-organizing structures. *Am. Sci.*, 75:252–259, 1987.

[6] S. Jakubith, H. H. Rotermund, W. Engel, A. von Oertzen, and G. Ertl. Spatiotemporal concentration patterns in a surface reaction — propagating and standing waves, rotating spirals, and turbulence. *Phys. Rev. Lett.*, 65(24):3013–3016, 1990.

[7] J. Lechleiter, S. Girard, E. Peralta, and D. Clapham. Spiral calcium wave propagation and annihilation in *Xenopus Laevis* oocytes. *Science*, 252(5002), 1991.

[8] T. Frisch, S. Rica, P. Coullet, and J. M. Gilli. Spiral waves in liquid crystal. *Phys. Rev. Lett.*, 72(10):1471–1474, 1994.

[9] M. C. Cross and P. C. Hohenberg. Pattern formation outside of equilibrium. *Rev. Mod. Phys.*, 65(3):851–1123, 1993.

[10] I. V. Biktasheva and V. N. Biktashev. On a wave-particle dualism of spiral waves dynamics. *Phys. Rev. E*, 67:026221, 2003.

[11] H. Verschelde, H. Dierckx, and O. Bernus. Covariant stringlike dynamics of scroll wave filaments in anisotropic cardiac tissue. *Phys. Rev. Lett.*, 99:168104, 2007.

[12] V. N. Biktashev and A. V. Holden. Resonant drift of autowave vortices in 2d and the effects of boundaries and inhomogeneities. *Chaos Solitons & Fractals*, 5(3,4):575–622, 1995.

[13] I. V. Biktasheva, D. Barkley, V. N. Biktashev, and A. J. Foulkes. Computation of the drift velocity of spiral waves using response functions. *Phys. Rev. E*, 81(6):066202, 2010.

[14] I. V. Biktasheva, D. Barkley, V. N.Biktashev, G. V. Bordyugov, and A. J. Foulkes. Computation of the response functions of spiral waves in active media. *Phys. Rev. E*, 79(5):056702, 2009.

[15] V. N. Biktashev and A. V. Holden. Resonant drift of an autowave vortex in a bounded medium. *Phys. Lett. A*, 181(3):216–224, 1993.

[16] V. A. Davydov, V. S Zykov, A. S. Mikhailov, and P. K. Brazhnik. Drift and resonance of spiral waves in a distributed excitable medium. *Radiofizika*, 31:574–582, 1988.

[17] K. I. Agladze, V. A. Davydov, and A. S. Mikhailov. The observation of the spiral wave resonance in a distributed excitable medium. *JETP Letters*, 45(12):601–605, 1987.

[18] V. N. Biktashev and A. V. Holden. Design principles of a low-voltage cardiac defibrillator based on the effect of feed-back resonant drift. *J. Theor. Biol.*, 169(2):101–113, 1994.

[19] A. M. Pertsov and E. A. Ermakova. Mechanism of the drift of a spiral wave in an inhomogeneous medium. *Biofizika*, 33(2):338–342, 1988.

[20] V. N. Biktashev, D. Barkley, and I.V. Biktasheva. Orbital motion of spiral waves in excitable media. *Phys. Rev. Lett.*, 104(5):058302, 2010.

[21] V. N. Biktashev, A. Arutunyan, and N. A. Sarvazyan. Generation and escape of local waves from the boundary of uncoupled cardiac tissue. *Biophys. J.*, 94:3726–3738, 2008.

[22] V. N. Biktashev, I. V. Biktasheva, and N. A. Sarvazyan. Evolution of spiral and scroll waves of excitation in a mathematical model of ischaemic border zone. *PLoS ONE*, 6(9):e24388, 2011.

[23] V. N. Biktashev, I. V. Biktasheva, G. Plank, and S. W. Morgan. Resonant drift of scroll waves. In preparation.

[24] V. N. Biktashev. A three-dimensional autowave turbulence. *Int. J. of Bifurcation and Chaos*, 8(4):677–684, 1998.

[25] H. Dierckx, H. Verschelde, Ö. Selsil, and V. N. Biktashev. Buckling of scroll waves. *Phys. Rev. Lett.*, 109(17):174102, 2012.

[26] V. N. Biktashev, A. V. Holden, and H. Zhang. Tension of organizing filaments of scroll waves. *Phil. Trans. Roy. Soc. Lond. ser. A*, 347:611–630, 1994.

[27] S. Alonso and A. V. Panfilov. Negative filament tension in the Luo-Rudy model of cardiac tissue. *Chaos*, 17:015102, 2007.

Научное издание

**Proceedings of the International Conference
"Instabilities and Control of Excitable Networks:
From Macro- to Nano-Systems"**

**Труды международной конференции
«Неустойчивости в возбудимых сетях и возможности
управления ими:
от макро- к нано-системам»**

Редакционно-издательская группа:
К.Е. Злобина, А.Р. Гагарина, О.А. Дудченко

Компьютерная верстка:
А.С. Рухленко

Дизайн обложки:
И.А. Романец, А.Н. Юнусова

ICENET 2012