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Mathematical Physics of Living Systems

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MOBILITY 1

Magneto-elastic instabilities in soft actuators

Jacopo Ciambella
Sapienza, Università di Roma, Italy

Development of micro- and nano-scale swimmers has become an area of interest in recent years due to the potential these systems have in transforming drug delivery systems, lab-on-chip devices and also cultivating new methods for performing micro-surgery and nano/micro fabrication. The main focus of research in this area has been based on the development of helical micro-swimmers that are propelled through the water using rotating magnetic fields, these systems show promise due to them having good steering ability and the potential to achieve high propulsion speeds. Biomimicry of aquatic propulsion has also led to the development of electro-active polymers that mimic the actuation surfaces of fish, with controlled bending and twisting configurations achievable and determined by the placement of electrodes on the surfaces. Other systems use alternative propulsion techniques such as chemical reactions, bubble oscillation and bacteria mimicry. Although these devices all show promise, there are still difficulties in developing swimmers that are easy to fabricate and reproduce, as well as being bio-compatible for use in the bio-medical field.

In this talk, we introduce a nonlinear model for magneto-elastic rod-like structures which is used to describe the experiments carried out by the authors on Polydimethylsiloxane (PDMS) films reinforced with short Nickel-coated Carbon Fibres (NiCF). The experimental results show the presence of an instability controlled by the magnetic torque, as predicted by the introduced model. The composite films undergo a transition from a bending-only deformed configuration for the 0 degrees fibre specimen, to a twisting-only configuration, achieved for fibres at 90 degrees, whereas all the intermediate angles show both bending and twisting. This behaviour mirrors that which is used to propel a selection of marine mammals.

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MOBILITY 2

Elastic rods and motility: two case studies.

Giancarlo Cicconofri
SISSA, Italy

In this talk I will present the key results from two studies on bio-inspired model locomotors: a snake-like flexible robot [1], and a flagellar microswimmer [2].

The snake-like robot is modeled as an active elastic rod. We will consider the motion of this system under two constraints: inside closely fitting channels, and on frictional surfaces where lateral slip of the rod is not allowed (but longitudinal sliding is). I will demonstrate the solvability of the equations of motion of the system in both cases. The propulsion mechanism of the system will be discussed.

For the flagellar microswimming study, we will consider a robot model made of a spherical cargo with a passive elastic tail attached to it (the flagellum). The swimmer is immersed in a fluid, swimming at low Reynolds number regime. The swimmer can flap its tail by controlling the angle of attachment with the cargo. I will address what, in control-theoretical terms, can be called the controllability of the system: given a generic periodic input for the controlled angle, I will show what is the resulting output in terms of motion of the body frame of the cargo.

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MOBILITY 3

Modeling of Carangiform Swimming

Michele Curatolo
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We reproduce the key features of carangiform swimming by modeling muscle functioning using the notion of active distortions, thus emphasizing the kinematical role of muscle, the generation of movement, rather than the dynamical one, the production of force. This approach, already proposed to model the action of muscles in different contexts, is here tested again for the problem of developing an effective and reliable framework to model and simulate swimming. We highlight the muscle function during fish locomotion describing the activation of muscles and the relation between the force production and the shortening–lengthening cycle of muscle. We found a great accordance between results and empirical relations, giving an implicit validation of our models.

MOBILITY 4

Biological and bio-inspired motility at microscopic scales

Antonio De Simone
SISSA, Italy

MOBILITY 5

Basic preliminaries to the biomechanical modelling of worm motility

Antonio Di Carlo
CECAM-IT-SIMUL Node, Director, Italy

In this talk I wish to discuss the peculiar features that make the study of worm motility both challenging and attractive, from the evolutionary, biological, and physical points of view. I will also sketch the basic theoretical ingredients of an actuatable soft rod model, meant to be applied to the simulation of the diverse regimes of worm locomotion. All of the above is preliminary to the development of a research programme joint with one of the meeting organisers (DA), which we started leisurely about one year ago and is obviously lagging far behind schedule.

MOBILITY 6

A cortex flow model for the craving motility of leukocytes

Christian Schmeiser
Universitat Wien, Austria

Rearward actin flow is observed in leukocytes crawling through artificial confined channels. A new model for cortex flow induced by the insertion of material at the protrusive side has been derived. In simulations it reproduces the motility behavior observed in experiments.

CELLS 1

Blood flow in venules: a mathematical model

Angiolo Farina
Università di Firenze, Italy

We study the blood flow of through vessels provided with valves ensuring a unidirectional motion and whose walls are animated by periodic peristaltic waves. The ultimate target is to describe the phenomenon of vasomotion, consisting in periodic oscillations of blood vessels walls which is particularly important for the blood flow in veins. We formulate a mathematical model based on approximations of the flow equations due to the smallness of the radius-to-length ratio.

CELLS 2

Influence of mechanical properties on cell migration and extracellular-matrix invasion.

Chiara Giverso
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The key factors for cell migration on flat substrates are the dynamic adhesion of cells on it via the expression of adhesive molecules (mainly integrins) and the generation of the force necessary for propulsion by contraction of the cytoskeleton. These are also the basic "ingredients" in the process of migration inside three-dimensional environments. However, in this case, the migratory and invasive process is associated with significant cell deformation while passing through constricted openings of the ECM, especially when the production of proteolytic enzymes is inhibited.
The introduction of microscopic mechanical properties of cells and subcellular structures into continuum macroscopic models of cell migration are therefore of fundamental importance in order to make a step towards a more comprehensive representation of tissue invasion.
Treating the nucleus as an elastic body covered by an elastic membrane, we formulate a mathematical model for a single cell entering cylindrical channels composed of extracellular matrix fibres.
The model leads to the definition of a necessary criterion for cells to pass through a regular network of fibres, depending on the traction forces exerted by the cells (or possibly passive stresses), the stretchability of the nuclear membrane, the stiffness of the nucleus, and the ratio of the pore size within the extracellular matrix with respect to the nucleus diameter.
The results obtained at the cell scale highlight the importance of the interplay between mechanical properties of the cell and microscopic geometric characteristics of the extracellular matrix and give an estimate for a critical value of the pore size that represents the physical limit of migration.
This critical value can finally be incorporated into a continuum macroscopic equation able to describe the process of cell aggregate invasion and segregation inside thick regions of extracellular matrix.

CELLS 3

Force Dependent Positioning of Myonuclei in Multinucleated Muscle Cells

Angelika Manhart
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The nucleus is the defining organelle in eukaryotic cells. Muscle cells contain several to several hundreds of myonuclei, which need to be positioned regularly to keep the muscle healthy. Positioning mechanisms most likely involve asters of microtubules emanating from the nuclei, as well as associated motors. Using a systematic force screen based on distance dependent forces, we discovered two candidate models that can explain the observed data in *Drosophila* larvae. Using bifurcation analysis I will discuss their properties and compare their predictions with detailed stochastic simulations performed in Cytosim. Joint work with Stefanie Windner, Mary Baylies and Alex Mogilner.

CELLS 4

A mechanical theory for cell contact inhibition

Pierre Recho
Universite Joseph Fourier, Grenoble, France

In this talk, we will show how a simple model of cell propulsion driven by cytoskeletal contraction provides a mechanical explanation for cell spontaneous polarization as well as cell contact inhibition; a process during which two cells enter in contact and subsequently repolarize and move apart from each other.

CELLS 5

Live cell motility under the FBLM-FEM prism: from numerical convergence to cell-cell adhesion

Nikolaos Sfakianakis
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The lamellipodium is a thin, sheet-like structure that is found in the propagating front of fast moving cells, such as fibroblasts, keratocytes, cancer cells, and more. It is a dense network of linear biopolymers of the protein actin, termed actin-filaments. These actin-filaments are highly dynamic structures that constantly polymerize by addition of new monomers on their one end, and participate in a plethora of other processes such as nucleation, capping, fragmentation, and many more.

These processes are important for the structure and functionality of the lamellipodium, and the motility of the cell. They are to a large extent affected by the extracellular environment; for example, the chemical landscape in which the cell of resides and the local composition and architecture of the Extracellular Matrix (ECM), lead to biased motility responses of the cell that are typically termed as chemotaxis, haptotaxis, and durotaxis.

In this talk, we present the main elements of the Filament Based Lamellipodium Model (FBLM); an anisotropic, two-phase, two-dimensional, continuum model that describes the dynamics the lamellipodium at the level of actin-filaments and their interactions. The FBLM was first proposed in [1] and later extended in [2,4]. When endowed with a problem specific Finite Element Method (FEM) that we have previously presented in [3], the combined FBLM-FEM is able to reproduce realistic,
crawling-like moving cells, [3,5].

We also present parts of our numerical study of the FBLM-FEM, while it is embedded in a complex extracellular environment with multiple chemical sources, and non-uniform, adaptive ECM. One of our focuses is on the convergence and sensitivity analysis of the FBLM-FEM.

Finally, we present and discuss some of our newest results in cell-cell interactions, i.e. cell-cell collision and adhesion.

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MATERIALS 1

Quasi-linear viscoelasticity for transversely isotropic materials under finite deformation

Valentina Balbi, NUI Galway, Ireland

The ability to predict deformation and stress distribution in soft compliant solids is important in a diverse range of materials modelling applications, e.g. reinforced polymers and rubbers, foams and of increasing importance in the context of soft tissue mechanics. In many of these applications the microstructure of the medium in question dictates that the material response is anisotropic and viscoelastic, particularly for soft tissues.

Additionally, given their compliant nature, it is necessary to accommodate finite strains. Here we propose a constitutive model based on the quasi-linear viscoelastic theory, where the total stress response is split into a time-dependent term, i.e. the relaxation function and a strain dependent term, i.e. the elastic stress response.

The key point of the model is that we employ a tensorial form for the relaxation function. This allows to fully account for the transversely isotropic nature of the tissue. Moreover, the components of the relaxation function can all be determined from small-strain experiments. As well as being an important and useful theory in its own right, this transversely isotropic Quasi Linear Viscoelastic model can be used as a starting point from which more general theories can be developed and in particular those associated with strain-dependent relaxations.

MATERIALS 2

Acoustic Wave Elastography of Arteries: Theory, Simulations, Experiments, Validation

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Understanding the dispersion relations (i.e., the variation of phase velocities with frequency) of guided waves in a material is an essential component of non-destructive evaluation. Dispersion relations are sensitive to physical and geometrical parameters, and their features can be exploited for the characterization of materials. Guided waves can be used not only on hard materials but also in the ultrasound elastography of soft thin-walled biological tissues.

These may be under large deformations due to pre-stress and fluid loading. Here we investigate theoretically, numerically, and experimentally the propagation of guided waves in pre-stressed soft plates and tubes surrounded by fluid. We find good agreement between the theory, the simulations and experiments on stretched silicone in a bath of water. The results may serve as fundamental solutions to characterize the mechanical properties of thin-walled soft tissues using the ultrasound elastography method.

MATERIALS 3

Biaxial Properties of the Vagina and its Apical Support

Raffaella De Vita
Virginia Tech, USA

Pelvic floor disorders such as urinary incontinence, fecal incontinence, and pelvic organ prolapse represent a major public health concern in the United States affecting one third of adult women. These disorders are determined by structural and mechanical alterations of the pelvic organs, their supporting muscles and connective tissues that occur mainly during pregnancy, vaginal delivery, and aging. In this talk, I will present our findings on characterizing the highly nonlinear biaxial properties of the vagina, the utero-sacral ligaments and the cardinal ligaments. Our findings can potentially transform current surgical reconstruction methods and post-operative rehabilitation protocols for pelvic floor disorders.

MATERIALS 4

On a hyperelastic model for ageing skeletal muscle tissue

Giulia Giantesio
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We present a hyperelastic model which describes the active and passive behavior of skeletal muscle tissue affected by sarcopenia, which is a geriatric syndrome characterized by the loss of muscle mass and efficiency. In the model that we propose, there will be four main constitutive prescriptions: one for the strain energy function when the tissue is not activated (passive energy), one for the activation (active strain), one for the loss of performance and one for the loss of mass. Some numerical results will be discussed.

MATERIALS 5

Structural evolution of fibre-reinforced biological tissues

Alfio Grillo
Politecnico di Torino

In this contribution, two aspects of the structural evolution of fibre-reinforced biological tissues are discussed. One is the reorientation of the fibres, and the other one is the development of irreversible strains. For both phenomena, the directional distribution of the fibres is described by a probability density that depends on a set of structural parameters. In order to model the reorientation of the fibres, such parameters are assumed to evolve in time. This evolution, in fact, is obtained by solving appropriate dynamic equations in which, together with stress-modulated external remodelling forces, also internal forces are accounted for. The latter ones are assumed to be derived from a free energy density featuring a remodelling part and capable of resolving the dependence of the structural parameters on the material point. The development of irreversible strains, instead, describes the rearrangement of cellular bonds, or the evolution of the microcracks that may occur in a tissue in the case of mechanical overloads. This type of remodelling addresses the redistribution of the mechanical stress in the presence of plastic-like distortions and the repercussion of those on other related phenomena.

MATERIALS 6

A predictive multiscale model for soft materials with unfolding macromolecules: anisotropic damage and residual stretches

Giuseppe Puglisi
Politecnico di Bari

We propose a multiscale model deducing the macroscopic mechanical behavior of macro-molecular soft materials undergoing strain-induced unfolding (such as protein and rubberlike materials). Starting from a (statistically based) energetic approach of the macromolecules unfolding, by extending classical multiscale approaches of polymer physics, we obtain a three-dimensional continuum model. Based on a limited number of experimental macromolecular parameters, including the persistence and contour length, we describe the complex history dependent macroscopic behavior observed in soft materials with anisotropic damage and residual stretches. The theoretical model are supported by our experimental cyclic tests on spider silk and keratin fibers (human, cow, and rabbit hair) that shows that our model is robust and reproduces with surprising accuracy the mechanical behavior of protein materials.

STRUCTURES 1

Coupled swelling and nematic reordering in liquid crystal gels

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Liquid crystal gels (LCGs) are fluid-swollen elastomers that contain mesogens. Like non-mesogenic polymer gels, these materials can swell or shrink in response to changes in the chemical potential of the swelling fluid. Additionally, changes in the temperature of the environment alter the nematic order, which in turn affects both the anisotropy and the magnitude of volume changes [1]. Reciprocally, swelling modifies the strength of nematic interactions and thus influences nematic order. These coupled effects may be exploited in applications, where the greater compliance of LCGs with respect to dry liquid crystal elastomers (LCEs) constitutes a plus, since it allows for an easier manipulation of the director orientation.

Here, we are interested in investigating the transient coupled phenomena that involve anisotropic swelling, nematic-isotropic phase transition and changes in the degree of order in LCGs. First, we derive a non-linear, coupled model for LCGs based on anisotropic Gaussian elasticity with active stretches [2], Flory-Rehner solvent-polymer mixing theory [3], and on the Landau-de Gennes theory of nematic interactions [4]. We then present a finite element implementation of the model.

To gather insight on the coupling between swelling and nematic order, we perform numerical simulations inspired by experiments [5] that involve concurrent swelling and phase transition in LCGs subject to a temperature change. Specifically, we demonstrate separation in time scales between solvent uptake and phase change, in agreement with experiments, which determines a kinetic decoupling between shape and volume changes. Finally, we discuss possible applications in the context of microswimmers, where such a kinetic decoupling is exploited to achieve non-reciprocal actuation and net motion in Stokes flow.

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STRUCTURES 2

Equilibrium of two nested elastic rings

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Elastic rods in contact provide a rich paradigm for understanding shape and deformation in interacting elastic bodies. Here, we consider the problem of determining the static solutions of two nested elastic rings in the plane. If the inner ring is longer than the outer ring, it will buckle creating a space between the two rings. This deformation can be further influenced by either adhesion between the rings or if pressure is applied externally or internally. We explore the role of the geometry, relative stiffness, capillary adhesion and pressure.

STRUCTURES 3

Compatibility issues in layered soft structures inspired by heart mechanics

Paola Nardinocchi
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The mechanical performances of the left ventricle (LV) determines the effectiveness of LV pump function, which is fundamental for heart functioning. LV mechanics is mainly based on inflation, longitudinal shortening, and torsion; driving forces are blood pressure and muscle contraction. Finally, myocardial fibers in LV play both as anisotropic reinforcement with respect to the passive response, and as uniaxial actuators in the active contraction [1, 2]. The contraction–driven component of the deformation poses serious compatibility issues, mainly charged to subendocardium layers due to their higher geometrical stiffness [3], and is largely determined by fibers orientation in the endocardial and epicardial layers. Overcoming loss of compatibility strongly determines LV deformative processes.

In the present work, we investigate this issue starting from a conceptual model of LV viewed as a soft tube, with a radially not uniform distribution of active fibers, whose contraction is modeled as growth. We find and discuss the compatibility conditions, i.e. the conditions to be satisfied to get a pair of compatible distortion/shape change, when different fields of fibers are assigned on the cylindrical body, through the specification of the fields of fiber angles [4]. In our opinion, a full comprehension of the relationships between compatible growth and shape changes in LV–like bodies may help the comprehension of LV deformative processes and drive the interpretation of these processes, usually based on the shape changes detected by clinical tools as speckle tracking echocardiography.

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STRUCTURES 4

Flexure and buckling actuation in bilayer gel beams

Eric Puntel
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Given the widespread usage of gels in biological devices and systems, we focus our attention on a bilayer beam as a prototypical example of actuator which can both bend and wrinkle. Our approach aims at obtaining simple design oriented formulas and as such stationary configurations are considered and the solvent swelling is modeled as a prescribed distortion. A one dimensional model is first introduced in which the finite strain curvature and extension of a bilayer beam made of gels with different properties is obtained. We observe that a concurrent and proportional reduction of the shear moduli of the two layers produces a non monotonic response in which the curvature first increases and then decreases. The investigation of this result allows for the generalization at finite strains of the well known Timoshenko's formula for the curvature of bilayer beams subject to thermal expansion. A two dimensional finite strain model for the same problem has also been obtained and its amenability to linear perturbation analysis demonstrated by a simple example in which wrinkling of a thinner and softer layer is characterized.

STRUCTURES 5

Indentation of elastic spherical shells: beyond 'mirror buckling'

Marco Taffetani
Oxford University, UK

When an elastic shell is indented, the classical picture suggests that it accommodates the so-called 'mirror buckling'. Surprisingly, despite this shape is regarded as a low energy configuration, an elastic shell under point indentation shows a large variety of behaviors, determined by its geometrical and mechanical parameters as well as the loading conditions applied.

The aim of this talk is to investigate the emergence and the evolution of buckling, wrinkling and crumpling in the indentation of pressurized and pressureless spherical shells. First, the `Near Threshold' behavior of such systems is considered in order to determine the buckling transition; hence, the evolution of the instabilities are analyzed `Far from Threshold', thus moving beyond the conditions for their onset. The relevant features in the patterns are shown using finite element simulations and analyzed employing the equations of the shallow shell theory.

The analysis of the stability of elastic shells and the investigation of the emergence of patterns in this kind of structures is relevant to link mechanics and biology. Since shell-like structures are common among living systems and indentation-based techniques are tools often used to derive their mechanical properties, studies that explain how to relate the loading conditions to the properties of the system are of great interest.

STRUCTURES 6

Liquid crystal models for active soft matter

Stefano Turzi
Politecnico di Milano, Italy

The mathematical modelling of biophysical and active materials pose new theoretical challenges for their unique features. Examples of active matter comprise bacterial swarms, the cellular cytoskeleton and in vitro cell extracts. Non-biological examples include vibrated granular material. These system are characterised by a strong deviation from thermal equilibrium due to the environmental energy supply and the active dynamics of the system's microscopic subunits. The simplest, yet successful, theoretical description of active matter is based on continuum models for single-component suspensions of rodlike objects. These models have been originally developed to describe (passive) nematic liquid crystals, e.g., Ericksen-Leslie theory.
The key features of an active system, namely, the viscoelastic response and the active dynamics due to energy consumption of the material sub-units, are usually added in an ad hoc manner to the passive physical model. Viscoelasticity is taken into account by postulating a Maxwell relaxation time and activity is usually introduced by assuming an active stress, proportional to the nematic ordering tensor. In the present talk I will show how a recent theory that models nematic liquid crystals as relaxing nematic elastomers yields a natural viscoelastic model for active gels. Furthermore, it also leads to a more transparent interpretation of the activity as an active strain.

GROWTH AND MORPHOGENESIS 1

On the relation between Eshelbian mechanics and growth in soft biological tissues

Christian J. Cyron, F.A. Braeu
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One of the most prominent properties of living soft tissues is their ability to grow and remodel, in particular under mechanical stimuli. For example, the walls of blood vessels are well-known to thicken under increased blood pressure. At the same time, atrophy has been observed, for example, in tendons under abnormally low mechanical loading. Growth in soft living tissues is often modeled on the basis of a multiplicative split of the deformation gradient into an inelastic part representing growth and an elastic part ensuring geometric compatibility and mechanical equilibrium [1]. To date it remains still highly controversial how to choose the inelastic growth part. Isotropic growth tensors are frequently assumed but have been demonstrated to provide unphysiological solutions even in simple scenarios such as growth of an artery in hypertension [2]. A theoretically more sophisticated and very elegant alternative to specify the growth tensor is the concept of accretive forces based on the framework of Eshelbian mechanics [3, 4]. However, unfortunately this concept also renders in various situations solutions that do not agree well with experimental observations, for example, during hypertension in blood vessels. Here we propose a novel way to apply the ideas of Eshelbian mechanics to growth in soft biological tissues that is based on a simple micromechanical model of growth and avoids previously observed unphysiological solutions.

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GROWTH AND MORPHOGENESIS 2

Growth and remodeling with application to AAA

Luis Dorfmann

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In this talk, we apply a mixture theory of growth and remodeling to study the formation and dilatation of abdominal aortic aneurysms. We adapt the continuum theory of mixtures to formalize the processes of production and removal of constituents from a loaded body. Specifically, we consider a mixture of elastin and collagen fibers, which endow the material with anisotropic properties. General formulations of the equations governing homeostatic state and aneurysm development are provided. In the homeostatic state the idealized geometry of the aorta is a thick-walled tube subject to constant internal pressure and axial stretch. The formation of an aneurysm induces an increase of mass locally achieved via production of new material that exceeds the removal of old material. The combined effects of loss of elastin, degradation of existing and deposition of new collagen as well as fiber remodeling results in a continuous enlargement of the aneurysm bulge. The numerical method makes use of a purposely written material subroutine, called UMAT, which is based on the constitutive formulation here developed.

Perspectives on the mathematics of biological patterning and morphogenesis

Krishna Garikipati
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A central question in developmental biology is how size and position are determined. The genetic code carries instructions on how to control these properties in order to regulate the pattern and morphology of structures in the developing organism. Transcription and protein translation mechanisms implement these instructions. However, this cannot happen without some manner of sampling of epigenetic information on the current patterns and morphological forms of structures in the organism. Any rigorous description of space- and time-varying patterns and morphological forms reduces to one among various classes of spatio-temporal partial differential equations. Reaction-transport equations represent one such class.

Starting from simple Fickian diffusion, the incorporation of reaction, phase segregation and advection terms can represent many of the patterns seen in the animal and plant kingdoms. Morphological form, requiring the development of three-dimensional structure, also can be represented by these equations of mass transport, albeit to a limited degree. The recognition that physical forces play controlling roles in shaping tissues leads to the conclusion that (nonlinear) elasticity governs the development of morphological form.

In this setting, inhomogeneous growth drives the elasticity problem. The combination of reaction-transport equations with those of elasto-growth makes accessible a potentially unlimited spectrum of patterning and morphogenetic phenomena in developmental biology. This perspective communication is a survey of the partial differential equations of mathematical physics that have been proposed to govern patterning and morphogenesis in developmental biology. Several numerical examples will be presented to illustrate these equations and the corresponding physics, with the intention of providing physical insight wherever possible.

GROWTH AND MORPHOGENESIS 4

Brain Mechanics and Brain Morphogenesis

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The human brain is an organ of extreme complexity, the object of ultimate intellectual egocentrism, and a source of endless scientific challenges. Despite a clear evidence that mechanical factors play an important role in regulating brain activity, current research efforts focus mainly on the biochemical or electrophysiological activity of the brain. However, classical concepts from mechanics including deformations, stretch, strain, strain rate, pressure, and stress also play a crucial role in both shaping the brain and modulating its functions. In this talk, I will review our current understanding of the brain and present several important mechanical problems and mathematical models related to brain mechanics and brain morphogenesis. In particular, I will study the variation of thickness appearing in the cortex and show how it results from a generic mechanical instability.

GROWTH AND MORPHOGENESIS 5

Chemo-mechanical feedback in solid tumor growth

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The experimental evidence that a feedback exists between growth and stress in tumors poses challenging questions. First, the rheological properties (the “constitutive equations”) of aggregates of malignant cells are still a matter of debate. Secondly, the feedback law (the “growth law”) that relates stress and mitotic-apoptotic rate is far to be identified.

We address these questions on the basis of a theoretical analysis of in vitro and in vivo experiments that involve the growth of tumor spheroids. We show that solid tumors exhibit several mechanical features of a poroelastic material, where the cellular component behaves like an elastic solid. When the solid component of the spheroid is loaded at the boundary, the cellular aggregate grows up to an asymptotic volume that depends on the exerted compression. Residual stress shows up when solid tumors are radially cut, highlighting a peculiar tensional pattern. By a novel numerical approach we correlate the measured opening angle and the underlying residual stress in a sphere. The features of the mechanobiological system can be explained in terms of a feedback of mechanics on the cell proliferation rate as modulated by the availability of nutrient, that is radially damped by the balance between diffusion and consumption. The volumetric growth profiles and the pattern of residual stress can be theoretically reproduced assuming a dependence of the target stress on the concentration of nutrient which is specific of the malignant tissue.