Année de publication : 2017

Julien G Dumortier, Jean-Léon Maître (2017 Dec 15)
Early embryos kept in check.
Nature : 178-179 : DOI : 10.1038/d41586-017-07436-w

Résumé

Jean-Léon Maître (2017 Dec 14)
[Mechanics of inner cell mass formation].
Biologie aujourd'hui : 137-148 : DOI : 10.1051/jbio/2017021

Résumé

During the very first days of mammalian development, the embryo forms a structure called the blastocyst. The blastocyst consists of two cell types: the trophectoderm (TE), which implants the embryo in the uterus and the inner cell mass (ICM), which gives rise to all cells of the mammalian body. Previous works identified how cells differentiate according to their position within the embryo: TE for surface cells and ICM for internal cells. It is therefore essential to understand how cells acquire their position in the first place. During the formation of the blastocyst, cells distort and relocate as a consequence of forces that are generated by the cells themselves. Recently, several important studies have identified the forces and cellular mechanisms leading to the shaping of the ICM. Here, I describe how these studies led us to understand how contractile forces shape the mammalian embryo to position and differentiate the ICM.

Jean-Léon Maître (2017 Jul 7)
Mechanics of blastocyst morphogenesis.
Biology of the cell : 323-338 : DOI : 10.1111/boc.201700029

Résumé

During pre-implantation development, the mammalian zygote transforms into the blastocyst, the structure that will implant the embryo in the maternal uterus. Consisting of a squamous epithelium enveloping a fluid-filled cavity and the inner cell mass, the blastocyst is sculpted by a succession of morphogenetic events. These deformations result from the changes in the forces and mechanical properties of the tissue composing the embryo. Here, I review the recent studies, which, for the first time, informed us on the mechanics of blastocyst morphogenesis.

S F Gabriel Krens, Jim H Veldhuis, Vanessa Barone, Daniel Čapek, Jean-Léon Maître, G Wayne Brodland, Carl-Philipp Heisenberg (2017 May 18)

Interstitial fluid osmolarity modulates the action of differential tissue surface tension in progenitor cell segregation during gastrulation.
Development (Cambridge, England) : 1798-1806 : DOI : 10.1242/dev.144964

Résumé

The segregation of different cell types into distinct tissues is a fundamental process in metazoan development. Differences in cell adhesion and cortex tension are commonly thought to drive cell sorting by regulating tissue surface tension (TST). However, the role that differential TST plays in cell segregation within the developing embryo is as yet unclear. Here, we have analyzed the role of differential TST for germ layer progenitor cell segregation during zebrafish gastrulation. Contrary to previous observations that differential TST drives germ layer progenitor cell segregation in vitro, we show that germ layers display indistinguishable TST within the gastrulating embryo, arguing against differential TST driving germ layer progenitor cell segregation in vivo We further show that the osmolarity of the interstitial fluid (IF) is an important factor that influences germ layer TST in vivo, and that lower osmolarity of the IF compared with standard cell culture medium can explain why germ layers display differential TST in culture but not in vivo Finally, we show that directed migration of mesendoderm progenitors is required for germ layer progenitor cell segregation and germ layer formation.

Jim H Veldhuis, Ahmad Ehsandar, Jean-Léon Maître, Takashi Hiiragi, Simon Cox, G Wayne Brodland (2017 Mar 29)

Inferring cellular forces from image stacks.
Philosophical transactions of the Royal Society of London. Series B, Biological sciences : DOI : 20160261

Résumé

Although the importance of cellular forces to a wide range of embryogenesis and disease processes is widely recognized, measuring these forces is challenging, especially in three dimensions. Here, we introduce CellFIT-3D, a force inference technique that allows tension maps for three-dimensional cellular systems to be estimated from image stacks. Like its predecessors, video force microscopy and CellFIT, this cell mechanics technique assumes boundary-specific interfacial tensions to be the primary drivers, and it constructs force-balance equations based on triple junction (TJ) dihedral angles. The technique involves image processing, segmenting of cells, grouping of cell outlines, calculation of dihedral planes, averaging along three-dimensional TJs, and matrix equation assembly and solution. The equations tend to be strongly overdetermined, allowing indistinct TJs to be ignored and solution error estimates to be determined. Application to clean and noisy synthetic data generated using Surface Evolver gave tension errors of 1.6-7%, and analyses of eight-cell murine embryos gave estimated errors smaller than the 10% uncertainty of companion aspiration experiments. Other possible areas of application include morphogenesis, cancer metastasis and tissue engineering.This article is part of the themed issue 'Systems morphodynamics: understanding the development of tissue hardware'.

K Guevorkian, J-L Maître (2017 Feb 21)
Micropipette aspiration: A unique tool for exploring cell and tissue mechanics in vivo.
Methods in cell biology : 187-201 : DOI : S0091-679X(16)30164-9

Résumé

Cell and tissue mechanical properties are paramount in controlling morphogenesis. Microaspiration techniques allow measuring the absolute values of mechanical properties in space and time in vivo. Here, we explain how to build a microaspiration setup that can be used for both cellular and tissue scale measurements. At the cellular scale, microaspiration allows the mapping in space and time of surface tensions of individual interfaces within a tissue to understand the forces shaping it. At the tissue scale, microaspiration can be used to measure macroscopic mechanical properties such as the viscoelasticity and tissue surface tension that regulate the dynamics of tissue deformation. Based on a simple and cost-effective apparatus, these two complementary microaspiration techniques provide unique tools for exploring cell and tissue mechanics in vivo.

Année de publication : 2016

Jean-Léon Maître, Hervé Turlier, Rukshala Illukkumbura, Björn Eismann, Ritsuya Niwayama, François Nédélec, Takashi Hiiragi (2016 Aug 4)
Asymmetric division of contractile domains couples cell positioning and fate specification.
Nature : DOI : 10.1038/nature18958

Résumé

During pre-implantation development, the mammalian embryo self-organizes into the blastocyst, which consists of an epithelial layer encapsulating the inner-cell mass (ICM) giving rise to all embryonic tissues. In mice, oriented cell division, apicobasal polarity and actomyosin contractility are thought to contribute to the formation of the ICM. However, how these processes work together remains unclear. Here we show that asymmetric segregation of the apical domain generates blastomeres with different contractilities, which triggers their sorting into inner and outer positions. Three-dimensional physical modelling of embryo morphogenesis reveals that cells internalize only when differences in surface contractility exceed a predictable threshold. We validate this prediction using biophysical measurements, and successfully redirect cell sorting within the developing blastocyst using maternal myosin (Myh9)-knockout chimaeric embryos. Finally, we find that loss of contractility causes blastomeres to show ICM-like markers, regardless of their position. In particular, contractility controls Yap subcellular localization, raising the possibility that mechanosensing occurs during blastocyst lineage specification. We conclude that contractility couples the positioning and fate specification of blastomeres. We propose that this ensures the robust self-organization of blastomeres into the blastocyst, which confers remarkable regulative capacities to mammalian embryos.

News & Views: Mammalian development: Mechanics drives cell differentiation

Année de publication : 2015

Hervé Turlier, Jean-Léon Maître (2015 Aug 11)
Mechanics of tissue compaction.
Seminars in cell & developmental biology : 110-7 : DOI : 10.1016/j.semcdb.2015.08.001

Résumé

During embryonic development, tissues deform by a succession and combination of morphogenetic processes. Tissue compaction is the morphogenetic process by which a tissue adopts a tighter structure. Recent studies characterized the respective roles of cells' adhesive and contractile properties in tissue compaction. In this review, we formalize the mechanical and molecular principles of tissue compaction and we analyze through the prism of this framework several morphogenetic events: the compaction of the early mouse embryo, the formation of the fly retina, the segmentation of somites and the separation of germ layers during gastrulation.

Jean-Léon Maître, Ritsuya Niwayama, Hervé Turlier, François Nédélec, Takashi Hiiragi (2015 Jun 16)
Pulsatile cell-autonomous contractility drives compaction in the mouse embryo.
Nature cell biology : 849-55 : DOI : 10.1038/ncb3185

Résumé

Mammalian embryos initiate morphogenesis with compaction, which is essential for specifying the first lineages of the blastocyst. The 8-cell-stage mouse embryo compacts by enlarging its cell-cell contacts in a Cdh1-dependent manner. It was therefore proposed that Cdh1 adhesion molecules generate the forces driving compaction. Using micropipette aspiration to map all tensions in a developing embryo, we show that compaction is primarily driven by a twofold increase in tension at the cell-medium interface. We show that the principal force generator of compaction is the actomyosin cortex, which gives rise to pulsed contractions starting at the 8-cell stage. Remarkably, contractions emerge as periodic cortical waves when cells are disengaged from adhesive contacts. In line with this, tension mapping of mzCdh1(-/-) embryos suggests that Cdh1 acts by redirecting contractility away from cell-cell contacts. Our study provides a framework to understand early mammalian embryogenesis and original perspectives on evolutionary conserved pulsed contractions.

Maté Biro, Jean-Léon Maître (2015 Feb 3)
Dual pipette aspiration: a unique tool for studying intercellular adhesion.
Methods in cell biology : 255-67 : DOI : 10.1016/bs.mcb.2014.10.007

Résumé

The dual pipette aspiration (DPA) assay is a highly versatile tool that enables the micromanipulation of cells and the precise measurement of a range of biophysical parameters in combination with concurrent high-resolution imaging. DPA permits the juxtaposition of cells, their manipulation using pressure and the controlled formation or separation of cell-cell contacts. The DPA set-up can thus readily be used to probe the dynamics and mechanics of cell-cell adhesion, notably adhesion strength and adhesion energy. In particular, the DPA set-up has been used to measure a wide range of separation forces between pairs of cells. Here, we describe how to build and use the DPA set-up in order to measure the separation force of cell doublets. We first describe how to prepare adequate pipettes, then how to assemble and calibrate the pipettes and pressure control devices, followed by how to manipulate cells in order to calculate separation forces. Finally, we give recommendations on how to use the DPA set-up and compare it to other methods used to study cell-cell contacts and adhesion strength in particular.

Année de publication : 2014

Hélène Berthoumieux, Jean-Léon Maître, Carl-Philipp Heisenberg, Ewa K Paluch, Frank Jülicher and Guillaume Salbreux (2014 Jun 10)

Active elastic thin shell theory for cellular deformations

New Journal of Physics : 16

Résumé

We derive the equations for a thin, axisymmetric elastic shell subjected to an internal active stress giving rise to active tension and moments within the shell. We discuss the stability of a cylindrical elastic shell and its response to a localized change in internal active stress. This description is relevant to describe the cellular actomyosin cortex, a thin shell at the cell surface behaving elastically at a short timescale and subjected to active internal forces arising from myosin molecular motor activity. We show that the recent observations of cell deformation following detachment of adherent cells (Maître J-L *et al* 2012 *Science* **338** 253–6) are well accounted for by this mechanical description. The actin cortex elastic and bending moduli can be obtained from a quantitative analysis of cell shapes observed in these experiments. Our approach thus provides a non-invasive, imaging-based method for the extraction of cellular physical parameters.

Année de publication : 2013

Jean-Léon Maître, Carl-Philipp Heisenberg (2013 Jul 27)

Three functions of cadherins in cell adhesion.

Current biology : CB : R626-33 : DOI : 10.1016/j.cub.2013.06.019

Résumé

Cadherins are transmembrane proteins that mediate cell-cell adhesion in animals. By regulating contact formation and stability, cadherins play a crucial role in tissue morphogenesis and homeostasis. Here, we review the three major functions of cadherins in cell-cell contact formation and stability. Two of those functions lead to a decrease in interfacial tension at the forming cell-cell contact, thereby promoting contact expansion–first, by providing adhesion tension that lowers interfacial tension at the cell-cell contact, and second, by signaling to the actomyosin cytoskeleton in order to reduce cortex tension and thus interfacial tension at the contact. The third function of cadherins in cell-cell contact formation is to stabilize the contact by resisting mechanical forces that pull on the contact.

Jean-Léon Maître, Hélène Berthoumieux, Simon Frederick Gabriel Krens, Guillaume Salbreux, Frank Jülicher, Ewa Paluch, Carl-Phillip Heisenberg (2013 Mar 5)
[Cell adhesion mechanics of zebrafish gastrulation].
Médecine sciences : M/S : 147-50 : DOI : 10.1051/medsci/2013292011

Résumé

Année de publication : 2012

Jean-Léon Maître, Hélène Berthoumieux, Simon Frederik Gabriel Krens, Guillaume Salbreux, Frank Jülicher, Ewa Paluch, Carl-Philipp Heisenberg (2012 Aug 28)
Adhesion functions in cell sorting by mechanically coupling the cortices of adhering cells.
Science (New York, N.Y.) : 253-6 : DOI : 10.1126/science.1225399

Résumé

Differential cell adhesion and cortex tension are thought to drive cell sorting by controlling cell-cell contact formation. Here, we show that cell adhesion and cortex tension have different mechanical functions in controlling progenitor cell-cell contact formation and sorting during zebrafish gastrulation. Cortex tension controls cell-cell contact expansion by modulating interfacial tension at the contact. By contrast, adhesion has little direct function in contact expansion, but instead is needed to mechanically couple the cortices of adhering cells at their contacts, allowing cortex tension to control contact expansion. The coupling function of adhesion is mediated by E-cadherin and limited by the mechanical anchoring of E-cadherin to the cortex. Thus, cell adhesion provides the mechanical scaffold for cell cortex tension to drive cell sorting during gastrulation.

Année de publication : 2011

Petra Stockinger, Jean-Léon Maître, Carl-Philipp Heisenberg (2011 Oct 4)

Defective neuroepithelial cell cohesion affects tangential branchiomotor neuron migration in the zebrafish neural tube.

Development (Cambridge, England) : 4673-83 : DOI : 10.1242/dev.071233

Résumé

Facial branchiomotor neurons (FBMNs) in zebrafish and mouse embryonic hindbrain undergo a characteristic tangential migration from rhombomere (r) 4, where they are born, to r6/7. Cohesion among neuroepithelial cells (NCs) has been suggested to function in FBMN migration by inhibiting FBMNs positioned in the basal neuroepithelium such that they move apically between NCs towards the midline of the neuroepithelium instead of tangentially along the basal side of the neuroepithelium towards r6/7. However, direct experimental evaluation of this hypothesis is still lacking. Here, we have used a combination of biophysical cell adhesion measurements and high-resolution time-lapse microscopy to determine the role of NC cohesion in FBMN migration. We show that reducing NC cohesion by interfering with Cadherin 2 (Cdh2) activity results in FBMNs positioned at the basal side of the neuroepithelium moving apically towards the neural tube midline instead of tangentially towards r6/7. In embryos with strongly reduced NC cohesion, ectopic apical FBMN movement frequently results in fusion of the bilateral FBMN clusters over the apical midline of the neural tube. By contrast, reducing cohesion among FBMNs by interfering with Contactin 2 (Cntn2) expression in these cells has little effect on apical FBMN movement, but reduces the fusion of the bilateral FBMN clusters in embryos with strongly diminished NC cohesion. These data provide direct experimental evidence that NC cohesion functions in tangential FBMN migration by restricting their apical movement.