FRIDAY, December 14, 2012

9.00 – 9.30	**Registration of participants**	
9.30 – 10.00	**Session I**	Opening Speech: Jürgen Haase, University of Leipzig
10.00 – 10.45		Thomas Risler (Institut Curie): Undulation instability of epithelial tissues and metastases' nucleation
10.45 – 11.00		Coffee break
11.00 – 11.45		Klaus Kroy (University of Leipzig): The stiffening-softening paradox in cell mechanics
11.45 – 12.30		Stefan Dhein (Herzzentrum Leipzig): Self-organization of intercellular communication in cardiomyocytes under stretch
12.30 – 13.45		**Lunch**
13.45 – 14.30	**Session II**	Jens Elgeti (Institut Curie): Simulating Tissue Growth and Motility
14.30 – 15.15		Benoit Ladoux (Université de Paris): Emerging modes of collective cell behaviors under physical constraints
15.15 – 15.45		Coffee break
15.45- 16.30		Andrew E. Ekpenyong (TU of Dresden): Viscoelastic properties of differentiating cells evolve to meet tissue-specific functions
16.30 – 17.15		Andreas Reichenbach (PFI, University of Leipzig): Postnatal Mammalian Retinal Development: Quantitative Data and General Rules
18.30		Christmas Market and city tour, meeting point: Bach monument in front of the Thomas Church

SATURDAY, December 15, 2012

9.00 – 9.45	**Session I**	Jae Hun Kim (Harvard School of Public Health, Boston): Physical Forces in Collective Cellular Migration
9.45 – 10.30		Paul Janmey (School of Medicine, Univ. of Pennsylvania, Philadelphia): Extracellular matrix physical properties alter cell mechanics, morphology, and proliferation
10.30 – 11.00		Coffee break
11.00 – 11.45		Claus Fütterer (University of Leipzig): Fluctuations and symmetry breaking during regeneration of Hydra vulgaris tissue toroids
11.45 – 12.30		Christoph Klingner (MPI München): Pulsatile contractility of apical acto-myosin networks in epithelial cells
12.30 – 13.45		**Lunch**
13.45 – 14.30	**Session II**	Albrecht Ott (University of Saarbrücken): All Cells are Equal – Hydra axis Formation
14.30 – 15.15		Josef Käs (University of Leipzig): Do Tumor Cells Care About Physics?
15.15 – 15.45		Coffee break
15.45- 16.30		Françoise Brochard-Wyart (Institut Curie): Mechanosensitivity and motility of cellular aggregates
16.30 – 17.15		Bert Hobmayer (University of Innsbruck): The role of f-actin in tissue bending in the simple metazoan Hydra
19.00		Social Event for invited speakers, venue: Magna Diagnostics GmbH Neumarkt 29 – 33, 7th floor 04109 Leipzig

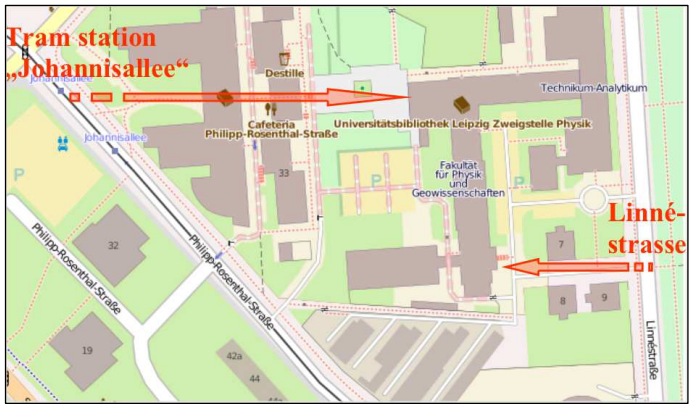
SUNDAY, December 16, 2012

9.00 – 9.45	**Session I**	Thomas Müller (MHH Hannover): The marmoset monkey - a preclinical supermodel for stem cell research and tissue engineering
9.45 – 10.30		Markus Affolter (University of Basel): Forces and the control of cell behavior in angiogenesis
10.30 – 11.00		Coffee break
11.00 – 11.45		Elisabeth Knust (MPI of Molecular Cell Biology and Genetics, Dresden): From epithelial cell polarity to retinal degeneration: lessons from *Drosophila*

11.45 – 12.30		Graham Sheridan (University of Cambridge): The importance of mechanics in central nervous system development
12.30 – 13.45		**Lunch**
13.45 – 14.30	**Session II**	Jacques Prost (Institut Curie)
14.30		Departure of participants

CONFERENCE VENUE:

Institute of Experimental Physics I
Linnéstr.5
04103 Leipzig, Germany



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Venue of the Social Event:

Magna Diagnostics GmbH
Neumarkt 29 – 33, 7th floor
04109 Leipzig, Germany

Conference Abstracts:

Markus Affolter, University of Basel	**Forces and the control of cell behavior in angiogenesis:** Anna Lenard, Lukas Herwig, Yannick Blum, Alice Krudewig,Loic Sauteur, Elin Ellertsdottir, Heinz-Georg Belting and Markus Affolter To form interconnected networks of endothelial tubes, sprouting vessels of the developing vasculature have to connect to each other, a process referred to as anastomosis. To better understand cell behavior during anastomosis, we studied how angiogenic sprouts connect to give rise to a fully lumenized vessel (DLAV) in different regions of the zebrafish embryos. To monitor cell behavior and lumen formation concomitantly, we generated novel transgenic fish lines expressing an eGFP-fused version of the AJ/TJ protein ZO1 under indirect control of an endothelial-specific enhancer using the Gal4 system. We found that during anastomosis, tip cells reach each other via filopodial extensions and subsequently establish new contact points by localizing eGFP-ZO1 and VE-Cad to such site of contact. These point-like initial contact sites subsequently elaborate into loop-like structures, suggesting that a pre-apical spot is enlarged into a larger apical membrane compartment between two tip/fusion cells. In 60% of the cases we recorded in vivo, we find that the lumen subsequently extends and grows through the former tip cells from the proximal-most position towards the novel, more distal apical side of the tip/fusion cell. This cell hollowing process is dependent on the previous lumenization of the participating sprouts, suggesting that apical membrane growth and invagination into the tip/fusion cell are driven by plasma pressure. We also find that a second mechanism is involved in vessel anastomosis. In this scenario, the novel apical membrane patches and the pre-luminal space they surround are brought together through cell rearrangements and eventually establish direct contact, resulting in lumen coalescence and the formation of an extracellular lumen embedded in a regular, multicellular tube. Thus, endothelial cells are rather plastic during the process of anastomosis and can connect using distinct mechanisms and generate tubes of different architectures. We have developed a new approach investigating cell behavior in vivo using gene-encoded nanobodies and will present first results from Drosophila work.
Françoise Brochard-Wyart, Institut Curie, Paris	**Mechanosensitivity and motility of cellular aggregates:** Françoise Brochard-Wyart, Damien Cuvelier, Stéphane Douezan, Sylvie Dufour, Julien Dumond, Gregory Beaune,David Gonzalez-Rodriguez, Karine Guevorkian We first describe the biomechanics of multicellular aggregates, a model system for tissues and tumors. We first characterize the tissue mechanical properties (surface tension, elasticity, viscosity) by a new pipette aspiration technique. The aggregate exhibits a viscoelastic response but, unlike an inert fluid, we

	observe aggregate reinforcement with pressure, which for a narrow range of pressures results in pulsed contractions or "shivering". We interpret this reinforcement as a mechanosensitive active response of the acto-myosin cortex. Such an active behavior has previously been found to cause tissue pulsation during dorsal closure of Drosophila embryo. We then described the spreading of spheroidal aggregates of cells, expressing a tunable level of cadherins, on glass substrates and polyacrylamide gels decorated with extracellular matrix (ECM) protein fibronectin. On glass substrate, we observe a precursor film with two possible states: in strongly cohesive aggregates this film is in liquid state, while in weakly cohesive aggregates the constitutive cells escape from the aggregate forming a 2D gas. The progression of a non-invasive tumor into a metastatic malignant carcinoma, known as the epithelial-mesenchyme transition, can be interpreted as a wetting (liquid-gas) transition. On soft gels decorated with fibronectin and strongly cohesive aggregates, we have observed a wetting transition induced by the substrate rigidity: on ultra soft gels, below an elastic modulus Ec the aggregates do not spread, whereas above Ec we observe a precursor film expending with a diffusive law. The diffusion coefficient D(E) present a maximum for E=Em. A maximum of mobility versus the substrate rigidity had also been observed for single cells. Near Em, we observe a new phenomenon: a cell monolayer expends outwards from the aggregate apparently under tension. In this tense monolayer, holes nucleate, and lead to a symmetry breaking as the entire aggregate starts to move in a similar fashion as a keratocyte. We can induce both spontaneous collective migration and directed motion in chemical or rigidity gradient, which are important process of embryonic development.
Stefan Dhein, Herzzentrum Leipzig	**Self-organisation of intercellular communication in cardiomyocytes under stretch:** Cyclic mechanical stretch (CMS) and angiotensin-II (ATII) play an important role in cardiac remodelling. Thus, we aimed to examine how CMS and ATII affect localisation and expression of the gap junction protein connexin43 (Cx43). Neonatal rat cardiomyocytes cultured on gelatine coated FlexCell cell culture plates were kept static or were exposed to CMS (110% of resting length, 1Hz) for 24hours without or with additional ATII (0.1µmol/L). Moreover, inhibitors of ATII-receptors (AT-R) were used (for AT1-R: losartan 0.1µmol/L, for AT2-R: PD123177 0.1µmol/L). Thereafter, the cardiomyocytes were investigated by immunohistology, PCR and Western Blot. After 24hours of CMS cardiomyocytes were significantly elongated and orientated 75±1.6° nearly perpendicular to the stretch axis. Furthermore, CMS significantly accentuated Cx43 at the cell poles. This was along with an orientation of the tubular system (alpha-tubulin). While elongation and orientation of the cells were permanent, Cx43 polarization returned to an un-organized pattern if cyclic stretch was discontinued. Additional ATII application significantly reduced Cx43 polarisation. The combined administration of ATII and losartan to CMS further reduced Cx43 polarisation to control levels while the AT2-R blocker PD123177 restored polarisation. Moreover, CMS and ATII application resulted in a significant Cx43-protein and Cx43-mRNA up-regulation which could be blocked by losartan, but not by PD123177. Thus, CMS results in a self-organisation of the cardiomyocytes leading to elongated cells orientated transverse towards the stretch axis with enhanced Cx43 expression and Cx43-accentuation at the cell poles. ATII enhances total Cx43-mRNA and -protein expression probably via AT1-R (=inhibitory effect of losartan) and reduces Cx43 polarisation presumably via AT2-R, since PD123177 (but not losartan) inhibited the negative effects of ATII on polarisation.
Andrew E. Ekpenyong, Biotec TU	**Viscoelastic properties of differentiating cells evolve to meet tissue-specific functions:** Although cellular mechanical properties are known to alter during stem cell differentiation,

Dresden	understanding of the functional relevance of such alterations is incomplete. Here, we show that during the course of differentiation of human myeloid precursor cells into three different lineages, the cells alter their viscoelastic properties, measured using an optical stretcher, to suit their ultimate fate and function. Myeloid cells circulating in blood have to be advected through constrictions in blood vessels, engendering the need for compliance at short time-scales (,seconds). Intriguingly, only the two circulating myeloid cell types have increased short time scale compliance and flow better through microfluidic constrictions. Moreover, all three differentiated cell types reduce their steady-state viscosity by more than 50% and show over 140% relative increase in their ability to migrate through tissue-like pores at long time-scales (.minutes), compared to undifferentiated cells. These findings suggest that reduction in steady-state viscosity is a physiological adaptation for enhanced migration through tissues. Our results indicate that the material properties of cells define their function, can be used as a cell differentiation marker and could serve as target for novel therapies.
Jens Elgeti, Institut Curie, Paris	**Simulating Tissue Growth and Motility:** The elementary building block of all living organisms is the cell. Cell division and apoptosis, adhesion and migration, differentiation and mutation are all determining factors of life. Over the past decades, the notion that physics, and especially mechanics plays an essential role in growth and development has evolved from hypothesis to fact. Even though an increasing number of experiments and theoretical works have focused on this puzzle, and many pieces have been found, we are still far from seeing the whole picture. In this work, tissue simulation techniques are used to connect some of the dots towards a coherent picture. The description of tissues is based on a mesoscopic particle based approach. Similar to mesoscopic hydrodynamic techniques, capturing the individual cell dynamics is of lesser importance. Instead, the goal is to attain the right meso- to macroscopic dynamics of the tissue, and extract generic properties arising from simple assumptions Here we present the basics of the simulation method and some applications. From growth of spheroids over rheology to wound healing a diverse set of phenomena are described well by very simple models.
Claus Fütterer, University of Leipzig	**Fluctuations and symmetry breaking during regeneration of *Hydra vulgaris* tissue toroids:** While much is known about the physics of single cells, the mechanics of self-organization and regeneration of cells in tissues and cell assemblies is largely unexplored. In order to close this gap we study bilayered tissue toroids dissected from *Hydra vulgaris* polyps and explain the macroscopic observations with the dynamics of force-generating mesoscopic structures of the cytoskeleton. The toroids fold to spheroids in a specific way and the rearrangement happens too fast for biochemical signalling or morphogenetic gradients. The initial pattern selection dynamics was studied by embedding toroids into hydro-gels and we found mechanical "critical fluctuations" tempting to break the toroidal symmetry. The evolution of the power spectra of these fluctuations is discussed for various gel stiffnesses. We also observed cells switching from tissue bound to a migrating state. We found this transition equally after tissue injury. The forces required for the folding process are created by a uniform supra-cellular actin ring which assembled along the toroid's inner edge. Its contraction can lead to the observed folding dynamics. We could confirm the mechanism by finite element simulations. The actin ring in the inner cell layer is assembled from mesoscopic filaments by myosin-driven length fluctuations of inter-cellular alpha-actin structures (myonemes) in the outercell-layer. *Hydra vulgaris* cells also possess beta-actin, which was not found to play an active role during folding. Only when cells switch to the mentioned individual migrating state, this actin isoform becomes important.

Bert Hobmayer, University of Innsbruck	**The role of f-actin in tissue bending in the simple metazoan Hydra:** 1Institute of Zoology and Center for Molecular Biosciences, University of Innsbruck, Austria. 2Max Planck Institute of Biochemistry, Max Planck Research Group Cellular Dynamics and Cell Patterning, Martinsried, Germany. 3Department of Anatomy and Cell Biology, The University of Kansas Medical Center, Kansas City, Kansas 66160, USA. Folding of epithelial cell sheets is a fundamental morphogenetic mechanism underlying the formation of the gut, the neural tube, extremities, and asexual reproduction in many multicelluar animals. Macroscopic shape changes in these developing tissues are based on spatially and temporally well co-ordinated activities of single cells, like cell shape changes and cell motility. At the molecular level, the actin cytoskeleton is the most important player responsible for shape and motility of eukaryotic cells. Much of our current knowledge about dynamic actin processes comes from *in vitro* studies and cultured cells. Considerably less is known about actin in multicelluar tissues of developing organisms. This is partly due to the fact, that proper, non-interfering methods for live visualisation of actin in developing tissues have been developed only in recent years. The freshwater polyp Hydra reproduces asexually by evagination of its body wall in the lower gastric column. This body wall is built up entirely by two epithelial layers with opposing apicobasal polarity, which are separated by a thin layer of extracellular matrix. Bud evagination is based on recruitment and reorganisation of parental tissue rather than on locally enhanced cell proliferation and only the activity of two cell types, the epitheliomuscular cells of the ectoderm and the endoderm, drive the tissue shape change. In the present study we analysed dynamic actin-processes *in vivo* during Hydra budding using two newly developed transgenic Hydra strains, which stably express lifeact-GFP, an *in vivo* marker for f-actin. Further, we applied phalloidin-labeling on fixed specimens. We report extensive reorganisation of the actin cytoskeleton, while cells are rearranging, moving and changing their shape, and these activities correlate with the bending and evagination of the body wall during budding. Based on our results we propose a model for tissue bending driven by endodermal contractile fibers and for a mechanism of cell locomotion in epitheliomuscular cells.
Paul Janmey, University of Pennsylvania	**Extracellular matrix physical properties alter cell mechanics, morphology, and proliferation:** Many cell types are sensitive to mechanical signals that are produced either by application of exogenous force to their surfaces or by the resistance that their surroundings place on forces generated by the cells themselves. Cell morphology, motility, proliferation, and protein expression all change in response to substrate stiffness. Changing the elastic moduli of substrates alters the formation of focal adhesions, the assembly of actin filaments into bundles, and the stability of intermediate filaments. The range of stiffness over which different primary cell types respond can vary over a wide range and generally reflects the elastic modulus of the tissue from which these cells were isolated. Mechanosensing depends on the type of adhesion receptor by which the cell binds, and therefore on both the molecular composition of the extracellular matrix and the nature of its link to the cytoskeleton. Many cell types can alter their own stiffness to match that of the substrate to which they adhere. The maximal elastic modulus that cells such as fibroblasts can attain is similar to that of crosslinked actin networks at the concentrations in the cell cortex. Simultaneous control of substrate stiffness and adhesive patterns suggests that stiffness sensing occurs on a length scale much larger than single molecular linkages and that the time needed for mechanosensing is on the order of a few seconds.

Josef Käs, University of Leipzig	**Do Tumor Cells Care About Physics?** Josef A. Käs, Anatol Fritsch, Tobias Kiessling, David Nnetu, Steve Pawlizak, Roland Stange, Franziska Wetzel, Mareike Zink With an increasing knowledge in tumor biology an overwhelming complexity becomes obvious which roots in the diversity of tumors and their heterogeneous molecular composition. Nevertheless in all solid tumors malignant neoplasia, i.e. uncontrolled growth, invasion of adjacent tissues, and metastasis, occurs. Recent results indicate that all three pathomechanisms require changes in the active and passive cellular biomechanics. Malignant transformation causes cell softening for small deformations which correlates with an increased rate of proliferation and faster cell migration. The tumor cell's ability to strain harden permits tumor growth against a rigid tissue environment. A highly mechanosensitive, enhanced cell contractility is a prerequisite that tumor cells can cross its tumor boundaries and that these cells can migrate through the extracellular matrix. Initial tumor growth is limited to the developmental compartments from which the tumor cells originate. The observation that compartmentalized cell growth is not merely found during development but throughout tumor progression does not only radically redefine how tumors have to be resected, it also has critical impact on how a tumor progresses and what the target cells must be when screening for new cytostatics. It is the cells that can cross compartment boundaries and thus are not restricted to local tumor growth that have to be fought by chemotherapy. Therefore, passive and active biomechanical behavior of tumor cells, cell jamming, cell demixing and surface tension-like cell boundary effects are investigated as key factors to stabilize or overcome compartment boundaries. Insights into changes of these properties during tumor progression may lead to selective treatments. Such drugs would not cure by killing cancer cells, but slow down tumor progression with only mild side effects and thus may be an option for older and frail patients.
Jae Hun Kim, Harvard School of Public Health	**Physical Forces in Collective Cellular Migration:** Jae Hun Kim, Chan Young Park, Dhananjay T. Tambe, James P. Butler, Jeffrey J. Fredberg Fundamental biological processes in development and disease involve collective cellular migration. In expanding monolayer sheet of cells, the direction of migration tends to align with the orientation of the maximal principal intercellular stress, which is a phenomenon called plithotaxis. However, whether there exist physical principles governing cellular navigation within advancing monolayer remains obscure. To expose the physical forces that cause constituent cells to move as they do, we placed in the path of an advancing epithelial cell sheet an island to which cells could not adhere. The monolayer impacts but cannot cover this island. Resulting systematic components of the nonuniform velocity field and underlying force fields were examined over an ensemble of geometrically similar systems. Far from the island region cells tend to exert traction forces that are aligned parallel to the migration velocity and along the orientation of maximal principal intercellular stress. Near the island region cells approaching the stagnation point turned without a noticeable stress gradient. Such behavior was inconsistent with a fluid-like behavior as might be described by the Navier-Stokes equation. These unanticipated observations reveal well-quantified mechanical behavior, which describe how cells comprising the monolayer exert forces as they move.
Christoph Klingner, Max Planck Institute of Biochemistry Martinsried	**Pulsatile contractility of apical acto-myosin networks in epithelial cells:** C. Klingner, A. Aufschnaiter, A.V. Cherian, and R. Wedlich-Söldner The cytoskeleton plays a central role in cellular morphogenesis by generating, sensing and transmitting physical forces. Actin filaments are key cytoskeletal elements that are mostly located close to the cell cortex. They can generate protrusive or contractile forces in combination with myosin motor proteins.

	We have now identified a highly dynamic acto-myosin network underlying the apical cell surface of epithelial cells. Using optical flow and image correlation, we found that this network exhibits characteristic pulsatile contractility. The resulting spatially restricted mechanical forces differ in directionality, leading to shear stress and friction within the apical cell cortex. Additionally, we identified a global oscillatory behavior using autocorrelation analysis. The actomyosin network switches between states of low and high activity. The identified features of subcellular cortex reorganization give important insights into how mechanical force generation and propagation control cell shape in epithelial cells.
Elisabeth Knust, Max Planck Institute of Molecular Cell Biology and Genetics, Dresden	**From epithelial cell polarity to retinal degeneration: lessons from Drosophila:** A polarised phenotype reflects the ability of a cell to establish functionally and spatially distinct plasma membrane compartments. Photoreceptor cells are polarised cells with a highly differentiated apical surface, specialised for phototransduction. The evolutionarily conserved Crumbs (Crb) protein complex is required for morphogenesis of photoreceptors and prevents light dependent retinal degeneration in both Drosophila and vertebrates. In both vertebrate and Drosophila photoreceptor cells, the protein complex is localised apical to the adherens junctions, in the inner segment/stalk membrane, respectively. Our studies aim to elucidate the cell biological role of this protein complex for cell morphogenesis and homeostasis.
Klaus Kroy, University of Leipzig	**The stiffening-softening paradox in cell mechanics:** Despite their notorious diversity, biological cells are mechanically well characterized by only a few robust and universal laws. Intriguingly, the law characterizing the nonlinear response to stretch appears self-contradictory. Various cell types have been reported to both stiffen and soften, or “fluidize” upon stretch. Within the classical paradigm of cells as viscoelastic bodies, this constitutes a paradox. Our measurements reveal that minimalistic reconstituted cytoskeletal networks (F-actin/HMM) exhibit a similarly peculiar response. A mathematical model of transiently crosslinked polymer networks, the so-called inelastic glassy wormlike chain (iGWLC) model, can simulate the data and resolve the apparent contradiction. It explains the observations in terms of two antagonistic physical mechanisms, the nonlinear viscoelastic resistance of biopolymers to stretch, and the breaking of weak transient bonds between them. Our results imply that the classical paradigm of cells as viscoelastic bodies has to be replaced by such an inelastic mechanical model.
Benoit Ladoux, University of Paris	**Emerging modes of collective cell behaviors under physical constraints:** SRK Vedula, MC Leong, AJ. Kabla, CT. Lim and B. Ladoux Fundamental biological processes such as morphogenesis and wound healing involve the dynamics of epithelial cells. I will present our recent studies on the collective behaviors of cells in response to the presence of physical constraints. We show that the geometrical properties of the environment regulate the dynamics of collective cell migration patterns through cell-cell interactions. Using microfabrication techniques to allow epithelial cell sheets to migrate into strips whose width can be varied from one up to several cell diameters, we have identified various modes of collective migration in response to these geometrical constraints. Furthermore, we have recently observed that such collective responses strongly depend on the cell type and consequently, our approach can be used to probe the mechanics of epithelial cell sheets. I will thus present and compare our results obtained with various epithelial cell lines such as MDCK cells and human keratinocyte epithelial cells.
Thomas	**The marmoset monkey - a preclinical supermodel for stem cell research and**

Müller, MHH Hannover	**tissue engineering:** Regenerative medicine is in need of a solid animal model as a link between rodents and human to evaluate functionality, immunogenicity and clinical safety of embryonic stem cells (ESCs), adult stem cells like mesenchymal stem cell or reprogrammed cell types (iPS). The common marmoset monkey (/Callithrix/ /jacchus/) is such an excellent large animal model, genetically closely related to the human and readily used worldwide in clinical research. Several embryonic stem cell lines of the animal exist next to ethically unproblematic obtainable placental or bone marrow derived MSCs and lately iPS from skin, bmMSCs and pMSCs. According to their origin, marmoset stem cells display different levels of pluripotency, plasticity and immunogenicity. Established protocols for adipocytes, chondrocytes, osteogenic progenitors, neuronal stem cells, definitive endoderm, granulocytes and megakaryocytes exist in our group. Additionally, expansion and differentiation protocols of the cells on collagen matrices were successfully established. After efficiency and clinical safety tests of the differentiated cell types they can be utilized for preclinical studies in the animal.
Albrecht Ott, Saarland University	**All Cells are equal: Hydra axis formation:** Hydra consists of a head and a foot connected by a tube. The animal is able to survive complete disintegration: it can reform from a random aggregate of about 10,000 cells. The process starts by forming a hollow sphere made of a cell bilayer. Here we ask how the cells of this sphere, without any molecular clues, decide on the position of a new animal-axis. Our results suggest that next-neighbour coupled, collective gene-expression fluctuations of these cells determine the nature of the axis establishing process. A weak temperature gradient of a fraction of a degree across the sphere defines the position of the head-foot axis if it is applied before WNT expression, first irreversible molecular step towards head formation. The hydra-specific gene ks1 has been described as a marker of 'cell head forming potential'. At the axis locking moment, *in-situ* hybridization reveals self-similar domains of ks1 expression on the surface of the cell sphere. Our observations can be understood in the framework of a dynamic critical-state. Simple cellular automata robustly reproduce the experimental observations. The head-foot orientation of the animal in a temperature gradient appears to depend on gradient steepness.
Andreas Reichenbach, University of Leipzig	**Postnatal mammalian retinal development: quantitative data and general rules:** In mammals the eye continues to grow, and the retina continues to expand, much after the end of retinal cytogenesis. Thus, although the total number of retinal cells remains constant after cessation of mitotic activity (and the end of 'physiological cell death'), the retinal surface area increases by a factor of two or more. In most mammals, ocular growth exceeds retinal expansion: the neural retina lines 70-80 % of the inner ocular surface at the beginning but only about 40-60 % in adults. Differential local expansion of the retina (the peripheral area increases more than the central one) can be explained by 'passive stretching' of the retinal tissue by the growing eye ball; it depends on the different biomechanical properties of the peripheral vs. central retinal tissue. The increasing retinal surface area allows for a redistribution of cells such that the thickness of the (particularly, outer) nuclear layer(s) decreases proportional to the areal expansion. This causes a considerable developmental reduction of the number of cell nuclei 'stacked above each other' by a factor of more than two, and requires a translocation of the somata against their neighbors. I will provide a physico-mathematical model of these oblique 'down-sliding' movements of the photoreceptor cell somata along the Müller cell process in the center of their columnar cell unit.
Thomas Risler,	**Undulation instability of epithelial tissues and metastases' nucleation:**

Institut Curie, Paris	We study the stability of the interface between a multilayered epithelium and its adjacent stroma. Treating the epithelium as a viscous fluid with cell division, we find a novel hydrodynamic instability that leads to the formation of fingering protrusions of the epithelium into the stroma [1]. Coupling cell division in the epithelium to the local concentration of nutrients diffusing from the stroma enhances the instability by a mechanism similar to that of the Mullins-Sekerka instability in single-diffusion processes of crystal growth [2]. This instability provides physical insight into a potential mechanism by which interfaces between epithelia and stroma undulate, and potentially by which tissue dysplasia leads to cancerous invasion. Later in the process of cancerous invasion, mechanics may also play an important part. We have recently proposed that one aspect of homeostasis is the regulation of tissues to preferred pressures, which can lead to a competition for space of purely mechanical origin and be an underlying mechanism for tumor growth. Surface and bulk contributions to growth lead to the existence of a critical size that must be overcome by metastases to nucleate macroscopic secondary tumors [3]. This property qualitatively explains the observed size distributions of metastases. Following these ideas, the influence of an externally applied osmotic stress on the long-term growth of cellular spheroids has been experimentally demonstrated [4]. Refrences: [1] M. Basan, J.-F. Joanny, J. Prost, and T. Risler, Phys. Rev. Lett., 106 (15), 158101 (2011). [2] T. Risler and M. Basan, under review [3] M. Basan, T. Risler, J.-F. Joanny, X. Sastre-Garau, and J. Prost, HFSP J., 3 (4), 265-272 (2009) [4] F. Montel, M. Delarue, J. Elgeti, L. Malaquin, M. Basan, T. Risler, B. Cabane, D. Vignjevic, J. Prost, G. Cappello, and J.-F. Joanny, Phys. Rev. Lett., 107 (18), 188102 (2011).
Graham Sheridan, University of Cambridge	**The Importance of Mechanics in Central Nervous System Development:** Neurobiological research over the past several decades has predominantly relied upon electrophysiology, biochemistry, molecular biology and genetics to better understand how the brain functions. The role that mechanics plays in neural processes has largely been overlooked, until recently. Cells of the central nervous system (CNS) are constantly subjected to mechanical forces which influence their underlying biology. The ability of CNS cells to sense and respond to mechanical cues in their surrounding environment suggests the presence of mechanoreceptors on their surface membranes. During development, for example, neuronal axons may navigate to their final destination by sensing not only chemical gradients (chemotaxis); but also changes in the stiffness (durotaxis) of neighbouring cells and extracellular matrix. CNS tissue is mechanically inhomogeneous. Neurons are slightly stiffer than astrocytes, for example. Similarly, astrocytes have also been shown to be mechanosensitive and can respond to changes in the mechanical properties of their surroundings. Taken together, it is clear that further research is needed to dissect the contribution that mechanics plays in both the physiology and pathology of the central nervous system.