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DYNAMICAL APPROACH IN BIOMATHEMATICS

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Abstract A short survey of topics in biomathematics is followed by a presentation of the mathematical models from biodynamics and medicine studied by the group of nonlinear dynamics and bifurcation of one of the authors (AG). Then a systematic approach of treating these models is formulated. Open problems and topics which can be investigated by this approach are presented. The state of the art in the joint studies on hydrodynamic stability carried out by the first two authors is sketched and possible connections with the field of interest of the third author are revealed.

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1. TOPICS IN BIOMATHEMATICS

Here we discuss the mathematical models associated with biological quantities and mathematical models governing their transformations. Then we briefly present the main topics in biomathematics.

Biomathematics is a branch of applied mathematics dealing with mathematical investigation of geometric, analytical, algebraic, statistical, probabilistic etc aspects involved into the mechanical, physical, chemical phenomena or equilibria occurring in biological systems. Indeed, in order to study biological systems from mathematical point of view, with a **biological characteristic** (object), we associate a **mathematical object**. If this characteristic undergoes changes in time and/or space, this means that in the biological system a motion (change, growth, transformation, phenomenon, process, dynamics) occurs. It is unanimously assumed that the corresponding biological phenomenon is a particular physico-chimical phenomenon. As a consequence, this motion must obey the general laws of physics and/or chemistry and some specific laws and "material relationships". From this perspective, biology can be viewed as the thermodynamics of biological systems. Here by thermodynamics (also referred to as the third thermodynamics) it is understood the most general science describing the motion and including all basic disciplines and all interdisciplinary area, e.g. mechanics, physics, electromagnetism, M.H.D.,

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classical thermodynamics, chemistry. In the resulting formalism there is no place for soul or other properties specific to living systems only: every biological concept is associated with a concept from particular subdomains of thermodynamics. Naturally, every mathematical model governing a biological modification belongs to such a subdomain and in it only concepts specific to that subdomain occur. The biological aspect appears mainly during the derivation of the model and in the biological interpretation of its solution.

Once formalized mathematically, the biological model becomes a topic of mathematics and it must be studied by specific tools. However, usually, simplifying ideas of biological nature must be incorporated if the resulted model is supposed to be solved at least numerically. For example, a bone may be conceived as a particular solid and, correspondingly, its displacement and/or deformation is governed by a model from mechanics of rigid bodies, or elasticity, or, more general, thermodynamics of elastica, in dependence on the practical needs.

Another example: the blood may be conceived as a particular non-Newtonian fluid the motion of which is governed by some model of fluid mechanics, or, more general, thermodynamics of fluids.

Therefore, every mathematical model of a biological quantity and every mathematical model governing its changes are borrowed from various branches of thermodynamics of inanimate bodies (matter and/or field).

In addition, as already mentioned, with a biological quantity or biological change several mathematical models can be associated, according to the complexity and needs one has in view. For example, for some purposes, it is sufficient to assimilate a bone with a rigid body, in other circumstances a finer model of elastic medium is necessary. Similarly, the blood, urine, saliva, tears, bile, sperm, lymph, cerebrospinal liquid, prespiration, mammary secretion, amniotic liquid can be assimilated with a Newtonian fluid, or a mixture of fluids in dependence on how accurate must be described its motion.

There is a key point in choosing one mathematical model or other for a quantity characterizing a biological, chemical, physical, mechanical, economical a.s.o. system and its change (evolution). This is the energy, and, correspondingly, the energy equation, establishing a balance between the rate of change of the total internal energy of the system and the energy, power, radiation etc. For instance, for pure mechanical systems, total internal energy consists of the kinetic and potential energies and its rate of change is balanced by the power. If the heat is important in the functioning of that system, its total internal energy must contain a new energy related to heat. As a result, the rate of change of this total internal energy is balanced by the mechanical power supplemented by heat and radiation. If the system is an electrically conductor, then the definition of the total internal energy must contain an electrical component too. Correspondingly, its rate of change is balanced by the former terms supplemented by an electrical power. Any time that the energy equation was not true, in the sense that the balance did not hold, it meant that the total internal energy was not defined suitably. It must contain a new part and, correspondingly, a new "power" must occur in the energy equation.

Some biochemists assert and some medical evidence plead for a specific energy for living bodies, but no mathematical model exist for it. This is why we frame our study in the thermodynamics.

In thermodynamics the geometric model (of a material system (substance)) is a continuum. There is an alternative geometric model, namely a totally discrete (disconnected) set. Correspondingly, there is another science dealing with the phenomena occurring in these systems: statistical physics (chemistry etc). There exists a connection between thermodynamics and statistical physics. In this paper we limit ourselves to thermodynamics.

There is a huge number of topics treated in mathematical biology. They are grouped in: mathematical biology in general; physiological, cellular and medical topics; genetics and population dynamics.

The second group treats: biophysics, biomechanics (including biomechanical solid mechanics), developmental biology, pattern formation, cell movement (chemotaxis etc.), neural biology, physiology (general), physiological flows (included in biological fluid dynamics which, in addition, treats biopropulsion in water and in air and other topics), cell biology, biochemistry, molecular biology, kinetics in biochemical problems (pharmacokinetics, enzime kinetics etc., related to chemical kinetics, reaction effects in flows, chemically reacting flows), medical applications, biomedical imaging and signal processing (related to Radon transformation, integral transforms, signal theory), medical epidemiology, plant biology.

The third group treats: genetics (related to genetic algebras), problems related to evolution, protein sequences, DNA sequences, population dynamics, epidemiology, ecology, animal behaviour.

In our opinion, due to the huge diversity of the biosphere, this enumeration reveals only a small part of the possible and necessary topics, namely those which at the time being are of interest for applied mathematicians, physicists and chemists. For others the association of the biological quantities and biological changes with mathematical models is not yet available.

An important conclusion for someone wishing to deal with mathematical biology is, first, to learn about the topics treated by thermodynamics and, second, to fix her/his biological objectives requiring a specific branches of thermodynamics. The first two authors of the paper are fluid dynamicists, therefore they fulfill the first requirement. The third author is a pure mathematician (geometer). Together, we attempt to study dynamics and bifurcation in mathematical models describing various aspects of the cancer.

Finally, we quote the **main subjects** dealt with in a few treatises of mathematics, some of them general, some others concerning only a narrower topic: continuous or discrete population models for single species, continuous models for interacting populations, discrete growth models for interacting populations, reaction kinetics, biological oscillators and switches, Belousov-Zhabotinskii reaction, perturbed and coupled oscillators and black holes, reaction-diffusion, chemotaxis and nonlocal mechanisms, oscillator generated wave phenomena, biological waves (single species models or multi-species diffusion models), travelling waves in reaction-diffusion systems with weak diffusion (analytical technique), spatial pattern formation with reaction/population interaction diffusion mechanisms, animal coat patterns and other practical applications of reaction-diffusion mechanisms, neural models of pattern formation, mechanical models for generating pattern and form in development (including morphogenesis, formation of microvili, cartilage formation), epidemic models and the dynamics of infections diseases, geographic spread of epidemics [1].

To **narrower topics** separate textbooks and proceedings are dedicated. An example is biological and biochemical oscillators [2] including : oscillatory behaviour, excitability, and propagation phenomena on membranes and membrane-like interfaces, stability properties of metabolic pathways with feedback interactions, damping of mitochondrial volume oscillations by propanolol and related compounds, glycolytic oscillations, oscillations in tissues, oscillations in growing cell populations, circadian oscillations.

The large diversity of biological phenomena was described in an enormous number of papers. We estimate this number of order of milions if we take into account that only to cancer more than 1.600.000 works are devoted. Usually, the books are published in series like Lecture Notes in Biomathematics [3] or Biomathematics [4]. A lot of books or chapters treating biological phenomena can be found in series in life sciences [5], or synergetics [6], or chemistry, or physics etc., or even applied mathematics [7].

This is due to the fact that, as we show in Section 2, the equations governing various types of phenomena (mechanical, physical, chemical, economical etc.) are derived from a common trunk and, when approximated, these equations are the same for several distinct phenomena. Indeed, the first approximations contain the same expansion functions. The difference occurs in the coefficients. In particular, frequently, the governing models in biology are presented together with models in economics, e.g. the Goodwin model, the Gompertz model. The Lotka-Volterra models are common to some phenomena in biology and chemistry; the Hodgkin-Huxley model is used in physiology and electric circuits. They are among the simplest and are derived as a result of severe approximations. Of course, the more simplifying hypotheses are assumed, the simpler and applicable to a more general domain are the resulting approximate equations. The largest number of papers on biological phenomena are short papers and they are spread through the existing journals. Only a few of these journals are devoted to biomathematics, e.g. [9], [10]. Most of them are devoted to other domains (especially physics, chemistry and applied mathematics) but contain applications to biology too.

The level and type of mathematics involved in these papers range from the heuristical and elementary mathematics till the most advanced achievements of (the conglomerate called) global analysis. We are interested in those mathematical treatments of models of biodynamics involving (ordinary or partial) differential equations and using techniques of dynamical systems theory and (static, imperfect and dynamic) bifurcation theory.

This paper was conceived as an address to scientists of various orientations willing to form a group intended to carry out analytically, numerically and experimentally some applications of biomathematics in medicine. This group must contain at least applied mathematicians and physicists.

2. MATHEMATICAL MODELS IN BIODYNAMICS

First, one of the most general models of thermodynamics is described. Then the particular models treated by the group of the first author are presented.

One among the most general models governing equilibria and motion of material systems (substances and fields), geometrically modelled as (mathematical) continua $\Omega \subset \mathbf{R}^3$ consists of some differential equations [11], referred to as global equations of motion

$$\frac{d}{dt}G(t,\Omega') = \Phi^G + p^G + s^G, \quad t \in \mathbf{R}, \quad \forall \Omega' \subset \Omega$$
(1)

constitutive equations (of material), which can be algebraic, differential, integral, integro-differential or, more general, functional

$$\Phi^G = \Phi^G(G),\tag{2}$$

constraints imposed by physical (generically speaking) reasons, e.g.

$$C(G) < 1 \tag{3}$$

initial conditions

$$G(0, \Omega') = G_0(\Omega'), \quad \forall \Omega' \subset \Omega$$

and boundary conditions

$$G_{|\partial\Omega} = G_W,\tag{5}$$

where $G(t, \Omega')$ is a global quantity, e.g. the mass, and it is a function of the time t and the subdomain Ω' of the domain Ω (occupied by the physical system (body)). The equation of motion (1) is a balance equation which shows that

the rate of change of the global quantity G is balanced by the sum of the flux Φ^G of the quantity G through the frontier $\partial\Omega'$ of Ω' , the production p^G of G and the supply s^G of G due to external influences on the part of the system from Ω' . If $p^G = 0$, then the balance equation is said to be a *conservative equation*. The terms in (1) are scalars, e.g. the mass, energy, entropy, or vectors, e.g. momentum, momentum of momentum. Equation (1) models a physical (biological) law, e.g. the second law of Newton, the mass balance or conservation, the total internal energy conservation. The components of (1) are present in all phenomena; of course, some of them can vanish for particular cases. Therefore the equation (1) is the common trunk leading to similar mathematical solutions and, correspondingly, to similar (in some nonevident always) aspects of the modeled phenomenon.

The superscript G shows that for each G, specific Φ^G , p^G and s^G correspond. For instance, if G is the mass, Φ^G , p^G and s^G are the mass flux, mass source and supply of mass respectively. In the case of a mechanical system, if G is the angular momentum, Φ^G , p^G and s^G are the stress terms, zero, and the body force. If G is the total internal energy and the system is mechanical, then $G = E_c + E_p$, where E_c and E_p are the kinetic and potential energy, respectively and $\Phi^G = p^G = 0$, while s^G is the power of the forces acting on the system. If the system is physical and is heat conducting, then $G = E_c + E_p + E_h$, where E_h is part of energy due to heat and Φ^G is the heat flux, $p^G = 0$ and s^G contains supplementary terms due to radiation. If the system is electromagnetic, then, apart from these quantities, influences of the electrical and magnetic fields must be considered. We already remarked that if the system is biological, this system.

In additional assumptions on the regularity of the functions occurring in equations (1), these equations become partial differential equations. For further simplified assumptions, equations (1) can become ordinary differential equations. For instance, in many cases the mass can be written as $m(t, \Omega') = \int_{\Omega'} \rho(t, \mathbf{x}) d\mathbf{x}$, where ρ is the mass density, the momentum can have the expression $\mathbf{M}(t, \Omega') = \int_{\Omega'} \rho(t, \mathbf{x}) \mathbf{u}(t, \mathbf{x}) d\mathbf{x}$, the total internal energy reads as $E(t, \Omega') = \int_{\Omega'} \rho(t, \mathbf{x}) \frac{\mathbf{u}^2}{2}(t, \mathbf{x}) + e(t, \mathbf{x}) d\mathbf{x}$, where $\mathbf{u}(t, \mathbf{x})$ is the velocity at the time t and point \mathbf{x} and e is the internal energy. The quantities ρ , \mathbf{u} and e are fields and they are called local quantities. In the adopted formalism [11], the internal energy (it is in e that possible types of energies, other than those from the inanimate world, would appear. But in this case, other global quantities, specific only to living systems, must be introduced). In regularity conditions for ρ , \mathbf{u} and e the global conservation equations (1) for the mass momentum and energy in a fluid system become local equations, namely

partial differential equations, valid for every $t \in \mathbf{R}, \mathbf{x} \in \Omega$,

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \mathbf{u}) = 0, \tag{6}$$

$$\frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \nabla \mathbf{u} = \frac{1}{\rho} \nabla \cdot \mathbf{T} + \frac{1}{\rho} \mathbf{F},\tag{7}$$

$$\frac{\partial e}{\partial t} + \mathbf{u} \cdot \nabla e = \frac{1}{\rho} \nabla \cdot \mathbf{q} + \mathbf{u} \cdot \frac{1}{\rho} \mathbf{F},\tag{8}$$

where in (7) and (8) we took into account (6), and (6) and (7) respectively, **T** is the stress tensor, **F** is the body force and **q** is the heat flux. If the fields ρ , **u**, e, **T**, **F** and **q** are homogeneous, i.e. they do not depend on **x**, then (6), (7) and (8) become the ordinary differential equations $\frac{d}{dt}\rho = 0$, $\frac{d}{dt}\mathbf{u} = \mathbf{F}$, $\frac{d}{dt}e = \mathbf{u} \cdot \mathbf{F}$, i.e. the equations characteristic to the rigid motion (the constant ρ was included in **F**). The first equation shows that the fluid is incompressible, the second equation is the Newton equation where **F** is the resultant of the forces acting upon the system and the third equation is the energy equation from mechanics of rigid bodies. These equations degenerate into algebraic equations characteristic to equilibria when **u** and *e* do not depend on time either.

More general, (1) become ordinary differential equations if the global quantities are homogeneous fields. This is the case of most equations in biomathematics. With them finite-dimensional dynamical systems are associated and their study, analytical as well as numerical, is easier than in the case of partial differential equations.

The equations (6), (7) and (8) (and, in general, (1)) are formally the same for any type of fluids (systems), which can have the property of having the momentum flux of the form $\mathbf{T} \cdot \mathbf{n}$, where \mathbf{n} is the outer normal to Ω' . The difference between various fluids, e.g. the blood, urine or amniotic fluid is mathematically specified by the constitutive equations connecting the fluxes and the global quantities, e.g. excitation and response. For instance, the stress in the blood depend on $\mathbf{D} = [\nabla \mathbf{u} + \nabla \mathbf{u}^T]/2$, the velocity of deformation tensor, as well as some of its derivatives, while the urine can be suitably modeled by $\mathbf{T} = -p\mathbf{I}$, where \mathbf{I} is the unit tensor and p is the static pressure. In general, in (2) $\Phi^G(G)$ are some operators, e.g. differential, integral or functional of the quantities G. These operators cannot be arbitrary; they must obey at most five principles, e.g. objectivity, isotropy. As a result the form of (2) simplifies and (2) become algebraic relationships relating the fluxes (e.g. \mathbf{T} , \mathbf{q} , e) to \mathbf{D} and other basic quantities and some of their derivatives.

In the constitutive equations and in the constitutive expressions for the fluxes (called the constitutive functions) the coefficients are functions of the temperature T and ρ or T and p taken at equilibrium. Their form is referred to

as the equations of state, e.g. for energy, entropy. The classical thermodynamic equation of state connects ρ , T, p, e.g. the Gay-Lussac equation.

Consequently, the material is characterized mathematically by constitutive equations and state equations. In the inanimate world the occurring coefficients are measured experimentally or are deduced from the statistical associated models. In living bodies it is only rarely possible to measure these coefficients. For instance, in order to characterize what kind of material is a tumor in its formation and development, when the quoted constitutive equations depend on the time too, we must know how look these equations and so, which are the numerical values of their coefficients.

The constraints (3) are related to the type of the physical, biological etc. quantity. For instance, the concentration cannot be greater than 1, the density is always positive.

The initial conditions (4) connect the phenomenon at the actual time to the past while the boundary conditions liberate the system existing in Ω from the exterior. In a more complex modeling the coefficients in the constitutive equations depend on the time derivative of u and other basic quantities. In this case we say that the *material has a memory*. We think that, in most of the circumstances, the living organs in a body or living beings are materials with memory.

We exemplify these by a few Cauchy problems for some systems of first order ordinary differential equations describing biological phenomena, which were studied by the first author group.

The FitzHugh-Nagumo (F-N) model, the mostly investigated by us, is the Cauchy problem [13], [12]

$$\dot{x}_1 = c(x_1 + x_2 - x_1^3/3 - A\cos\omega t), \quad c\dot{x}_2 = -(x_1 + bx_2 - a), \quad x_1(0) = x_1^o, x_2(0) = x_2^o$$
(9)

where $\cdot \equiv d/dt$, t, the time, is the independent variable, $x, y : \mathbf{R} \to \mathbf{R}$, x = x(t), y = y(t) are the unknown functions, a, b, c, A and ω are real parameters. The problem (9) is also called the Bonhoeffer-Van der Pol (BVP) model and describes the electrical behaviour along a neuronal membrane subject to the action of a periodic external stimulus. It also governs the initiation of the heart beats and follows from the reaction-diffusion equations governing the wave propagation in excitable media

$$\epsilon \frac{d}{dt}x_1 = \epsilon^2 D_1 \bigtriangleup x_1 + f(x_1, x_2), \quad \frac{d}{dt}x_2 = \epsilon^2 D_2 \bigtriangleup x_2 + g(x_1, x_2) \tag{10}$$

where D_1 and D_2 are the transport coefficients, f and g are reaction terms and ϵ is some parameter. In the case of the cardiac muscle x_1 is the electrical potential. FitzHugh derived (9) from the four-dimensional experimental model of Hodgkin and Huxley and put it as the basis of the axon physiology. The problem (9) generalizes the electrical Van der Pol oscillator. If x_1 and x_2 do not depend on space variables and $f(x_1, x_2) = x_1 + x_2 - x_1^3/3$, and $g(x_1, x_2) = -(x_1 + bx_2 - a)$, the system (10) reduces to (9), for the case of $A = \omega = 0$, i.e. when the forcing is absent.

Mainly we dealt with the case without forcing [12], [13], which, for a, b and c fixed, generates a two-dimensional dynamical system. The static and dynamic bifurcation diagrams were determined by analytic [12], [13] and numerical [14] methods. Two asymptotic dynamics as $\mu = c^{-2} \rightarrow 0$ and (a, b) is very close to the curve of the Hopf bifurcation values were studied analytically and numerically [15]. The attention was focused on the relaxation oscillations of the heart and oscillations in two and three times, related to concave limit circles (French canards). When the forcing is present, the dynamical F-N system is three-dimensional. In this case, for specific situations, the chaotic dynamics was studied by reducing the continuous dynamics to a discrete one [13] and by treating numerically the resulting discrete dynamical system [16].

In [17] the static, dynamic and perturbed bifurcation was studied for the Gray-Scott model

$$\dot{u} = a(1-u) - uv^2 - bu, \quad \dot{v} = a(c-v) + uv^2 + bu - dv,$$
 (11)

where the unknown functions u and v are the concentrations of the two reactants, while the parameters a, b, c and d are related to the sedimentation time, noncatalyzed conversion, influence of the catalyzer and rate of decomposition of the catalyzer respectively. The Cauchy problem for (11) governs a chemical reaction in the presence of the noncatalyzed enzymes.

Two models in oncology are dealt with in [18]. The first is the lymphocytestumor model

$$\dot{x} = \alpha x - xy, \quad \dot{y} = xy - (y/\alpha) - kx + \sigma, \quad x(0) = x_0, y(0) = y_0, \quad (12)$$

where the unknown functions x and y represent the number of malign cells and the number of lymphocytes, respectively and the real parameters α , k and σ are related to the coefficients of the rates of change of the cells (action of the immunitary system on the malign cells), the natural death of the malign cells and the tumor surface interacting with lymphocytes, diffusion of lymphocytes. In the case of a treatment, the number of unknown functions and parameters increases. The second model is a immuno-tumoral model

$$\dot{x} = -x - x^2 + xy, \quad \dot{y} = -(e+b)x + ly - ex^2 + (l+c)xy - b, \quad x(0) = x_0, y(0) = y_0, \quad (13)$$

where the state functions x and y represent the free lymphocytes situated on the tumor surface and the total number of tumoral cells. The parameters have meanings similar to those in (12). For both these models the static and dynamic bifurcation diagrams were determined analytically and the results were represented graphically. It was found that the large number of parameters

leads to notable difficulties of the theoretical study and the graphs must be based on the perturbed bifurcation theory. These two features are common to the majority of mathematical models of cancer, which explains the existence of a small number of papers devoted to rigorous mathematical treatment in the field, in spite of the huge quantity of studies devoted to the topic. Keeping only a few parameters means a poor model of the cancer, its evolution and its treatment.

A form specific to biochemistry of a balance equation is the mass action law: the velocity of reaction is a sum of two terms. The first is proportional to the product of the concentrations of the reactants while the second is proportional to the product P of the biochemical reaction. More exactly, the rate of change of the concentrations c_1 and c_2 of the reactants has the quoted properties. Therefore the mathematical model of this law is [17]

$$\dot{c}_1 = -k_1c_1c_2 + k_{-1}p, \quad \dot{c}_2 = -k_1c_1c_2 + k_{-1}p, \quad \dot{p} = k_1c_1c_2 - k_{-1}p.$$
 (14)

An extensive list of references on the mathematical models in biodynamics can be found in [19].

3. DYNAMICS AND BIFURCATION IN SOME BIOLOGICAL MODELS

The synthetic results on the dynamics and bifurcation associated with the Cauchy problem $\mathbf{u}_{t=0} = \mathbf{u}_0$ for the differential vector equation

$$\mathbf{u} = \mathbf{f}(\alpha, \mathbf{u}) \tag{15}$$

are presented in the form of static, imperfect and dynamic bifurcation diagrams. Let us present the main steps to obtain them.

The static bifurcation diagram (sbd) is a graphical representation of the stationary solution set $\mathbf{u}(\alpha)$ in dependence on the (scalar or vector) parameter α .

If dim $\mathbf{u} + \dim \alpha > 3$, then only sections in this diagram can be represented. But, in this case, the problem of finding all nonequivalent sbd's arises. This problem is solved by considering one component, say $\alpha_1 = \lambda$, of α as a control parameter, all others being assumed small. In addition, λ is supposed to vary near some value λ_0 , usually taken as equal to zero. Denote $\tau_1 = \alpha_2, \dots, \tau_m = \alpha_{m+1}$. Then the sbd existing for $\tau \equiv (\tau_1, \dots, \tau_m) = \mathbf{0}$ is deformed when τ vary in a neighborhood of $\mathbf{0}$. If the number m of the small scalar parameters is smaller than 5, then only a finite number of nonequivalent sbd's exist. Correspondingly, in the small parameter space τ there are some manifolds \mathcal{B}, \mathcal{H} and \mathcal{D} separating some zones. All sbd's corresponding to all τ from one zone are equivalent. Therefore, up to this equivalence, in each zone some bifurcation diagram persists and, consequently, it suffices to draw a single sbd. Then the *imperfect* or (*perturbed*) bifurcation diagram (ibd) consists of these zones and the corresponding one sbd in each of them.

The dynamic bifurcation diagram (dbd) is similar to the ibd. The parameter space is divided into zones (strata) such that the dynamical systems (of a dynamical scheme, i.e. family of dynamical systems) corresponding to the points (parameters) belonging to one zone are topologically equivalent. Then the phase portrait of one dynamical system corresponding to a point in each zone suffices to characterize topologically the dynamic behavior for the entire zone. The configuration represented by strata is called the *parameter portrait*. The dbd consists of the parameter portrait and one phase portrait for each stratum.

A combined dynamics and bifurcation study proceeds in several steps [20]: the stationary solutions (corresponding to equilibria of the dynamical system associated with (15)) are deduced; for each equilibrium the linearized system around that point is written; the eigenvalues are computed. If the real part of all eigenvalues are non null, then the equilibrium is hyperbolic and, by Hartman-Grobman theorem, the nonlinear dynamical system is locally equivalent to the linearized dynamical system. In this case no other study is necessary; if at least one eigenvalue has a null real part, then the equilibrium $\overline{\mathbf{u}}$ is non hyperbolic. Assume that we are in the two-dimensional case for \mathbf{u} and assume that $\overline{\mathbf{u}}$ corresponds to $\overline{\alpha}$; let us transform \mathbf{u} and α such that $\overline{\mathbf{u}}$ and $\overline{\alpha}$ are carried at the origin; let us form the problem (15) for $\overline{\alpha}$, called the problem at the point; determine the normal form for the problem (15) at the point; this form indicates which are the corresponding miniversal unfoldings. We determine them by means of the existing theories; let us perform the same study around each non-hyperbolic point; during these investigations some important manifolds occur(the manifold S of the double equilibria, the manifold $\mathcal{H}_{\mathbb{C}}$ of the Hopf bifurcation values, the manifold Q of the double zero eigenvalues (i.e. of the Bogdanov-Takens bifurcations), the manifolds B-T of the homoclinic bifurcations, the manifold B_a of the Bautin bifurcation, manifolds of degenerate bifurcations). All these manifolds are separating in the parameter space the so-called strata. The configuration of strata represents the parameter portrait; for one point of each stratum the phase portrait is represented; if the mentioned manifolds are complicated in geometrical structure, the manifolds \mathcal{B}, \mathcal{H} and \mathcal{D} are determined. These manifolds are extra strata in the parameter portrait.

All these steps were used systematically in the studies of the first author's group, in the hope to realize as complete an analysis as possible, using all existing theoretical and numerical approaches. These studies ended by publication of research monographs devoted to a single or at most two models. Later on, it was proved that other new directions of research arose even for the very minutely investigated models. Presently, a lot of open problems re-

vealed are waiting for their solution: the asymptotic behavior for the parameter portrait and the corresponding phase portraits; the perturbed bifurcation diagrams for the above-mentioned manifolds; global bifurcations; the geometric and mechanics classification of the periodic oscillations; the degenerated bifurcations; the French canard phenomenon etc.; for the three-dimensional case the presence of chaos is probable and a systematic and complete study is not conceivable in general.

4. THERMAL CONVECTION

The collaboration of the first two authors in the framework of hydrodynamic stability theory, developed during the last 16 years, mainly concerned the derivation of stability criteria for mechanical equilibria of fluid layers, which can be a premise for interesting applications to biological fluid dynamics. Their studies were devoted to complex fluids subject to several physical influences (thermal, electrical, magnetic fields, concentration, porosity, compressibility, non Newtonicity). Variational methods (extending some of the existing ones), Fourier series combined with backwards integration techniques and a direct method based on the characteristic equation were frequently used in these studies [21].

For most of the fluid flows of interest in real-world applications, the direct use of the methods of functional analysis lead to results very unsatisfactory for users. This is due, in principle, to the fact that some changing-sign terms are estimated by their norm. In addition, some physical effects disappear by projection (and, so, symmetrization of some operators) on the problem spaces. These types of problems remain for dozens of years as a challenge for fluid dynamicists. Such a problem was solved by us by means of several ideas (borrowed from simpler cases of ode's): a change of the governing problem is necessary before applying to it the projection; this change must contain several parameters to be chosen so that the remained symmetric operators preserve all physical parameters; the changing-sign terms must be included in sign-preserving terms by suitable definition of the Liapunov functional; it is necessary an optimal change of the parameters for stability bounds as well as for the simplicity of usually cumbersome computations. Thus, the problem governing the nonlinear stability of the mechanical equilibrium of a horizontal layer Ω of a binary fluid mixture subject to two competing effects temperature and concentration when the Soret and Dufour thermodiffusive currents are present reads [21]

$$\frac{\partial \mathbf{v}}{\partial t} + \mathbf{v}\nabla\mathbf{v} = -\nabla p + (\mathcal{R}\theta - s\mathcal{C}\gamma)\mathbf{k} + \Delta\mathbf{v},$$
$$P_r\left(\frac{\partial\theta}{\partial t} + \mathbf{v}\cdot\nabla\theta\right) = (1 + N\lambda^2\tau^{-1})\Delta\theta + \mathcal{R}\mathbf{v}\cdot\mathbf{k} + N\lambda\sigma\Delta\gamma, \quad (t,\mathbf{x}) \in (o,\infty) \times \Omega,$$

$$S_c \left(\frac{\partial \gamma}{\partial t} + \mathbf{v} \cdot \nabla \gamma \right) = \Delta \gamma + \lambda \sigma^{-1} \tau^{-1} \Delta \theta + \mathcal{C} \mathbf{v} \cdot \mathbf{k}, \tag{16}$$

where t is the time, $\mathbf{v}, \theta, \gamma$ are perturbed velocity, temperature and concentration unknown field, while $R, \mathcal{C}, s, P_r, N, \lambda, \tau, \sigma, S_c$ are physical parameters. Boundary conditions and the requirement of the solenoidality are imposed energy method yielding results much better than the existing ones.

An inspired handling with algebraic (Young) and integro-differential (Poincaré) inequalities made possible the improvement of the Navier-Stokes spectrum of the bounds for the model [23]

$$\frac{d\mathbf{v}}{dt} + \widetilde{A}\mathbf{v} = R(v),\tag{17}$$

where $A\mathbf{v} = A\mathbf{v} + M_{\mathbf{u}}\mathbf{v}$, A is related to the projection of the Laplacian on the space N of solenoidal vectors (17), $M_{\mathbf{u}}$ is the projection on N of the linearization of the advective nonlinear term in the Navier-Stokes equations about the basic vector fields \mathbf{u} , and R is the projection on N of the nonlinear advective term in perturbation velocity \mathbf{v} .

The assumption of normal mode perturbations transformed the pde's into ode's and the boundary conditions became two-point conditions. The trace of the complexity of the fluid and physical effects can be pursuited in the very high order of differentiation in the ode's and in the presence of physical parameters. The complexity of flow can be viewed in the complicated boundary conditions. An example of such a two-point eigenvalue problem is

$$\left[\left(D^2 - a^2 \right)^2 - M^2 D^2 \right] \left(D^2 - a^2 \right) w - b_1 a^2 w = 0, \ z \in [-0.5, 0.5],$$
$$W = DW = \left[\left(D^2 - a^2 \right)^2 - M^2 D^2 \right] w = 0, \ \text{at} \ z = \pm 0.5.$$
(18)

where W(z) is the unknown function and a, M, b_1 are physical parameters. By adapting the direct method in the theory of ode's to, in [24] was determined the secular equation. False secular points, not detected by a straightforward application of a numerical method, were found by a bifurcation analysis of the characteristic manifold.

It is in these bifurcation problems and in the study of dynamics generated by ode's possessing several parameters that the third author can help the first ones. The geometric forms involves are extremely complicated; some of them are fractals. Therefore a specialist in fractal geometry, integral geometry and computation geometry is necessary.

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