Pacific Institute *for the* Mathematical Sciences

MATHEMATICS AT THE FRONTIER OF DEVELOPMENTAL BIOLOGY

Workshop Program

July 2-4, 2014

Pacific Institute for the Mathematical Sciences
Rm 2012 Earth Sciences Building (ESB)
2207 Main Mall, Vancouver

PIMS

PWIAS
PETER WALL INSTITUTE FOR ADVANCED STUDIES
THE UNIVERSITY OF BRITISH COLUMBIA | VANCOUVER

UBC

Mathematics at the Frontier of Developmental Biology, PIMS-PWIAS workshop, room 2012 Earth Sciences Building (ESB), 2207 Main Mall]

Wednesday July 2nd

8:45am - 9:00am	Registration and package pick up
9:00am - 10:00 am	**Eric Cytrynbaum:** *Estimating the bending modulus of a FtsZ bacterial-division protein filament*
10:00 am - 11:00 am:	**Rodrigo Fernandez-Gonzalez** *: Force generation, cytoskeletal architecture and junctional dynamics in embryonic wound repair*
11:00am - 11:20 am:	Coffee break (ESB 2012 Lobby)
11:20am - 12:20 pm:	**Len Pismen:** *Non-equilibrium patterns in polarisable active layers*
12:30 - 12:35 pm :	Group Photo
12:35pm - 2:00 pm:	Lunch (hosted- ESB Magma Café, **Please have your name tag)
2:00pm - 3:00 pm:	**Tony Harris:** *Molecular circuits controlling cell polarity in the Drosophila embryo*
3:00pm-3:30 pm:	Preview of poster session (short presentations)
3:30pm – 4:00pm:	Second chance: questions about all talks of the day
6:30pm:	Dinner for invited speakers (Provence, 4473 W. 10th Ave.)

Thursday July 3rd

9:00am - 10:00 am	**Kees Weijer :** *Cellular mechanisms underlying the formation of the primitive streak formation in the chick embryo*
10:00 am - 11:00 am	**Emmanuel Farge :** *Evolutionary conservation of early mesoderm specification by mechanotransduction in Bilateria*
11:00am - 11:20 am:	Coffee break (ESB 2012 Lobby)
11:20am - 12:20 pm:	**Guy Tanentzapf**: *Cell-matrix adhesion and morphogenesis: A systems biology approach*
12:30pm - 2:00 pm:	Lunch (Self Catered)
2:00pm - 3:00 pm:	**Bill Bement** : *Control of the single cell wound response by upstream signals (Alison Moe, Matt Larson and Bill Bement)*
3:00pm – 4:30pm:	Student poster competition and light reception (ESB Museum of Planet Earth)
4:30pm-5:30pm:	Student-led social evening (Mahoney & Sons, 5990 University Blvd.)

Friday July 4th

9:00 am - 10:00 am	**Bill Holmes :** *Spatio-temporal regulation of early blastocyst development*
10:00 am - 11:00 am	**James Feng** : *Modeling dorsal closure during Drosophila embryogenesis*
11:00am - 11:20 pm:	Coffee break (ESB 2012 Lobby)
11:20am – 12:20 am:	Roundtable for invited speakers: brainstorm for collaborative research plan and joint grant proposal 2

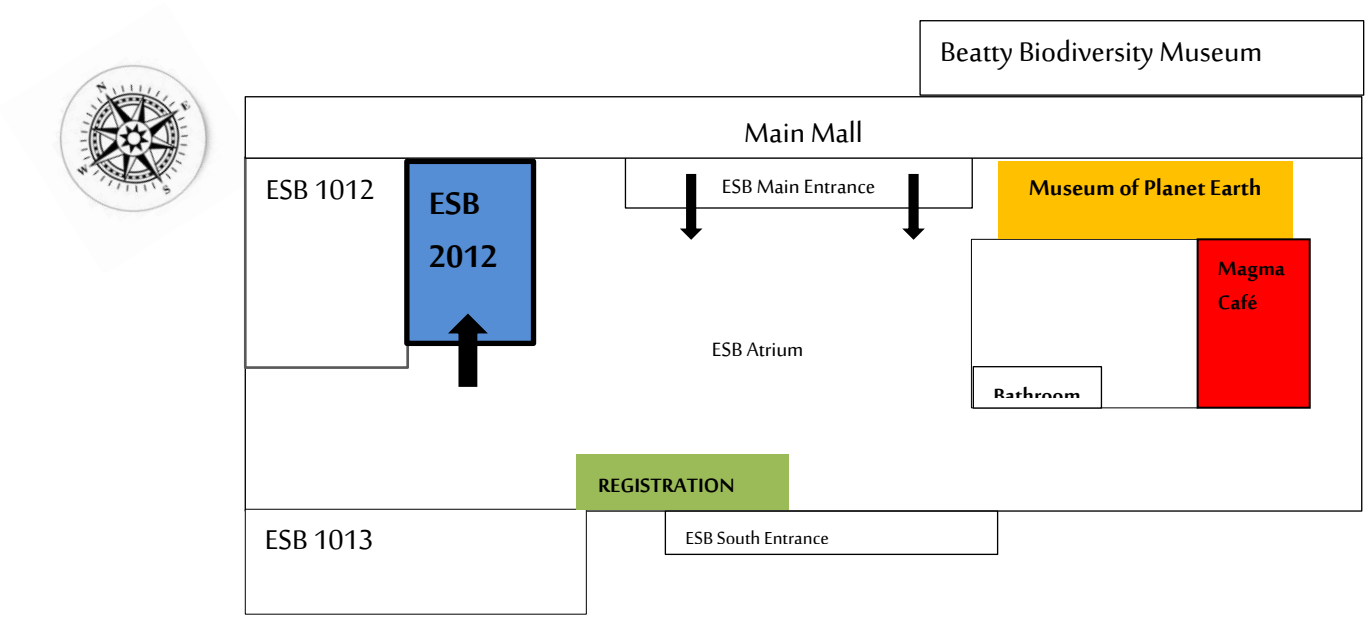
12:30am Lunch for invited speakers (Point Grill, 2205 Lower Mall)

2:00 pm Closing of workshop

Getting Started:

- **Get connected:** Select the "ubcvisitor" wireless network on your wireless device. Open up a web browser, and you will be directed to the login page.
- **Speaker Abstracts:** begin on page 3
- **Event Evaluation Survey**: Please help PIMS to improve the quality of its events and plan for the future by filling out the survey at the end of the conference. It is located at: http://goo.gl/zH6MJw

Building Floor Plan:



Speaker Abstracts

Bill Bement (University of Wisconsin - Madison):

Control of the single cell wound response by upstream signals (Alison Moe, Matt Larson and Bill Bement)

Damage to single cells initiates a rapid repair mechanism that has at least two complementary components: membrane fusion-dependent resealing of the hole in the plasma membrane triggered by damage, and cytoskeletal reorganization to repair the cortex. Both the membrane fusion and the cytoskeletal events triggered by wounding are highly complex but poorly understood. This situation reflects in part the surprising complexity of the repair process. For example, we have found that more than 40 different proteins rapidly accumulate around wounds in concentric rings, most of which differ from each other in terms of position and timing. How their recruitment is controlled is mysterious, but we assume that it ultimately reflects the influence of several several upstream gradients that form as an immediate consequence of woun wounding. These include gradients of calcium, gradients of lipids, and mechanical gradients. Clearly linking recruitment patterns of specific healing participants to multiple upstream gradients that are themselves dynamic in space and time is a serious challenge. We will discuss some of the steps we have taken to address this challenge and point out how it is related to challenges faced by others studying seemingly different biological processes such as cell division or polarization.

Eric Cytrynbaum (UBC):

Estimating the bending modulus of a FtsZ bacterial-division protein filament

FtsZ, a cytoskeletal protein homologous to tubulin, is the principle constituent of the division ring in bacterial cells. It is known to have force-generating capacity in vitro and has been conjectured to be the source of the constriction force in vivo. In this talk, I will describe our recent efforts to use modeling and data fitting to identify possible mechanisms by which the division ring generates force.

Emmanuel Farge (Institut Curie, Paris):

Evolutionary conservation of early mesoderm specification by mechanotransduction in Bilateria

The modulation of developmental biochemical pathways by mechanical cues is an emerging feature of animal development[1-5], but its involvement in evolution has not been explored. Here we show that a common mechanosensitive pathway involving β-catenin specifies early mesodermal identity at gastrulation in zebrafish and *Drosophila*. Mechanical strains developed by zebrafish epiboly and *Drosophila* mesoderm invagination trigger the phosphorylation of β-catenin-tyrosine-667. This leads to the release of β-catenin into the cytoplasm and nucleus, where it triggers and maintains, respectively, the expression of zebrafish *brachyury* ortholog *notail* and of *Drosophila* Twist, both crucial transcription factors for early mesoderm identity. The role of the β-catenin mechanosensitive pathway in mesoderm identity has been conserved over the large evolutionary distance separating zebrafish and *Drosophila*. This suggests mesoderm mechanical induction dating back to at least the last bilaterian common ancestor more than 570 million years ago, the period during which mesoderm is thought to have emerged.

[1] Desprat, N., Supatto, W., Pouille, P.A., Beaurepaire, E., and Farge, E. (2008). Tissue deformation modulates twist expression to determine anterior midgut differentiation in Drosophila embryos. Dev Cell *15*, 470-477.

[2] Pouille, P.A., Ahmadi, P., Brunet, A.C., and Farge, E. (2009). Mechanical Signals Trigger Myosin II Redistribution and Mesoderm Invagination in Drosophila Embryos. Science signaling *2*, ra16.

[3] Brunet, T., Bouclet, A., Ahmadi, P., Mitrossilis, D., Driquez, B., Brunet, A.C., Henry, L., Serman, F., Bealle, G., Menager, C., et al. (2013). Evolutionary conservation of early mesoderm specification by mechanotransduction in Bilateria. Nature communications *4*, 2821.

[4] Kahn, J., Shwartz, Y., Blitz, E., Krief, S., Sharir, A., Breitel, D.A., Rattenbach, R., Relaix, F., Maire, P., Rountree, R.B., et al. (2009). Muscle contraction is necessary to maintain joint progenitor cell fate. Dev Cell *16*, 734-743.
[5] Fernandez-Gonzalez, R., Simoes Sde, M., Roper, J.C., Eaton, S., and Zallen, J.A. (2009). Myosin II dynamics are regulated by tension in intercalating cells. Dev Cell *17*, 736-743.

James Feng (UBC):

Modeling dorsal closure during Drosophila embryogenesis

We report a mathematical model for the dynamic interaction among signaling proteins that control dorsal closure of the fruit fly Drosophila. Recent experiments have implicated the Par-family proteins as prominent players. In particular, aPKC suppresses the apicomedial actomyosin network, while Bazooka tends to inhibit aPKC. Their spatial recruitment from the cortex to the apicomedial surface introduces a delayed negative feedback loop. Our model represents the interaction among the signaling proteins through delayed differential equations, and further couples these kinetic equations with mechanical equations governing the dynamic contraction of the cells due to the actomyosin network. Thus, we are able to predict sustained oscillations of the cells in the early stage of dorsal closure, and a natural transition to a later stage of sustained areal contraction. These predictions are in good agreement with observations.

Rodrigo Fernandez-Gonzalez (University of Toronto):

Force generation, cytoskeletal architecture and junctional dynamics in embryonic wound repair

Epithelial tissues are protective barriers that display a remarkable ability to repair wounds. Wound repair is often associated with an accumulation of actin and non-muscle myosin II around the wound, forming a supracellular cable whose contraction drives wound closure. Wound closure is also accompanied by a redistribution of cell-cell adhesion proteins around the wound. However, the mechanisms that regulate cytoskeletal and junctional rearrangements at the wound margin are not well understood. We are investigating the molecular rearrangements associated with wound repair in the epidermis of *Drosophila* embryos. Using automated image analysis, we demonstrate that the junctional proteins β-catenin and E-cadherin accumulate at discrete points of contact between cells adjacent to the wound. This redistribution of junctional proteins follows actomyosin contractility. We find that the conserved non-receptor tyrosine kinase Abl is necessary for the redistribution of β-catenin at the wound margin, and also for proper actin organization at the purse string. We propose that Abl controls adhesion dynamics during wound repair through the organization of actin around the wound to promote contractile forces and growth of mechanosensitive cadherin-catenin complexes.

Tony Harris (University of Toronto):

Molecular circuits controlling cell polarity in the Drosophila embryo

My lab pursues several related questions. How are plasma membranes formed in the early *Drosophila* embryo? How are plasma membranes polarized to distinguish the two ends of epithelial cells? How are epithelial cells connected to form tissues? How are cell shape changes regulated for epithelial morphogenesis? To address these questions, we use *Drosophila* genetics and microscopy to identify and characterize molecular circuits that regulate each process. For example, robust cell polarization relies on positive feedback mechanisms for assembling molecular complexes locally, coupled with inhibitory mechanisms for preventing complex assembly elsewhere. The polarization of epithelial cells involves the assembly of Bazooka (Baz)/Par-3 complexes around the apical cell circumference where adherens junctions form. Basolaterally, the kinase Par-1 phosphorylates Baz and inhibits Baz complex assembly. Apicolaterally, cytoskeletal landmarks are important for Baz recruitment, but positive feedback mechanisms were unknown. We have identified a positive feedback loop in which Baz and centrosomes recruit each other to specific sites around the apical circumference of newly formed epithelial cells of the embryo. Strikingly, we find that Par-1 promotes this positive feedback. Thus, Par-1 is responsible for both the local assembly of Baz complexes, next to centrosomes, and the inhibition of assembly elsewhere. This polarization pathway is, however, counteracted by the apical kinase aPKC for a more even distribution of Baz around the apical circumference. aPKC appears to modulate the pathway by phosphorylating and displacing Par-1 from the apical domain as embryos transition

from cellularization to gastrulation. The ability of a single kinase, Par-1, to both locally promote and globally inhibit assembly of its substrate's complexes provides a simple mechanism for inducing robust polarity. Indeed, the pathway can produce an extreme polarization of Baz when left unchecked and is normally tuned down by aPKC. These and other aspects of epithelial cell polarity will be discussed.

Bill Holmes (University of California - Irvine):

Spatio-temporal regulation of early blastocyst development

The central question of developmental biology is how a single cell can produce an organism with exquisitely complex spatial structure, reproducibly and robustly. The first step in mammalian embryonic development is the specification of two cell types: trophoectoderm (TE) cells that later form the placenta, and pluripotent inner cell mass (ICM) cells that form the embryo proper. We combine modeling and experiments to investigate the events that choreograph this process. Using two and three dimensional multiscale spatial models of the developing embryo, it is shown that contact mediated fate commitment is sufficient to initially direct cells to the correct lineage but incapable of maintaining proper embryonic structure. Further, gene expression noise (at endogenous levels, as determined by immunofluorescence) is both necessary and sufficient to maintain cells plasticity, a requirement for them to continually integrate positional information in the highly dynamic early embryonic environment.

Len Pismen (Technion):

Non-equilibrium patterns in polarisable active layers

I explore a class of macroscopic continuous models with feedback interactions inducing spontaneous vector or nematic polarisation and mechanical deformation of elastic active media. Linear stability analysis predicts, depending on the sign of feedback interaction coefficients, either monotonic or oscillatory instability of the homogeneous isotropic state. In the former case, the emerging pattern undergoes a slow coarsening process but permanent polarity may emerge when the system is topologically constrained. Oscillatory instabilities emerge in active systems on a finite wavelength and lead to complex wave patterns. Transition to a deformed polarised state may be frustrated in constrained geometry but leads to boundary undulations in free-boundary settings.

Guy Tanentzapf (UBC):

Cell-matrix adhesion and morphogenesis: A systems biology approach

Our lab is interested in how complex tissue architecture arises during animal development through the process of morphogenesis. Our primary focus is on Cell adhesion to the ExtraCellular Matrix (ECM), which has numerous roles during development. Cell-ECM adhesion is largely mediated by the integrin family of adhesion receptors. We wish to elucidate how integrins mediate a vast diversity of roles during development. To address this question we are using a cross-disciplinary systems-level approach. We start by deriving knowledge from structural and single molecule biophysical studies of integrin and its associated proteins. This knowledge is then applied, using molecular and transgenic approaches, to alter the regulation and mechanical properties of integrin-mediated adhesion on the level of the cell. Using localization studies, FRAP, and other quantitative imaging approaches, combined with mathematical modeling we analyze the regulation of the assembly and stability of the adhesion complex. Information from cell-level studies is then used to study tissue level functions of integrin. Using live imaging combined with mathematical modeling we can analyze the mechanical properties of tissues undergoing morphogenesis. By integrating these levels of analysis, from molecule to cell to tissue, we are uncovering the fundamental mechanisms that regulate Cell-ECM adhesion during development.

Kees Weijer (University of Dundee):

Cellular mechanisms underlying the formation of the primitive streak formation in the chick embryo

Collective cell movement is a key process during the development of many organisms. We are interested in understanding how cell-cell signalling guides and coordinates large scale collective cell movements and how these movements feedback on cell-cell signalling to result in tissue morphogenesis. Collective cell movement is especially important during gastrulation, the process in which the mesendoderm cells take up their

correct positions in the embryo. Chick embryos are a widely used model system for the study of gastrulation in amniotes. Gastrulation in the chick embryo starts with the formation of the primitive streak. The streak forms in a posterior to anterior direction and is the site of ingression of the mesendoderm cells. Streak formation involves extensive large scale counter rotating cell flows in the epithelial cell layer of the epiblast. These flows merge at the site of the forming streak and transport the forming mesendoderm into the midline of the embryo. The mechanisms controlling the formation of the primitive streak in amniote embryos are still not well understood. It has been suggested that streak formation could result from chemotaxis, local cell-cell intercalation and or oriented division, based on experimental observations and modelling studies. However detailed quantitative data on cell behaviours to back up the statements are still lacking. The cells in the epiblast form a highly polarised epithelial sheet and the cells are connected with well-developed apical adherens and tight junctions. It remains to be determined by which mechanisms the cells in the epiblast and forming streak move and how much relative cell movement exists. To answer some of the questions and study most cells in the embryo (3-4 mm across) we have developed a dedicated light sheet microscope that in combination with a new transgenic chick line that expresses a membrane targeted GFP now allows us to investigate cellular dynamics of the epiblast cells in great detail. We have developed algorithms to segment and track up to 100.000 cells in the epiblast, which allows us to monitor *in vivo* cell shape changes, cell division and cell movement. Our results show that streak formation is driven by active deformation of the mesendoderm leading to the formation of the observed embryo wide vortex flows. Our analysis shows that mesendoderm precursor cells undergo an extensive apical contraction, ultimately culminating in their ingression through the streak. Simultaneously groups of cells all over the sickle shaped mesendoderm show sequential directional contractions of aligned junctions. These coordinated junctional contractions result in oriented cell-cell intercalations. Our experiments show that junctional contraction is mediated by conventional and unconventional myosins. Inhibitor and knockdown studies show that junctional contraction is mediated by myosin II but that the assembly of MyosinII filaments is regulated by in a myosin I dependent manner and which may be involved in a tension sensing pathway. At present we attempt to identify secreted factors that may help to coordinate these processes and we are developing cell based computational models to test our understanding of the system.

Poster Session Abstracts

Stephanie Ellis:

Integrin-mediated cell-ECM adhesion controls morphogenesis through modulation of the biomechanical properties of a tissue

Integrin-mediated Cell-ECM adhesion is essential for tissue morphogenesis during development. An inherent aspect of morphogenesis is that it involves massive changes in the mechanical properties of tissues. Integrins are known to integrate mechanical signals to regulate the formation of complex tissue architecture, but the mechanisms involved are poorly understood. Dorsal closure (DC), an integrin-dependent morphogenetic process that occurs during fly embryogenesis, provides a model to study integrin function during tissue morphogenesis. We have identified integrin-containing adhesive structures on the basal surface of the amnioserosa, an extra-embryonic epithelium that is essential for DC. These adhesive structures bear striking resemblance to focal adhesions, thus we term them Focal Adhesion-Like Structures (FALS). FALS are dynamic, motile structures; their morphology and relative stability is tied to the developmental stage of the tissue. Upon application of ectopic force, we observe striking changes in FALS morphology and dynamics. Genetic modulation of actomyosin contractility and/or FALS attachment to actin also perturbs FALS dynamics and behavior suggesting that FALS are mechano-responsive structures. Mutations in integrin and its ECM ligands disrupt FALS and lead to a failure of DC. Intriguingly, mutations that act to increase cell-ECM adhesion through FALS also result in DC defects. Using quantitative image analysis and mathematical modeling, we show that FALS regulate the mobility of amnioserosa cells during DC. Misregulation of integrin function in this context changes the biomechanical properties of the tissues involved, and in particular, alters the friction forces between tissue layers, leading to impaired cell mobility and disrupted DC. Altogether, our study illustrates how modulation of cell-ECM adhesion can alter the fundamental biomechanical properties of a tissue to regulate morphogenetic events.

*I will co-present a poster with Katie Goodwin.

Katharine Goodwin:

Functional analysis of Cell-ECM adhesion during Dorsal Closure using quantitative imaging and mathematical modeling

During morphogenesis cells undergo dynamic processes of migration, rearrangement, and shape changes in order to form complex tissue architecture. Essential for these morphogenetic processes is the ability of cells to form adhesive contacts to their neighbors and to the underlying extracellular matrix (ECM). Cell-Cell adhesion and Cell-ECM adhesion is mediated by transmembrane adhesion receptors that link the extracellular environment and intracellular cytoskeletal networks. Our lab is interested in the studying the morphogenetic roles of integrins, which form the primary link between the ECM and the actin cytoskeleton. To this end we are studying integrin function during dorsal closure (DC), a morphogenetic event that involves cell migration and fusion of epithelial sheets over an extra-embryonic tissue, the amnioserosa (AS). Integrins and their associated adhesion complex play important and diverse roles during DC. We are utilizing a toolkit, generated in our lab, containing various regulatory mutations in integrins and their associated proteins. We identified a number of regulatory mutations that disrupt specific aspects of integrin-mediated adhesion and lead to defective and/or abnormal DC. We will present the results of an intensive quantitative analysis of cell behavior during DC that was carried out using high-resolution live imaging in Cell-ECM mutants that exhibit abnormal DC. To contextualize and interpret our image analysis data we are utilizing a cell-level biomechanical mathematical model of dorsal closure that includes many of the quantitative parameters we measure. Modifying this mathematical model in order to recapitulate a mutant phenotype can help us to understand the mechanical effects of the mutation on cell behavior and tissue dynamics during DC. With this quantitative approach, we will provide novel mechanistic insight into the role of Cell-ECM adhesion in the formation and maintenance of complex tissue architecture.

Leah Keshet:

Using CHASTE (Oxford) to explore tissue dynamics

(Dhanajay Bhaskar and Leah Edelstein-Keshet)

Mathematicians have developed models of biological mechanisms across multiple spatial and temporal scales: ranging from subcellular level to population of organisms. Accurate simulation of biological processes like cell migration, cell sorting, wound healing, etc. requires interaction between models at more than one scale. In this undergraduate summer project, DB and LEK work on mathematical models of movement and mechanical interaction between epithelial cells arranged in a 2-dimensional layer including subcellular models of cell growth, proliferation and tissue-level models of geometric constraints. Multiscale simulations of epithelial monolayers created using the CHASTE (Cancer, Heart and Soft Tissue Environment) simulation package, developed at University of Oxford, is being used to visualize how these mathematical models interact and capture complex dynamics of biological processes.

Haihan Lan:

A Biomechanical Model for Cell Polarization and Intercalation

In this paper we present a biomechanical model for planar cell polarization and dynamic tissue remodelling during intercalation in Drosophila embryo. Our model is based on the myosin positive feedback mechanism observed by Fernandez-Gonzalez et al. We model the kinetics of four chemical species: Rho-kinase, non-muscle myosin-II, Bazooka/Par-3 and Shroom, and model the mechanical dynamics by imposing linear force laws on the cell edges. After setting the initial perturbations and allowing the system to evolve, the results observed are promising. Our current work focuses on incorporating experimentally measured parameters into the model and extracting key biological predictions and insights for future experiments.

Laura Liao:

Signaling in single cell wound healing

A single cell, such as a frog egg, repairs injuries by orchestrating an intracellular signalling response. The signalling response is spatiotemporally localized, recruiting proteins to the plasma membrane, around the wound site. Proteins such as Rho GTPases assemble at the wound edge, where fluorescent probes reveal Rho GTPase patterning in concentric rings. Patterning allows testable hypotheses to be made about the structure of the signalling network. In this work, a Rho GTPase signalling model was extended to test how a family of enzymes, protein kinase C (PKC), play a role in cell repair signalling. The partial differential equation model allowed PKCs to affect Rho GTPase basal rates of activation and/or inactivation, with increasing spatial detail. Spatially constant and spatially detailed PKC activity profiles were considered. Ultimately, this approach did not account for Rho GTPase patterning data. However, several results on PKC regulation of Rho GTPases were found: (1) Modulation of Rho inactivation rates, rather than activation rates, by PKCs were more likely to quantitatively account for patterning data. (2) The basal Rho activation rates must saturate with PKC, rather than exhibit a linear dependence. (3) Certain Rho insensitivities to PKC indicated an oversimplified model view. These results suggested that PKCs likely acted as suppressors for Rho GTPases. Conversely, if PKCs were activators for Rho GTPases, their activity must be finite, which is biologically consistent with resource-limited lipid activation of PKCs. Finally, PKC competition for lipids was proposed as a model revision, in order to account for patterning data.

Mary Anne Mata:

Mathematical Analysis of Actin Waves Model

Actin cytoskeleton reorganization is highly regulated in eukaryotic cells and spatio-temporal patterns such as localized and propagating waves are observed in experiments. In this study, we describe and analyze a minimal reaction diffusion model depicting the feedback between signalling proteins and filamentous actin (F-actin) which we refer to as the actin wave model. We show using numerical simulation that this model displays a rich variety of patterning regimes. Moreover, a relatively recent nonlinear stability method, the Local Perturbation Analysis (LPA), is used to map the

parameter space of this model and explain the genesis of patterns in various linear and nonlinear patterning regimes. We show, using LPA, that the spatially distributed model gives rise to dynamics that are not present in the kinetics alone.

Brian Merchant:

A cell motility model coupling Rho-GTPase interactions with cell geometry

Polarization of the Rac and Rho family of small Rho GTPases is critical for single cell motility, but is not well studied in multicellular contexts. We present a simple model of Rac/Rho polarization coupled to a cell motility model that recapitulates important aspects of cell motility. The simplicity of the model is well suited for further study in a multicellular context. By considering Rac/Rho interactions only at specific points on the cell membrane boundary, the model can make use of ODEs to capture Rac/Rho interactions instead of the PDEs used in more complex models. The behaviour of the cytoskeleton (in protrusion and retraction) is abstracted in order to keep focus on Rac/Rho interactions while still capturing important aspects of biological detail. Thus, simple algorithms are used to capture feedback from cell geometry to Rac/Rho interaction parameters. The model predicts a polarized pattern of GTPases coupled with a deformed cell geometry and a steady movement.

Tenghu Wu:

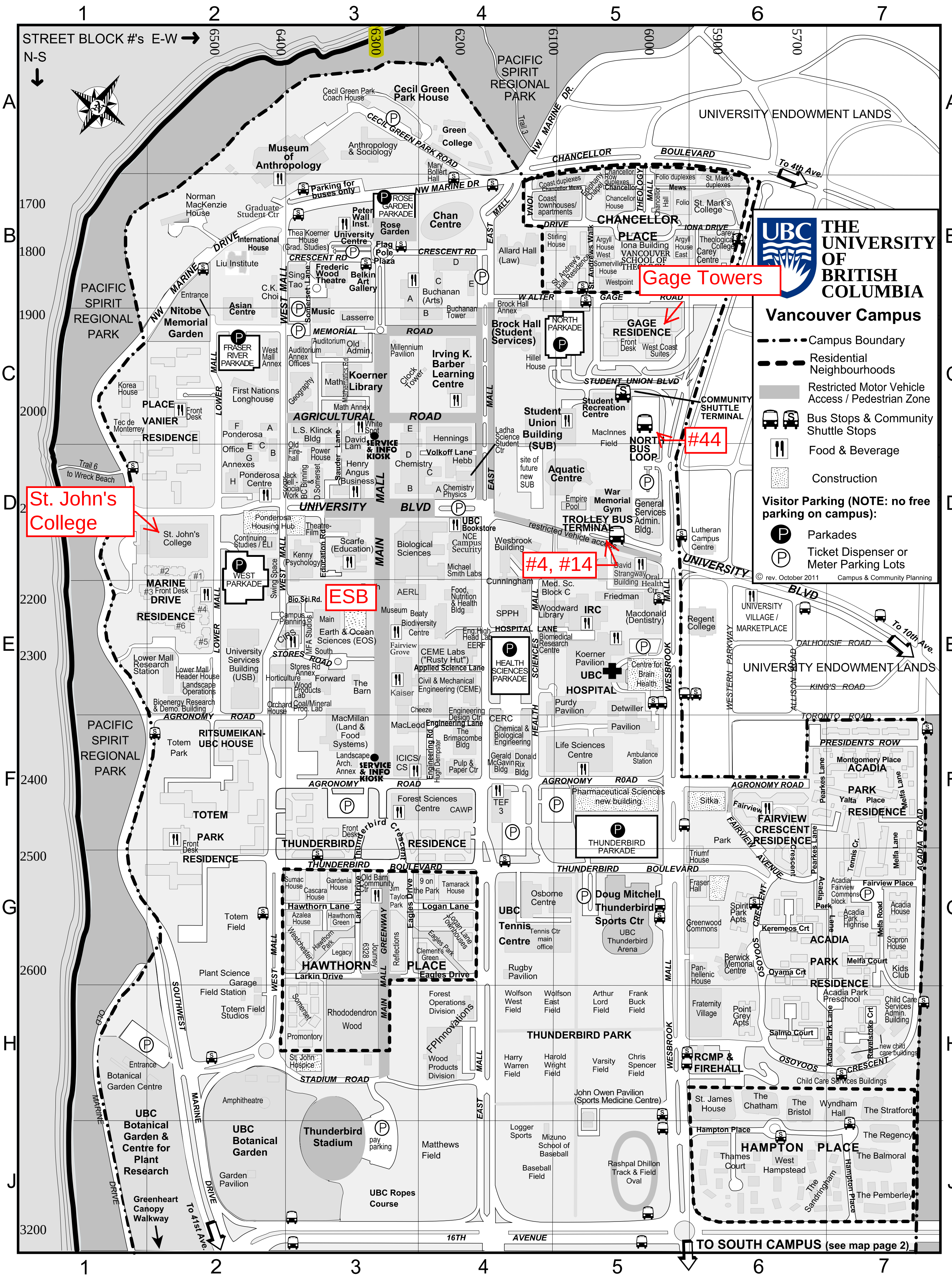
A bio-mechanical model for fluidization of cells under dynamic strain

Recently, Fredberg and coworkers have investigated the response of human airway smooth muscle cells under a transient stretch-compress (SC) and compress-stretch (CS) maneuvers. Their results indicate that the transient SC maneuver causes a sudden fluuidization of the cell while the CS maneuver does not. We have built a model to probe the asymmetric behavior of the stress fibers under the CS and SC maneuvers. The model couples the crossbridge cycle of myosin motors with a viscoelastic Kelvin-Voigt element representing the stress fiber. Simulation results suggest that the sensitivity of the myosin detachment rate to the stress fiber tension may have caused the asymmetric behavior of the stress fiber under the CS and SC maneuvers. For the SC maneuver, the stretch increases the tension of the stress fiber and suppresses the myosin detachment rate. The subsequent compression then causes a large proportion of the myosin population to disengage from actin filaments. This leads to the disassembly of the stress fibers and the observed fluidization.

Jessica Yu:

The role of mechanical tension during axis elongation in Drosophila

Convergent extension is a conserved process in which a tissue elongates along one axis and narrows along a second, orthogonal axis. Convergent extension is necessary in processes such as limb bud development, kidney tubule elongation, and the extension of the anterior-posterior axis of the embryo. In Drosophila, axis elongation results largely from cell intercalation, a cell behaviour in which cell-cell interfaces parallel to the dorsal-ventral axis of the animal contract, forming a transient vertex where four or more cells meet. The vertex is then resolved through the assembly of new cell interfaces parallel to the anterior-posterior axis of the animal. We use quantitative fluorescence microscopy and biophysical methods to measure the cellular and molecular dynamics involved in vertex resolution during Drosophila axis elongation. Using laser ablation and particle tracking velocimetry, we found that new cell interfaces resulting from vertex resolution sustained 32% more mechanical tension than older, more stable interfaces. We found that the elongation rate of new interfaces increased by 1.81-fold when we applied ectopic tension on the elongating interface. Together, these data suggest that the elongation of new interfaces during axis elongation results from a pulling force. We are currently investigating the molecular mechanisms by which tension determines the rate of elongation of new edges, the origin of the tensile stresses involved in vertex resolution, and if mechanical signals can also determine the direction of new interface elongation. In addition to these, we found a population of cells on the ventral surface of the Drosophila germband that undergoes oriented cell divisions parallel to the anterior-posterior axis during axis elongation, and we are investigating the role of mechanical tension in orienting these divisions. Characterizing the mechanical signals behind axis elongation will be crucial to understand animal development, as well as birth defects such as spina bifida and limb malformations.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SW MARINE DRIVE
STADIUM ROAD
AGRONOMY ROAD
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To 10th Ave.
To 41st Ave.
TO SOUTH CAMPUS (see map page 2)

Map Directory

Site or Building Name & Address	Grid
Abdul Ladha Science Student Ctr, 2055 East Mall	D4
Acadia/Fairview Commonsblock, 2707 Tennis Cres	G7
Acadia House, 2700-2720 Acadia Rd	G7
Acadia Park Residence	F/H-6/7
Acadia Park Highrise, 2725 Melfa Rd	G7
Acadia Park Preschool, 2750 Acadia Park Lane	H7
Allard Hall [Faculty of Law], 1822 East Mall	B4
Anthropology & Sociology Bldg, 6303 NW Marine Dr	A3
Aquatic Centre, 6121 University Blvd	D5
Aquatic Ecosystems Research Lab (AERL), 2202 Main Mall	E3
Asian Centre, 1871 West Mall	B2
Auditorium (a.k.a. "Old Auditorium"), 6344 Memorial Rd	C3
Auditorium Annex Offices, 1924 West Mall	C3
Barn (daycare), 2323 Main Mall	E3
B.C. Binning Studios (formerly Hut M-17), 6373 University Blvd	D3
Beaty Biodiversity Centre & Museum, 2212 Main Mall	E3/4
Belkin (Morris & Helen) Art Gallery, 1825 Main Mall	B3
Berwick Memorial Centre, 2765 Osoyoos Cres	G6
Bioenergy Research & Demonstration Bldg., 2337 Lower Mall	E2
Biological Sciences Bldg [Science Faculty office], 6270 University Blvd	D3
Biomedical Research Ctr, 2222 Health Sciences Mall	E4
Biotechnology Laboratory, 2125 East Mall	D4
Bollert (Mary) Hall, 6253 NW Marine Dr	A4
Bookstore, 6200 University Blvd	D4
Botanical Garden Centre/Gatehouse, 6804 SW Marine Dr	H1
Botanical Garden Pavilion (enter at Gatehouse, 6804 SW Marine Dr)	J2
Botan. Gard. Greenhses/ Workshops, 6088 S. Campus Rd	South Campus
Brimacombe Building, 2355 East Mall	F4
BROCK HALL: Student Services & Welcome Centre, 1874 East Mall	**C4**
Brock Hall Annex, 1874 East Mall	C4
Buchanan Building (Blocks A, B, C, D, & E) [Arts], 1866 Main Mall	B3/4
Buchanan Tower, 1873 East Mall	C4
C.K. Choi Building for the Institute of Asian Research, 1855 West Mall	B2
Campus & Community Planning, 2210 West Mall	E3
Campus Security, 2133 East Mall	D4
Carey Centre, 5920 Iona Drive	B6
Carey Theological College, 1815 Wesbrook Mall	B6
CAWP (Centre for Advanced Wood Processing), 2424 Main Mall	F4
Cecil Green Park Coach House, 6323 Cecil Green Park Rd	A3
Cecil Green Park House, 6251 Cecil Green Park Rd	A3
CEME — *see Civil & Mechanical Engineering Building*	
Centre for Comparative Medicine, 4145 Wesbrook Mall	South Campus
Centre for Interactive Research on Sustainability (CIRS), 2260 West Mall	E3
CERC (Clean Energy Research Ctr), 2360 East Mall	F4
Chan Centre for the Performing Arts, 6265 Crescent Rd	B4
Chancellor Place neighbourhood	B5
Chemical & Biological Engineering Bldg, 2360 East Mall	F4
Chemistry A Block - Chemistry Physics Building, 6221 University Blvd	D4
Chemistry B,C,D & E Blocks, 2036 Main Mall	D3
Child Care Services Administration Bldg, 2881 Acadia Rd	H7
Child Care Services Bldgs, Osoyoos Cresc and Revelstoke Crt	H7
CIRS — *see Centre for Interactive Research on Sustainability...*	
Civil & Mechanical Engineering Bldg (CEME), 6250 Applied Science Lane	E4
Civil & Mechanical Eng. Labs ("Rusty Hut"), 2275 East Mall	E4
Coal & Mineral Processing Lab, 2332 West Mall	E3
Continuing Studies Bldg [English Language Institute], 2121 West Mall	D2
Copp (D.H.) Building, 2146 Health Sciences Mall	D5
Cunningham (George) Building [Pharmaceutical Sc.], 2146 East Mall	E4
David Lam Learning Centre, 6326 Agricultural Rd	C3
David Lam Management Research Ctr, 2033 Main Mall	C3
Donald Rix Building, 2389 Health Sciences Mall	F4
Doug Mitchell Thunderbird Sports Centre, 6066 Thunderbird Blvd	G5
Dorothy Somerset Studios (formerly Hut M-18), 6361 University Blvd	D3
Earth Sciences Building (ESB) under construction, 2207 Main Mall	E3
Earth & Ocean Sciences (EOS) - Main and South, 6339 Stores Rd	E3
Earthquake Engineering Research Facility (EERF), 2235 East Mall	E4
Engineering High Head Room Lab, 2225 East Mall	E4
English Language Institute (E.L.I.) — *see Continuing Studies Building*	
Environmental Services Facility, 6025 Nurseries Rd	South Campus
Fairview Crescent Residence, 2600-2804 Fairview Cres	F6
Fire Department, 2992 Wesbrook Mall	H6
First Nations Longhouse, 1985 West Mall	C2
Flag Pole Plaza (Main Mall & Crescent Rd)	B3
Food, Nutrition and Health Bldg, 2205 East Mall	E4
Forest Sciences Centre [Faculty of Forestry], 2424 Main Mall	F4
Forward (Frank) Building, 6350 Stores Rd	E3
FPInnovations (Forest Operations & Wood Products), 2601/2665 E. Mall	H4
FPInnovations (Pulp & Paper Division), 3800 Wesbrook Mall	South Campus
Fraser Hall (public rental housing), 2550 Wesbrook Mall	G6
Fraternity Village, 2880 Wesbrook Mall	H6
Frederic Wood Theatre, 6354 Crescent Rd	B3
Friedman Bldg, 2177 Wesbrook Mall	E5
Gage Residence, 5959 Student Union Blvd	C5
General Services Administration Bldg (GSAB), 2075 Wesbrook Mall	D5
Geography Building, 1984 West Mall	C3
Gerald McGavin Building, 2386 East Mall	F4
Graduate Student Centre — *see Thea Koerner House*	
Green College, 6201 Cecil Green Park Rd	A4
Greenheart Canopy Walkway, Botanical Garden, 6804 SW Marine Dr	H1
Greenwood Commons (public rental housing), 2660 Wesbrook Mall	G6
Hampton Place neighbourhood	H/J-6/7
Hawthorn Place neighbourhood	G/H3
Hebb Building, 2045 East Mall	D4
Hennings Building, 6224 Agricultural Rd	C4
Henry Angus Building [Sauder School of Business], 2053 Main Mall	D3
Hillel House - The Diamond Foundation Centre for Jewish Campus Life, 6145 Student Union Blvd	C4
Horticulture Building/Greenhouse, 6394 Stores Rd	E2/3
Hugh Dempster Pavilion, 6245 Agronomy Rd	F4
ICICS/CS (Institute for Computing, Information & Cognitive Systems/Computer Science), 2366 Main Mall	F4
Instructional Resources Centre (IRC), 2194 Health Sciences Mall	E5
International House, 1783 West Mall	B2
In-Vessel Composting Facility, 6035 Nurseries Road	South Campus
Irving K. Barber Learning Centre, 1961 East Mall	C4
Jack Bell Building for the School of Social Work, 2080 West Mall	D3
John Owen Pavilion & Allan McGavin Sports Medicine Centre, 3055 Wesbrook Mall	H5
Kaiser (Fred) Building [Faculty of Applied Science], 2332 Main Mall	E3
Kenny (Douglas T) Building, 2136 West Mall	D3
Kids Club, 2855 Acadia Rd	G7
Klinck (Leonard S.) Bldg, 6356 Agricultural Rd	C3
Koerner (Walter C.) Library, 1958 Main Mall	C3
Landscape Architecture Annex, 2371 Main Mall	F3
Lasserre (Frederic) Building, 6333 Memorial Rd	C3
Law, Faculty of — *see Allard Hall*	
Leon and Thea Koerner University Centre, 6331 Crescent Rd	B3
Life Sciences Centre, 2350 Health Sciences Mall	F5
Liu Institute for Global Issues, 6476 NW Marine Dr	B2
Lower Mall Header House, 2269 Lower Mall	E2
Lower Mall Research Station, 2259 Lower Mall	E2
Macdonald (J.B.) Building [Dentistry], 2199 Wesbrook Mall	E5
MacLeod (Hector) Building, 2356 Main Mall	F3
MacMillan (H.R.) Bldg [Faculty of Land & Food Systems], 2357 Main Mall	F3
Marine Drive Residence (Front Desk in Bldg #3), 2205 Lower Mall	E2
Material Recovery Facility, 6055 Nurseries Rd	South Campus
Mathematics Annex, 1986 Mathematics Rd	C3
Mathematics Building, 1984 Mathematics Rd	C3
Medical Sciences Block C, 2176 Health Sc. Mall	E4
M.F.A. Studios (formerly B.C. Binning MFA Studios), 6363 Stores Rd	E3
Michael Smith Laboratories, 2185 East Mall	D4
Museum of Anthropology (MOA), 6393 NW Marine Dr	A2/3
Music Building, 6361 Memorial Rd	B/C3
Networks of Ctrs of Excellence (NCE), 2125 East Mall	D4
Nitobe Memorial Garden, 1895 Lower Mall	B/C2
Nobel Biocare Oral Heath Centre (David Strangway Bldg), 2151 Wesbrook Mall	E5
Norman MacKenzie House, 6565 NW Marine Dr	B2
NRC Institute for Fuel Cell Innovation, 4250 Wesbrook Mall	South Campus
Old Administration Building, 6328 Memorial Rd	C3
Old Auditorium — *see Auditorium*	
Old Barn Community Centre, 6308 Thunderbird Blvd	G3
Old Firehall, 2038 West Mall	D3
Orchard House, 2336 West Mall	E2
Osborne (Robert F.) Centre/Gym, 6108 Thunderbird Blvd	G4
Panhellenic House, 2770 Wesbrook Mall	G6
Peter Wall Institute for Advanced Studies, 6331 Crescent Rd	B3
Place Vanier Residence, 1935 Lower Mall	C/D2
Plant Ops Nursery/Greenhouses, 6029 Nurseries Rd	South Campus
Plant Science Field Station & Garage, 2613 West Mall	H2
Point Grey Apartments, 2875 Osoyoos Cresc	H6
Police (RCMP) & Fire Department, 2990/2992 Wesbrook Mall	H6
Ponderosa Centre, 2071 West Mall	D2
Ponderosa Office Annexes: A, B, & C, 2011-2029 West Mall	C/D2
Ponderosa Office Annexes: E to H, 2008-2074 Lower Mall	C/D2
Power House, 2040 West Mall	D3
Pulp and Paper Centre, 2385 East Mall	F4
Ritsumeikan-UBC House, 6460 Agronomy Rd	F2
Rose Garden	B3
Roy Barnett Recital Hall - in Music Building	
Rugby Pavilion, 2584 East Mall	G4
Scarfe (Neville) Building [Education], 2125 Main Mall	D3
School of Population & Public Health (SPPH), 2206 East Mall	E4
Simon K.Y. Lee HKU-UBC House — Bldg #1, Marine Drive Residence	E2
Sing Tao Building, 6388 Crescent Rd	B3
Sopron House, 2730 Acadia Rd	G7
South Campus Warehouse, 6116 Nurseries Rd	South Campus
Spirit Park Apartments, 2705-2725 Osoyoos Cresc	G8
St. Andrew's Hall/Residence, 6040 Iona Dr	B5
St. John's College, 2111 Lower Mall	D2
St. Mark's College, 5935 Iona Dr	B6
Staging Research Centre, 6045 Nurseries Rd	South Campus
Stores Road Annex, 6368 Stores Rd	E3
Student Recreation Ctr, 6000 Student Union Blvd	C5
Student Union Bldg (SUB), 6138 Student Union Blvd	C4
TEF3 (Technology Enterprise Facility 3), 6190 Agronomy Rd	F4
Thea Koerner House [Faculty of Graduate Studies], 6371 Crescent Rd	B3
Theatre-Film Production Bldg, 6358 University Blvd	D3
Thunderbird Residence, 6335 Thunderbird Cresc	F3/4
Thunderbird Stadium, 6288 Stadium Rd	J3
Thunderbird Winter Sports Ctr — *see Doug Mitchell Thunderbird Sports...*	
Totem Field Studios, 2613 West Mall	H2
Totem Park Residence, 2525 West Mall	F/G2
TRIUMF, 4004 Wesbrook Mall	South Campus
Triumf House (TRIUMF Visitor's Residence), 5835 Thunderbird Blvd	G6
UBC Bookstore, 6200 University Blvd	D4
UBC Farm, 6182 Wesbrook Mall	South Campus
UBC Hospital, 2211 Wesbrook Mall	E5
UBC Tennis Centre, 6160 Thunderbird Blvd	G4
UBC Thunderbird Arena (in Doug Mitchell Centre), 2555 Wesbrook Mall	G5
University Centre (Leon & Thea Koerner), 6331 Crescent Rd	B3
University Neighbourhoods Association, 5923 Berton Ave	South Campus
University Services Building (USB), 2329 West Mall	E2
Vancouver School of Theology, 6000 Iona Drive	B5
Walter H. Gage Residence, 5959 Student Union Blvd	C5
War Memorial Gymnasium, 6081 University Blvd	D5
Wayne & William White Engineering Design Ctr, 2345 East Mall	E4
Wesbrook Bldg, 6174 University Blvd	D4
Wesbrook Place neighbourhood	South Campus
Wesbrook Village shopping centre	South Campus
West Mall Annex, 1933 West Mall	C2
West Mall Swing Space Bldg, 2175 West Mall	D2
Wood Products Laboratory, 2324 West Mall	E3
Woodward IRC, 2194 Health Sciences Mall	E4/5
Woodward Library, 2198 Health Sciences Mall	E4/5

SOUTH CAMPUS MAP

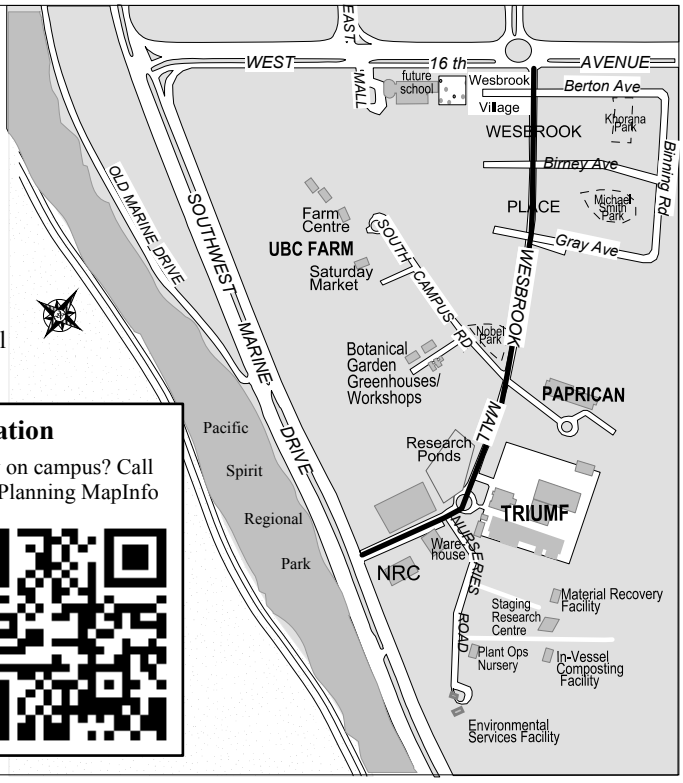
Campus & Community Planning
www.planning.ubc.ca

Note:
Local traffic only along Wesbrook Mall on South Campus

Map Information

Need help finding your way on campus? Call the Campus & Community Planning MapInfo Line at 604-827-5040, M-F, 8:30-4:30

Or use the online searchable colour map at www.maps.ubc.ca



Campus Dining

at the University of British Columbia

Student Union Building (1)

Pacific Spirit Place Cafeteria
The cafeteria includes a Bake Shop, Pasta Bar, Pho Soup Bar, and Salad Bar, as well as fast food outlets A&W, Koya Japan, Manchu Wok, and Subway.

Blue Chip Cookies
Assorted cookies, pastries, and coffee

The Delly
Sandwiches, soups, curries, assorted hot and cold savory pastries, and baked goods

Pie R Squared
Pizza by the slice

The Pit Burger Bar
Variety of burgers and fries, daily burger specials

The Pit Pub
No. 1 bar on campus, student-friendly pricing

Bernoulli's Bagels
Montreal-style bagels, sandwiches

The Gallery
Variety of take-out or dine-in options including pasta, quesadillas, and salads

The Moon
Noodle and wonton soups, stir fries, and rice bowls

The Honour Roll
Freshly made sushi and assorted Japanese dishes

The Patio BBQ
Beef and Veggie Burgers

University Village (2)

University Village has many take out and dine in options; diner-style breakfasts, coffee shops, pizza by the slice, bubble tea, a full-service sushi restaurant, a small grocer selling fresh produce and assorted goods, as well as an international food court

Blenz	Booster Juice	Mio Japan	Granville Island Produce
McDonalds	Pearl Fever Tea House	FreshSlice Pizza	One More Sushi
Only U Café	Starbucks	Pita Pit	Vera's Burger Shack
Subway	Red Burrito	Well Tea	

International Food Court

A-1 Vietnamese Food	Curry Point	Donair Town	Leona Mediterranean
Malasian Cuisine	Osaka Sushi	Timpo Mongolian BBQ	Yi Kou Xiang

Wesbrook Village (3)

Wesbrook Village, located on south campus, offers shops, services and elegant homes within a quaint, pedestrian-friendly setting, with easy access to Pacific Spirit Park, countless beaches and all the amenities of the UBC campus.

Save-On-Foods
Large grocery store with a deli and small café

Chef Hung Taiwanese Beef Noodle
Noodles, soups, rice dishes, and sides

Jugo Juice
Fresh fruit smoothies

Menchie's Frozen Yogurt
Frozen yogurt and sorbet bar

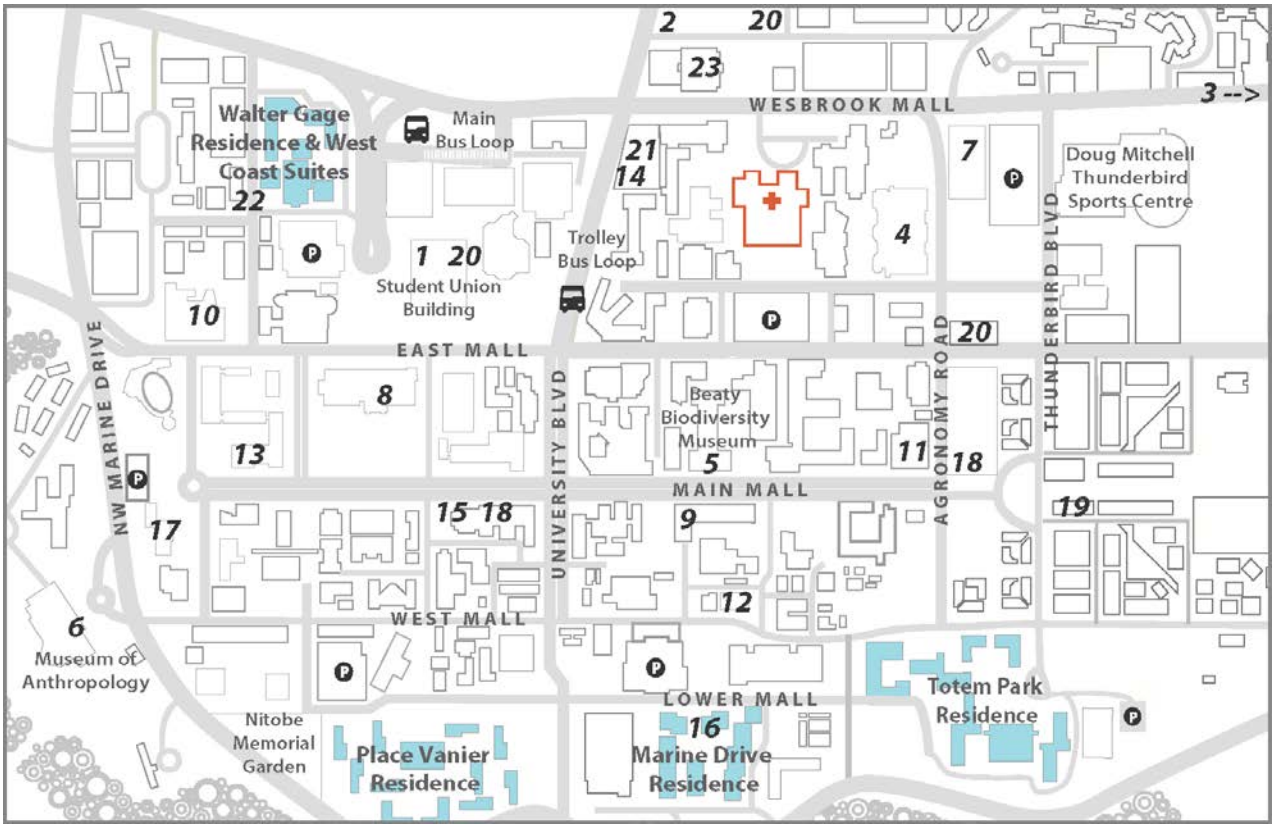
Togo Sushi
Fresh sushi made to order

Blenz
Coffee shop

UBC Mobile App

Campus Dining

at the University of British Columbia



Full-Service Restaurants

Mahoney & Sons Public House (14)
Irish-style pub serving salads, appetizers, pizzas, and a sampling of classic pub fare

Triple O's (15)
Dine in or take out - breakfast sandwiches, beef, chicken, and veggie burgers, and milkshakes

The Point Grill (16)
Burgers and sandwiches, salads, local seafood, and an outdoor patio to enjoy the sun

Sage (17)
Reopening September 2013

Coffee Shops

Tim Hortons (18)
Bean Around the World (19)

Starbucks (20)
The Boulevard Coffee Roasting Co (21)

Great Dane Coffee (22)
The Well Café (23)

Quick-Service Cafés

These cafés, located in convenient spots across campus, offer a range of snacks and lunch items, including soups, sandwiches, salads, and a variety of hot dishes

Caffe Perugia (4)
Niche Café (5)

Café MOA (6)
Pharmacy Café (7)

Ike's Café (8)
Magma Café (9)

Law Café (10)
Reboot Café (11)

The Loop Café (12)
Stir It Up Café (13)