Mathematical Foundations of Mechanical Biology
27 September to 1 October 2010

Organizers: Alain Goriely, Krishna Garikipati, Marcelo Epstein

MEALS

*Breakfast (Buffet): 7:00–9:30 am, Sally Borden Building, Monday–Friday
*Lunch (Buffet): 11:30 am–1:30 pm, Sally Borden Building, Monday–Friday
*Dinner (Buffet): 5:30–7:30 pm, Sally Borden Building, Sunday–Thursday
Coffee Breaks: As per daily schedule, 2nd floor lounge, Corbett Hall
***Please remember to scan your meal card at the host/hostess station in the dining room for each meal.**

MEETING ROOMS

All lectures will be held in Max Bell 159 (Max Bell Building accessible by walkway on 2nd floor of Corbett Hall). LCD projector, overhead projectors and blackboards are available for presentations. Note that the meeting space designated for BIRS is the lower level of Max Bell, Rooms 155–159. Please respect that all other space has been contracted to other Banff Centre guests, including any Food and Beverage in those areas.

SCHEDULE

Sunday

16:00	Check-in begins (Front Desk - Professional Development Centre - open 24 hours)
17:30–19:30	Buffet Dinner, Sally Borden Building
20:00	Informal gathering in 2nd floor lounge, Corbett Hall (if desired)
	Beverages and a small assortment of snacks are available on a cash honor system.

Monday

7:00–8:45	Breakfast
8:45–9:00	Introduction and Welcome by BIRS Station Manager, Max Bell 159
9:00-9:30	**William Klug** (UCLA) *Structural Mechanics of Viral Shells: Stretching the Limits of Continuum Models*
9:30-10:00	**Marino Arroyo** (Universitat Politecnica de Catalunya) *Active force generation in biological tissues*
10:00-10:30	Coffee Break, 2nd floor lounge, Corbett Hall
10:30-11:00	**Luigi Preziosi** (Politecnico di Torino) *Cell Adhesion and Re-organisation in a Multiphase Model Describing Tumour and Tissue Growth*
11:00-11:30	**Martine Ben Amar** (Ecole Normale Suprieure, Paris) Shape instability of growing tumors
11:30-12:00	**Krishna Garikipati** (University of Michigan) *The non-equilibrium thermodynamics and kinetics of focal adhesion dynamics*
12:00–13:00	Lunch
13:00–14:00	Guided Tour of The Banff Centre; meet in the 2nd floor lounge, Corbett Hall
13:50	Group Photo; meet on the front steps of Corbett Hall
14:00-14:30	**Yibin Fu** (Keele University) *Characterization and stability of localized bulgingin inflated membrane tubes*
14:00-14:30	**Jean-François Ganghoffer** (ENSEM) *Equilibrium shapes of biological membranes using analytical techniques. Application to Beaded Nerve Fibers and generalized cylinders.*
15:00-15:30	Coffee Break, 2nd floor lounge, Corbett Hall
15:30-16:00	**Marcelo Epstein** (University of Calgary) *Field Equations of Boundary Growth*
16:00-16:30	**Patrick Shipman** (Colorado State University) *Diffusion to Capture with Mechanical Stresses*
17:30–19:30	Dinner

Tuesday

7:00–8:45 Breakfast

9:00-9:30 **Przemyslaw Prusinkiewicz** (University of Calgary)
Relating mechanics and geometry of form development

9:30-10:00 **Sébastien Neukirch** (Université Pierre et Marie Curie)
Competition between curls and plectonemes near the buckling transition of stretched supercoiled DNA

10:00-10:30 Coffee Break, 2nd floor lounge, Corbett Hall

10:30-11:00 **Luis Dorfmann** (Tufts University)
Modeling muscle properties in a soft-bodied arthropod

11:00-11:30 **Derek moulton** (University of Oxford)
Mucosal folding in growing elastic tubes

11:30-12:00 **Elena Di Martino** (University of Calgary)
Effect of smooth muscle contraction on residual stresses in the aorta

12:00–13:00 Lunch

13:30–14:00 **Tim Secomb** (University of Arizona)
Structural adaptation in microvessel networks: Learning the rules

14:00-14:30 **Rebecca Shipley** (University of Oxford)
Theoretical Models of Blood Flow in the Vasculature

14:30-15:00 **Ellen Kuhl** (Stanford University)
A multiscale model for cardiac growth through sarcomerogenesis.

15:00-15:30 Coffee Break, 2nd floor lounge, Corbett Hall

15:30-16:00 **Stephen C. Cowin** (The City University of New York)
Centers of growth and growth gradients in preference to a growth tensor

16:00-16:30 **Gérard Maugin** (Université Pierre et Marie Curie)
Reflections on the problem of the longitudinal growth of long bones in mammals

16:30-17:00 **Vaclac Klika** (Czech Technical University, Prague)
Biochemical model of bone remodelling including mechano-chemical coupling

17:30–19:30 Dinner

Wednesday

7:00–9:00	Breakfast
9:00-9:30	**Anja Geitmann** (Université de Montreal)
	Size matters: how the pollen tube controls cell shape
9:30-10:00	**Michael Tabor** (University of Arizona)
	A twisted life: the mechanics of spontaneous rotational reversal in Phycomyces
10:00-10:30	Coffee Break, 2nd floor lounge, Corbett Hall
10:30-11:00	**John Lowengrub** (University of California Irvine)
	Feedback, lineages and cancer
11:00-11:30	**Sarah Waters** (University of Oxford)
	Mathematical models for tissue engineering applications
11:30–13:00	Lunch
	Free Afternoon
17:30–19:30	Dinner

Thursday

7:00–9:00	Breakfast
9:00-9:30	**Arash Yavari** (Georgia Tech) *Riemannian geometry of bulk growth*
9:30-10:00	**Cameron Hall** (University of Oxford) *Kinematics of bulk growth*
10:00-10:30	Coffee Break, 2nd floor lounge, Corbett Hall
10:30-11:00	**Isaac Chenchiah** (University of Bristol) *Continuum limits of discrete growing systems*
11:00-11:30	**Davide Ambrosi** (Politecnico di Milano) *Active force generation in biological tissues*
11:30-12:00	**Markus J. Buehler** (Massachusetts Institute of Technology) *Turning weakness to strength*
12:00–13:00	Lunch
	Free Afternoon
17:30–19:30	Dinner

Friday

7:00–9:00	Breakfast
9:00-9:30	**Alan Newell** (University of Arizona) *How universal are Fibonacci patterns?*
9:30-10:00	**Prashant Purohit** (University of Pennsylvania) *Heterogeneous fluctuating rod models for unfolded proteins and application to fibrin networks*
10:00-10:30	Coffee Break, 2nd floor lounge, Corbett Hall
10:30-11:00	**Sachin Goyal** (Emory University) *Effect of Polyamines on the Mechanical Properties of DNA*
11:00-11:30	**Gert van der Heijden** (University College London) *Multistability of inextensible helical strips with applications to self-assembled cholesterol ribbons*
11:30-12:00	**Mohamed Assidi** (ENSEM, Nancy) *Equivalent properties of biological membranes from lattice homogenization*
Checkout by 12 noon.	
12:00–13:00	Lunch

** 5-day workshops are welcome to use BIRS facilities (2nd Floor Lounge, Max Bell Meeting Rooms, Reading Room) until 3 pm on Friday, although participants are still required to checkout of the guest rooms by 12 noon. **

Mathematical Foundations of Mechanical Biology
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ABSTRACTS
(in alphabetic order by speaker surname)

Speaker: **Ambrosi, Davide** (Politecnico di Milano)
Title: *Active force generation in biological tissues*
Abstract: The application of the methods of classical continuum mechanics to living tissues, namely the cardiac muscle, faces a peculiar behavior: the ability of a living body to deform by its own action, even without external loads. The mathematical representation of this fact is usually approached in the engineering literature by the introduction of an additive surface force contribution, the "active stress tensor", to be included in the force balance equation. An alternative approach, recently proposed, models the activity of muscles as an "active deformation" that enters in the equations thanks a multiplicative decomposition of the gradient of deformation, reminiscent of classical approaches in plasticity. In my talk I will point out some mathematical aspects and open questions that pertain both approaches.

Speaker: **Arroyo, Marino** (Universitat Politecnica de Catalunya)
Title: *The role of membrane viscosity in the dynamics of fluid membranes*
Abstract: Fluid membranes made out of lipid bilayers are the fundamental separation structure in eukaryotic cells. Many physiological processes rely on dramatic shape and topological changes (e.g. fusion, fission) of fluid membrane systems. Fluidity is key to the versatility and constant reorganization of lipid bilayers. Here, we study the role of the membrane intrinsic viscosity, arising from the friction of the lipid molecules as they rearrange to accommodate shape changes, in the dynamics of morphological changes of fluid vesicles. In particular, we analyze the competition between the membrane viscosity and the viscosity of the bulk fluid surrounding the vesicle as the dominant dissipative mechanism. We consider the relaxation dynamics of fluid vesicles put in an out-of-equilibrium state, but conclusions can be drawn regarding the kinetics or power consumption in regulated shape changes in the cell. On the basis of numerical calculations, we find that the dynamics arising from the membrane viscosity are qualitatively different from the dynamics arising from the bulk viscosity. When these two dissipation mechanisms are put in competition, we find that for small vesicles the membrane dissipation dominates, with a relaxation time that scales as the size of the vesicle to the power 2. For large vesicles, the bulk dissipation dominates, and the exponent in the relaxation time vs. size relation is 3.

Speaker: **Assidi, Mohamed** (LEMTA-ENSEM, Nancy)
Title: *Equivalent properties of biological membranes from lattice homogenization*
Abstract: One of the essential aims of bioengineering today is to answer the basic question of how individual cells and/or cell networks interact with each other or behaves under different loading, such as thermal or chemical or mechanical one. In a general case, cells are composed by filaments which are linked together as a part of a network or are associated with the cell membrane to built an effective two-dimensional structure. In a first approach, this cellular structure displays an elastic behaviour, due to the individual entropic elastic behavior of the constituting macromolecular chains.
The goal of this work is an application of the asymptotic homogenisation technique to derive the effective elastic behavior of planar and non-planar repetitive networks viewed as continua versus the geometrical and mechanical micro-parameters of the underlying network, considering a repetitive unit cell. The derivation of mechanical properties of cellular biological structures is interesting in order to understand the somewhat peculiar observed behaviour (anisotropy, negative Poisson's ratio) and to possibly test the limit of the membrane architecture to bear certain loading conditions.
Different biological membranes are analysed using this methodology within the small displacement framework and their effective moduli are calculated and recorded versus the geometrical lattice parameters.

Speaker: **Ben Amar, Martine** (Ecole Normale Supérieure, Paris)
Title: *Shape instability of growing tumors.*

Speaker: **Buehler, Markus J.** (Massachusetts Institute of Technology)
Title: *Turning weakness to strength*
Abstract:Biology exquisitely creates hierarchical structures, where initiated at nano scales, are exhibited in macro or physiological multifunctional materials to provide structural support, force generation, catalytic properties, or energy conversion. This is exemplified in a broad range of biological materials such as hair, skin, bone, spider silk or cells. For instance, despite its simple building blocks spider silk is one of the strongest, most extensible and toughest biological materials known, exceeding the properties of many engineered materials including steel. This is particularly puzzling since despite its great strength, spider silk is made of some of the weakest chemical bonds known, H-bonds. We have discovered that the great strength and extensibility of spider silk can be explained based on its particular structural makeup, which involves several hierarchical levels from the nano- to the macro-scale. Thereby, the structural confinement of H-bonds into ultra-small beta-sheet nanocrystals with dimensions of only a few nanometers is the key to overcome the intrinsic limitations of H-bonds, creating mechanically strong, tough and resilient cross-linking domains between a semi-amorphous phase composed of 3_1 protein helices (Keten, Buehler *et al., Nature Materials*, 2010). Our work unveils a material design strategy that enables silks to achieve superior material properties despite its simple and structurally inferior material constituents. Exploiting this concept could lead to a novel materials design paradigm, where enhanced functionality is not achieved using complex building blocks but rather through the utilization of universal repetitive constitutive elements arranged in hierarchical structures. We discuss analogies with other protein materials such as collagen and intermediate filaments, and present approaches towards the design of adaptable, mutable and active materials.

Speaker: **Chenchiah, Isaac** (University of Bristol)
Title: *Continuum limits of discrete growing systems*
Abstract: We investigate continuum limits of discrete growing systems, beginning with simple two-dimensional node-spring systems that "grow" by adding springs, adding nodes or changing the rest-length of the springs. In particular we explore circumstances under which the (continuum) energy-density of the grown system is related to that of the initial system through a multiplicative decomposition of the deformation.

Speaker: **Cowin, Stephen C.** (The City University of New York)
Title: *Centers of growth and growth gradients in preference to a growth tensor*
Abstract: Two distinct methods of modeling the growth of an organism were inspired by D'Arcy Thompson's method of coordinate transformations. One is based on the solid mechanics concept of the deformation of an object and other based on the fluid mechanics concept of the velocity field of a fluid. Although proposed more that 70 years ago, they were not given names until recently. The solid mechanics model was called the distributed continuous growth (DCG) model by Skalak et al. (1982) and the fluid mechanics model is called the graphical growth velocity field representation (GVFR) by Cowin (2010). The GVFR is a minimum or simple model based only on the assumption that a velocity fields may be used effectively to illustrate experimental results that reveal the centers of growth and growth gradients first described by Julian Huxley in 1932. It is the method with a future that earlier writers considered, inappropriately, as an aspect of the DCG model. The prospects for the DCG model itself are less attractive as it does not allow mass change of the organism, does not recognized centers of growth and growth gradients and it requires a closed system that permits no transport across it boundaries. These statements about the literature are demonstrated with interesting and extensive graphic illustrations, mostly historical.
References Cowin SC. 2010. Continuum kinematical modeling of mass increasing biological growth, *Int. J. Engr. Sci. in press, available online now;* Huxley JS. 1932. *Problems of Relative Growth*, New York, Lincoln MacVeagh, 1st ed. (2nd ed. 1972 New York, Dover); Skalak R, DaGupta G, Moss M, Otten E, Dullemeijer P, Vilmann H. 1982. Analytical description of growth, *J. theor. Biol*. **94**:555-577

Speaker: **DiMartino, Elena** (University of Calgary)
Title: *Effect of smooth muscle contraction on residual stresses in the aorta*
Abstract: In health, the wall of blood vessels is optimized to sustain the time-dependent stress arising during the cardiac cycle. Together with the wall structural characteristics and the loads due to the oscillating blood pressure, residual stresses play an important role in determining a homeostatic stress level or, in other words, a stable environment. Any alteration in composition and arrangement of the wall microstructure modifies vascular mechanics and changes wall stress, inducing remodeling. This process, intended to restore homeostasis, can lead to the onset of vascular pathologies. Residual stress represent a good target to relate the macroscopic effects of remodeling with the changes at the microscopical level, since they arise directly from vascular adaptation, depend on the contribution of the different wall constituents and can be assessed with experimental measurements on excised vessels. This talk will focus on experiments performed on canine aortic tissue to ascertain the role of smooth muscle contraction on residual stresses. Analytical and computational models were developed to interpret the results, which support the hypothesis that smooth muscle contraction contributes to the homogenization of stresses in the aortic wall, reducing the gradient of stress across the vessel thickness. Experiments were also performed on isolated smooth muscle cells seeded on different substrates to study the effect of matrix stiffness on smooth muscle cell behaviour.

Speaker: **Dorfmann, Luis** (Tufts University)
Title: *Modeling muscle properties in a soft-bodied arthropod*
Abstract: Muscles in soft-bodied arthropods perform multiple functions in addition to acting as biological actuators, including dissipating energy and providing structural support. In this talk, we examine the mechanical properties of the ventral interior lateral muscle of the tobacco hornworm caterpillar, *Manduca sexta*. Most of the previous studies focus on the active properties of the muscle tissue and do not account for the passive or transitioning states. In this work, a constitutive model is derived to represent the change in mechanical properties between active and passive conditions based on new experimental data. In formulating the model, a phenomenological approach is used to capture the complex mechanisms by which passive and active forces change during stimulation and deformation.

Speaker: **Epstein, Marcelo** (University of Calgary)
Title: *Field Equations of Boundary Growth*
Abstract: Boundary growth is defined as a particular case of surface growth. Within this restricted context, it is shown that the field equations of boundary growth are not essentially distinguishable from those of volumetric growth and that, consequently, the a-priori notion of material particle may be devoid of an intrinsic meaning.

Speaker: **Fu, Yibin** (Keele University)
Title: *Characterization and stability of localized bulgingin inflated membrane tubes*
Abstract: When a cylindrical membrane tube is inflated by an internal pressure (through, for instance, air pumping), a localized bulge will form when the pressure reaches a critical value $p_{\rm cr}$. As more air is pumped into the tube, the pressure actually drops but the radius at the center of the bulge will increase until it reaches a maximum value $r_{\rm max}$. With continued inflation, the pressure stays at a constant value $p_{\rm m}$, and the bulge spreads in both directions while the radius at the center of the bulge maintains the maximum value $r_{\rm max}$. This process is well-known and has been much studied both analytically, numerically and experimentally; see, for instance, Yin (1977), Chater and Hutchinson (1984), Kriakides and Chang (1991), and Shi and Moita (1996). This problem also shares some features with a family of other problems such as phase transformations in metals, and kink band formation and propagation in layered structures and fibre-reinforced composites. It is also hoped that a full understanding of this problem will help understand the more complicated problem of aneurysm formation and growth in human arteries.

We have recently carried out a series of studies offering improved understanding of the above inflation process. In the first of this series, Fu {\it et al.} (2008), the initial bulging/necking was recognized as a bifurcation problem and the corresponding bifurcation condition was derived using two different methods. The bifurcation condition was in fact not new: the expression had previously appeared in the bifurcation analysis of Haughton and Ogden (1979) and the stability analysis of Chen (1997), but in either case its connection to localized bulging/necking was not fully recognized since the corresponding eigenmode was simply an extra uniform inflation – seemingly unable to describe a localized deformation. It was shown in Fu *et al.* (2008) that the eigenmode is a localized deformation when weakly nonlinear terms were brought in to eliminate the degeneracy in the linear analysis.

In the second of the above-mentioned series, Pearce and Fu (2010), our attention was turned to a detailed description of the fully nonlinear bulging/necking solutions and a study of their stability. It turned out that the entire inflation process could be described by a graphical method aided by some simple analysis. In particular, the exact nature of the transition from radial growth to axial spreading (i.e. from a solitary-wave type solution to a kink-wave type solution) was clarified. A stability analysis was conducted for the case of pressure control, and it was found that all the possible bulging/necking solutions were unstable with respect to axially symmetric perturbations. In a more recent paper, Fu and Xie (2010), stability of localized bulging solutions under volume control was studied using an energy stability criterion, and it was shown that the solutions in the early stages of bulging are unstable whereas those in the later stages of bulging are stable. To be more precise, it is found that the unstable solutions correspond exactly to the snap-back section of the associated pressure-volume diagram.

In this talk we shall present our most recent results on the effects of material inhomogeneities and variable wall thickness. We shall show how such effects drastically reduce the critical pressure for the onset of localized bulging.

Speaker: **Ganghoffer, Jean-François** (ENSEM)
Title: *Equilibrium shapes of biological membranes using analytical techniques. Application to Beaded Nerve Fibers and generalized cylinders.*
Abstract: We presently investigate the equilibrium shapes of some biological membranes, using analytical techniques. Delaunay surfaces (axisymmetrical) represent one class of solutions of the shape equation; the plane elastica which generates generalized cylinders is another type of solutions. Preliminary results for both types of membranes are presented. Pure bilayer tubes such as myelinated fibers, or axons of unmyelinated nerve fibers which are subjected to stretch exhibit beaded shapes, resulting in a succession of expansions and constrictions observed along the axis of longitudinally sections of the fibers. The mechanics of beading is investigated from an analytical viewpoint, adopting the mechanical model exposed in Markin *et al*, based on membrane tension and hydrostatic pressure as the basic factors responsible for the axonal constriction of unmyelinated nerve fibers. Solutions of the determining equation for the shape of axisymmetrical beads are expressed in closed form in terms of elliptic functions, and the effects of two principal geometrical parameters, the oscillation amplitude and the neck length are analyzed.
Symmetry methods represent another quite general and efficient mathematical tool to analyse the shape of membranes form the underlying governing differential equation. Using the Lie algorithm, the knowledge of admitted symmetries of the shape equation allows finding invariants expressing the shape (for a given parameterization) versus the membrane geometrical and physical relevant parameters, such as surface tension. Such solutions are exhibited for generalized cylinders which constitute another class of solution of the membrane shape equation.

Speaker: **Garikipati, Krishna** (University of Michigan)
Title: *The non-equilibrium thermodynamics and kinetics of focal adhesion dynamics*
Abstract: Focal adhesions are a type of matrix-attachment formed by certain cell types, prominently by fibroblasts. They play important roles in cell migration, signalling and cytoskeletal dynamics. The formation, growth and resorption of focal adhesions has been shown to be mechano-sensitive, and furthermore, they demonstrate a rich dynamic response. We consider a focal adhesion to be made up of molecular complexes, each consisting of a ligand, an integrin molecule, and associated plaque proteins. Free energy changes drive the binding and unbinding of these complexes and thereby control the focal adhesion's dynamic modes of growth, treadmilling and resorption. We have identified a competition among four thermodynamic driving forces for focal adhesion dynamics: (1) the work done during the addition of a single molecular complex of a certain size, (2) the chemical free energy change associated with the addition of a molecular complex, (3) the elastic free energy change associated with deformation of focal adhesions and the cell membrane, and (4) the work done on a molecular conformational change. We have developed a theoretical treatment of focal adhesion dynamics as a nonlinear rate process governed by a classical kinetic model. We also express the rates as being driven by out-of-equilibrium thermodynamic driving forces, and modulated by kinetics. The mechanisms governed by the above four effects allow focal adhesions to exhibit a rich variety of behavior without the need to introduce special constitutive assumptions for their response. For the reaction-limited case growth, treadmilling and resorption are all predicted by a very simple chemo-mechanical model. Treadmilling requires symmetry breaking between the ends of the focal adhesion, and is achieved by driving force (1) above. In contrast, depending on its numerical value (2) causes symmetric growth, resorption or is neutral, (3) causes symmetric resorption, and (4) causes symmetric growth. In addition to explaining focal adhesion dynamics, this treatment can be coupled with models of cytoskeleton dynamics and contribute to the understanding of cell motility.

Speaker: **Geitmann, Anja** (Université de Montreal)
Title: *Size matters: how the pollen tube controls cell shape*
Abstract: The pollen tube is a cellular tunnel transport system that is generated to connect the male **gametophyte** with its female counterpart during sexual reproduction in plants. Through this cellular protuberance the sperm cells are delivered from the pollen grain to the ovule. To be competitive, the pollen tube elongates extremely rapidly. At least two opposing mechanical constraints determine the size of this tubular protuberance: For mechanical reasons, a smaller cell can invade the pistillar tissues with greater ease. However, a sufficiently large diameter is required to allow the sperm cells to pass through the tube. In a mechanical model based on finite element techniques we demonstrate how the pollen tube has to control the mechanical properties of its apical cell wall in order to produce a cylinder with the desired size.
In order to overcome the mechanical impedance to invasion generated by the pistillar tissues the pollen tube limits potential loss of energy caused by friction during cell expansion. It does so by focusing all growth activity to the tube tip. This mechanism also enables it to respond rapidly and efficiently to guidance cues. This tip-focused growth activity raises the question of how the tube coordinates its intracellular transport logistics. How does it provide the material required for cell wall and membrane assembly to the continuously expanding extreme end of the cell? A mathematical model based on actin polymerization and vesicular dynamics successfully explains numerous experimentally observed phenomena that are associated with this transport challenge.

Speaker: **Goyal, Sachin** (Emory University)
Title: *From Atomistic Simulations to Continuum Modeling*
Abstract: Twisting and bending deformations of micron-scale bio-filaments, such as DNA, play a central role in their biological functions. The elastic rod model, which uses a continuum approximation, has emerged as a viable tool to model the large, nonlinear deformations of bio-filaments. Rod model predictions are however very sensitive to the constitutive law (springiness) of the filament, which follows from the atomistic-level interactions. Estimation of the constitutive law from experimental data and molecular dynamics simulations remains a significant challenge. In this

presentation, we will illustrate our recently developed two-step inverse technique that can use a rod model in combination with high-fidelity molecular dynamics simulation data to estimate the constitutive law.

Speaker: **Hall, Cameron** (Oxford University)
Title: *Kinematics of bulk growth*
Abstract: In growing tissues, it becomes difficult to define strain in a way that is both coherent and informative. On the one hand, it is possible to define strain in terms of the difference between the current state and some specified reference configuration (e.g. the initial state). This leads to a simple and coherent definition of strain, but the resulting 'apparent strain' will have a complicated relationship with stress that makes it difficult to formulate constitutive laws. Alternatively, it is possible to define strain in terms of the difference between the current state and a locally defined zero stress state; this leads to the 'effective strain', where zero strain corresponds to zero stress and standard constitutive laws can be used. Unfortunately, the kinematic definition of effective strain is complicated by growth, remodelling and other phenomena that cause the zero stress state to evolve over time.
In this talk, the kinematics of a growing body will be examined, leading to the construction of an evolution equation for the effective strain. The starting point for this work is the well-known multiplicative decomposition of the deformation gradient, in which the deformation from the initial state to the current state is separated into an elastic part and a plastic/growth part. This talk will show how this can be used to develop the growth tensor, a frame-indifferent tensorial measure of the rate of change of the zero stress state, and we demonstrate how the growth tensor can be related to the evolving effective strain. If time permits, physical interpretations of the growth tensor and preliminary work on solving the strain evolution equation will be presented.

Speaker: **Klika, Vaclav** (Czech Technical University, Prague)
Title: *Biochemical model of bone remodelling including mechano-chemical coupling*
Abstract: Based on the current knowledge of bone remodelling process, a biochemical model is proposed which describes the essential interactions that governs the whole bone remodelling process. Further, the influence of mechanical stimulation on bone tissue is well known. Considerations from non-equilibrium thermodynamics are used to quantify this effect and moreover to stress the importance of dynamic character of the loading. This rather different approach from the classical ones can predict bone density distribution as will be shown on some examples including the effect of stem insertion or osteoporosis.

Speaker: **Klug, William** (UCLA)
Title: *Structural Mechanics of Viral Shells: Stretching the Limits of Continuum Models*
Abstract: As revealed by techniques of structural biology, the protein shells of viruses (capsids) are some of nature's most beautiful and robust examples of highly symmetric multiscale self-assembled structures. The ability of viral capsids to respond structurally and mechanically to physical and chemical stimuli also gives them tremendous potential as components for the design of synthetic materials with adaptive properties. A series of recent indentation experiments using atomic force microscopy (AFM) has shown that capsids also possess impressive overall mechanical properties of strength and elasticity. Moreover, these experiments pose a unique opportunity to probe the internal conformational degrees of freedom and the molecular interactions that regulate macromolecular assembly. However, full advantage of these experiments can be made only through the development of new mathematical models that capture the multiscale hierarchical structure of proteins. In this talk I will present some analytical and numerical models of viral capsids based on continuum mechanics and Ginzburg-Landau theory, and I will discuss what we've learned about (1) the elastic response and mechanical failure of viral capsids, (2) coupling of global capsid mechanical response to local protein conformational change, and (3) the role of mechanics in capsid self-

assembly. Lastly I will describe our ongoing efforts to push the limits of usefulness of continuum theory via coupled continuum-atomistic multiscale modeling of capsids and other large protein assemblies.

Speaker: **Kuhl, Ellen** (Stanford University)
Title: *A multiscale model for cardiac growth through sarcomerogenesis*
Abstract: We present a novel computational model for maladaptive cardiac growth in which kinematic changes of the cardiac chambers are attributed to alterations in cytoskeletal architecture and in cellular morphology. We adopt the concept of finite volume growth characterized through the multiplicative decomposition of the deformation gradient into an elastic part and a growth part. The functional form of its growth tensor is correlated to sarcomerogenesis, the creation and deposition of new sarcomere units. In response to chronic volume-overload, an increased diastolic wall strain leads to the addition of sarcomeres in series, resulting in a relative increase in cardiomyocyte length, associated with eccentric hypertrophy and ventricular dilation. In response to chronic pressure-overload, an increased systolic wall stress leads to the addition of sacromeres in parallel, resulting in a relative increase in myocyte cross sectional area, associated with concentric hypertrophy and ventricular wall thickening. We explore a generic bi-ventricular heart model in response to volume- and pressure-overload to demonstrate how local changes in cellular morphology translate into global alterations in cardiac form and function.

Speaker: **Lowengrub, John** (University of California Irvine)
Title: *Feedback, lineages and cancer*
Abstract: A multispecies diffuse-interface continuum model is used to simulate dynamics of cell lineages in solid tumors. The model consists of Cahn-Hilliard type equations for the cell species interacting through cell proliferation logic. Following biological considerations borrowed from developmental biology, a feedback system is proposed to control the cell populations in the lineages via diffusible chemical factors. The origin and consequences of tumor heterogeneity is investigated. The highly nonlinear/numerically stiff equations are solved using fully adaptive, nonlinear-multigrid schemes.

Speaker: **Maugin, Gérard** (Université Pierre et Marie Curie)
Title: *Reflections on the problem of the longitudinal growth of long bones in mammals*
Abstract: The slow lengthening of long bones in mammals via the evolution of the so-called growth plate is an interesting problem of mechanobiology. First analogies and differences between the evolution of the growth plate and the progress of phase-transformation fronts are noted. Second, on account of biophysical data several modellings of the growth plate itself and its progress are considered. Finally, the special modelling that views the growth plate as a zone of gradient variation of its structural properties but in very slow time evolution is considered. The possibility to exploit nonlinear signals (bell shapes, kinks) in the nonlinear elasticity of the considered tissues superimposed on this quasi-static evolution, is then envisaged delivering various signatures for these signals, which are characteristic of the considered growth plate structure. Works in co-operation with A.B. Freidin and A.V. Porubov (St Petersburg) and M. Rousseau (Paris).

Speaker: **Moulton, Derek** (Oxford University)
Title: *Mucosal folding in growing elastic tubes*
Abstract: When an elastic tube is under external radial pressure, a circumferential instability may develop at a critical pressure in which the tube buckles to a non-circular cross section. This phenomenon is observed in a number of biological tissues, where it is referred to as mucosal folding, and represents an instability of the inner mucosal edge. Previous mechanical investigations have quantified the effect of wall thickness on the instability; however, absent from previous work is the effect of growth. Here, we analyze a model to study mucosal folding in a growing elastic tube, and in

particular explore the impact of differential growth on the instability. We study the problem in a generic setting and also focus the analysis on the problem of airway remodeling in patients with chronic asthma.

Speaker: **Neukirch, Sebastien** (Univ. Paris 6 / CNRS)
Title: *Competition between curls and plectonemes near the buckling transition of stretched supercoiled DNA*
Abstract: Recent experiments have observed that formation of a plectonemically supercoiled region in a stretched, twisted DNA proceeds via discontinuous formation of a small plectonemic domain. We present a microscopic model for the nucleation of the small plectonemic bubble, including the influence of small chiral loops or "curls" along the extended DNA. Curls are induced just before plectoneme formation, and play an important role in stabilizing the extended state and in delaying formation of the plectonemic bubble. Curls are a natural transition state for binding of DNA-loop-trapping enzymes.

Speaker: **Newell, Alan** (University of Arizona)
Title: *How universal are Fibonacci patterns?*
Abstract: Not provided

Speaker: **Preziosi, Luigi** (Politecnico di Torino)
Title: *Cell Adhesion and Re-organisation in a Multiphase Model Describing Tumour and Tissue Growth*
Abstract: The main aim of the talk is to describe how to embed the experimental results recently obtained studying the detachment force of single adhesion bonds in a multiphase model developed to describe the growth of tumours and tissues in general. In order to do that the microscopic infomation is upscaled to the macroscopic level to describe the dependence of some crucial terms appearing in the PDE model on the sub-cellular dynamics involving, for instance, the density of bonds on the membrane, the probability of bond rupture and the rate of bond formation. In fact, adhesion phenomena influence both the interaction forces among the constituents of the mixtures and the constitutive equation for the stress of the cellular components.
Studying the former terms a relationship between interaction forces and relative velocity is found. The dynamics presents a behaviour resembling the transition from epithelial to mesenhymal cells or from mesenchymal to ameboid motion though the chemical cues triggering such transitions are not considered here.
The latter terms are dealt with using the concept of evolving natural configurations consisting in decomposing in a multiplicative way the deformation gradient of the cellular constituent distinguishing the contributions due to growth, to cell rearrangement and to elastic deformation. This allows to describe situations in which if in some points the ensemble of cells is subject to a stress above a threshold, then locally some bonds may break and some others may form, giving rise to an internal re-organisation of the tissue that allows to relax exceedingly high stresses.

Speaker: **Prusinkiewicz, Przemyslaw** (University of Calgary)
Title: *Relating mechanics and geometry of form development*
Abstract: Very briefly, I will consider several case studies where closely related developmental problems are sometime considered from a geometric perspective and sometime from a mechanical perspective. I will then look at relations between these approaches, and their respective advantages and drawbacks.

Speaker: **Purohit, Prashant** (University of Pennsylvania)
Title: *Heterogeneous fluctuating rod models for unfolded proteins and application to fibrin networks*

Abstract: Biofilaments, such as, actin and DNA, have for long been modeled as thermally fluctuating elastic rods with homogeneous material properties. Such models are adequate if the length scale of the filaments being studied is much larger than the scale of the heterogeneity. However, advanced single molecule experimental techniques have now made it possible to probe the properties of biomolecules at the scale of a few nanometers. The data emerging from these experiments ought to be greeted with appropriately detailed models. In this presentation we study the mechanics of a thermally fluctuating elastic rod whose moduli are a function of position. Such a rod can be used as a model for DNA whose sequence specific properties are known or for a protein oligomer in an AFM where some of the monomers might be unfolded. The mechanics of these rods is understood by first evaluating a partition function through path integral techniques. Similar methods can also be applied to heterogeneous networks of filaments. In this presentation we will show how protein unfolding at the level of a single filament can determine the macroscopic mechanical behaviour of a fibrin network.

Speaker: **Secomb, Timothy** (University of Arizona)
Title: *Structural adaptation in microvessel networks: Learning the rules*
Abstract: The number and structure of blood vessels change continuously during development and in response to changing demands. While the locations of major arteries and veins are under genetic control, the microcirculation contains more than 10^9 vessels, whose structure cannot be individually controlled. Instead, each vessel must react to local conditions and stimuli according to a common set of 'rules.' We adopted a 'top-down' approach to deduce these rules by observing network structures and analyzing the constraints imposed by the requirements for stability and functionally adequacy. In the resulting theoretical model, vessel diameters change in response to shear stress caused by flow, circumferential stress resulting from pressure, and oxygen level. We showed that upstream communication of signals along vessel walls is essential for efficient distribution of blood flow. By comparing networks from normal and tumor tissues, we deduced that this communication is impaired in tumor networks. This approach was also applied to the control of vascular wall thickness and vessel number.

Speaker: **Shipley, Rebecca** (University of Oxford)
Title: *Theoretical Models of Blood Flow in the Vasculature*
Abstract: The vasculature is a 3D multiscale network comprised of a hierarchy of vessels that is frequently categorized according to vessel size. Although the geometry and topology of the vasculature is organ-specific, blood flows into an organ from a feeding artery, through the arterioles into the capillary bed (or microcirculation), and exits through the venules then veins. Gas exchange occurs primarily in the microcirculation and, indeed, the function of the vasculature is to bring oxygenated blood within a small distance of every tissue point in the body in order to meet metabolic demands. Understanding and predicting the flow of blood through these networks could play a crucial role in, for example, developing novel anti-cancer treatments that “normalize” the tumour vasculature, and understanding how we might promote angiogenesis and vascular remodelling to treat myocardial ischaemia.
Traditional modelling approaches have employed a discrete approach by solving equations for blood flow in each vessel of a network. However, recent advancements in imaging methods have led to a wealth of imaging data that describe vascular structure in a highly detailed way. As the resolution of this data increases further, it will become too computationally intensive to simulate flow and mass transport in the complete vascular tree using a discrete approach. As such, continuum models must be developed that can be used alongside a discrete approach to capture the key functional properties of blood flow.
In this talk we present multiscale models, derived using the mathematical process of asymptotic homogenization, that describe blood transport in the arteriole, capillary and venule components of a vascular tree. This technique separates the network into three disparate length scales to determine the dependence of tissue-scale blood perfusion properties on the underlying vascular structures. We discuss the advantages and disadvantages of such a method compared to a discrete approach, and

finally discuss the option of coupling discrete and continuum models to simulate blood flow in explicit examples of rat mesentary networks.

Speaker: **Shipman, Patrick** (Colorado State University)
Title: *Diffusion to Capture, with Mechanical Stresses.*
Abstract: Patterns that form as iodine (for example) diffuses into organic gels are influenced by stresses on the gels.

Speaker: **Tabor, Michael** (University of Arizona)
Title: *A twisted life: the mechanics of spontaneous rotational reversal in Phycomyces*
Abstract: The growth of Phycomyces have long been a source of fascination. The aerial growth phase of stage IV sporangiophores of Phycomyces blakesleeanus displays a rotation that can change handedness as the sporangiophore elongates. We propose a continuum mechanical model of this process through the use of nonlinear, anisotropic, elasticity and show how the combination of a helical anisotropy (associated with the cell wall structure) and growth can induce spontaneous rotation and, under appropriate circumstances, the reversal of rotational handedness in a growing bioelastic filament. This talk represents joint work with Alain Goriely (University of Oxford).

Speaker: **van der Heijden, Gert** (University College London)
Title: *Multistability of inextensible helical strips with applications to self-assembled cholesterol ribbons*
Abstract: We derive new equilibrium equations governing the deformation of helical strips of inextensible material. For certain values of the elastic parameters we find instabilities and associated hysteresis behaviour for end-loaded helices of sufficiently large ratio of radius to pitch. We also find that the unstressed strip may have two stable helical configurations if the effect of material anistropy is taken into account. The results may help explain the experimentally observed bistability as well as the tension-induced straightening transition in self-assembled cholesterol ribbons that form in gallbladder bile as precursors to gallstones.

Speaker: **Waters, Sarah** (Oxford University)
Title: *Mathematical models for tissue engineering applications*
Abstract: The broad goal of tissue engineers is to grow functional tissues and organs in the laboratory to replace those which have become defective through age, trauma, and disease and which can be used in drug screening applications. To achieve this goal, tissue engineers aim to control accurately the biomechanical and biochemical environment of the growing tissue construct, in order to engineer tissues with the desired composition, biomechanical and biochemical properties (in the sense that they mimic the in vivo tissue). The growth of biological tissue is a complex process, resulting from the interaction of numerous processes on disparate spatio-temporal scales. Advances in the understanding of tissue growth processes promise to improve the viability and suitability of the resulting tissue constructs. In this talk, I highlight some of our recent mathematical modelling work that aims to provide insights into tissue engineering applications.

Speaker: **Yavari, Arash** (Georgia Institute of Technology)
Title: *Riemannian Geometry of Bulk Growth*
Abstract: In this seminar we present a geometric theory of the mechanics of growing solids. Bulk growth is modeled by a material manifold with an evolving metric. In this theory time dependence of metric represents the evolution of the stress-free (natural) configuration of the body in response to changes in mass density. We show that time dependency of material metric will affect the energy balance and the entropy production inequality; both must be modified. We then obtain the governing equations covariantly by postulating invariance of energy balance under time-dependent spatial

diffeomorphisms. We use the principle of maximum entropy production in deriving an evolution equation for the material metric. In the case of isotropic growth, we find those growth distributions that do not result in residual stresses. We then look at Lagrangian field theory of growing elastic solids. We will use the Lagrange-d'Alembert's principle with Rayleigh's dissipation functions to derive all the governing equations. We make an explicit connection between this geometric theory and the conventional multiplicative decomposition of deformation gradient $\mathbf{F} = \mathbf{F}e\mathbf{F}g$ into growth and elastic parts. We will also comment on the linearized theory.