wavefront curvature, which makes different regions of the substrate more susceptible to propagation block and spiral wave formation. To quantify this observation, we found that instabilities predicted by curves relating the action potential duration and the pacing frequency at different spatial locations predict sites of wave break initiation, and, hence, spiral wave chirality.
[1] T. Quail, A. Shrier, L. Glass, Spatial Symmetry Breaking Determines Spiral Wave Chirality, Phys. Rev. Lett., In Press, (2014).

1566-Pos Board B517
Signaling Delays Preclude Defects in Lateral Inhibition Patterning
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Developmental biology is extraordinarily robust in its ability to self-organize exquisite spatio-temporal patterns despite an intrinsically noisy set of parts. Lateral inhibition is one mechanism commonly implicated in the formation of such precise emergent behavior. Models of lateral inhibition's patterning capabilities usually implicitly assume, however, that cells receive expression signals from their neighbors without delay. Here we explicitly investigate the effects of signaling delays as well as their relation to cis-interactions in lateral inhibition patterning. We find that rather than being a source of error, signaling delays counter-intuitively allow biology to ensure defect-free patterning, which together with cis-interactions can be both fast and robust to noise and parameter variation. This suggests that overlooking time delays in developmental signaling does not just ignore a potential source of error, but rather ignores a knob with which evolution may tune patterning robustness in general.

1567-Pos Board B518
Modeling Epithelial-Mesenchymal Transitions in Metastatic Cancer
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Cancer metastasis is responsible for more than 90% of cancer deaths. Yet, understanding epithelial mesenchymal transition (EMT) during cancer metastasis remains a major challenge in cancer biology. It is now established that cells use genetic regulatory circuits to make functional decisions of whether to undergo EMT or not. In this study, we constructed a theoretical model of the circuitry involved in the EMT. The core regulatory unit for the decision consists of two highly interconnected chimeric modules - the miR-34/SNAIL and the miR-200/ZEB mutual-inhibition feedback circuits. We developed a theoretical framework for modeling microRNA-based circuit and applied it to study the chimeric modules. We showed that the miR-34/SNAIL module functions as a noise-buffering signal integrator, and the miR-200/ZEB module functions as a three-way switch, allowing not only for the epithelial and mesenchymal phenotypes, but also for a hybrid phenotype with mixed epithelial and mesenchymal characteristics. We further studied EMT in a multi-cell environment by coupling the EMT circuit to cancer-related signaling pathways and by including cell-cell communications. Our model explains recent data on the observation of unusual intermediates with specialized cell behavior, such as collective migration, and phonotypical heterogeneity of the EMT observed in various lung cancer cell lines.

1568-Pos Board B519
The Density of Competitors in a Stratified Environment Determines the Relative Fitness of Biofilm Structures
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Multicellular organisms consist of many billions of individual cells, whose spatial location, gene expression and reproduction are closely coordinated to produce a functional whole. Understanding how cells assemble into three-dimensional, multicellular structures, and how these structures' spatial organization influences their function, is a fundamental challenge in biology and biophysics, while controlling cellular aggregation and growth for regenerative or therapeutic purposes is a major goal in bioengineering and medicine. Biofilms are three-dimensional sessile communities of interacting unicellular organisms, and even in a biofilm of genetically-identical clones the constituent cells can differentiate into different patterns of gene expression and growth rates; this differentiation is often linked to the cells' positions in the biofilm structure, which controls transport and intercellular contacts in the biofilm. P. aeruginosa is an opportunistic human pathogen and a widely-studied model system for biofilm formation. It has recently been found that P. aeruginosa tends to form multicellular aggregates even when grown in shaken liquid culture. Here, we use a combination of confocal laser-scanning microscopy experiments and individual-based computer simulations to track the fate of pre-aggregated and initially-un-aggregated cells as they compete for resources during the development of a biofilm in a flow cell. We find that pre-formed aggregates do not have an intrinsic growth advantage over single cells, but nevertheless biofilm regions that are initiated by pre-formed aggregates can outgrow regions that are initiated by single cells if competition for growth substrate is high. Our results show that preformed aggregates can assist a strain in colonizing a surface, under conditions of high competition from other strains. However, within the aggregate itself, a form of cooperation exists, in which cells on the top of an aggregate benefit at the expense of lower cells.

1569-Pos Board B520
How Do Bacterial Growth Rates Relate to Evolutionary Fitness Landscapes for Energy-Efficiency?
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We are interested in energy flows in bacteria, and how energy gets trafficked between producing ribosomal and nonribosomal proteins under different growth conditions. We describe an analytical model that leverages extensive data on experimental growth laws to infer the underlying fitness landscape in E. coli. This model gives insight into some of the complex nonlinear relationships between energy utilization and ribosomal and non-ribosomal production as a function of cell growth conditions. We draw inferences about what evolution has optimized in E. coli. Is E. coli optimized for growth speed or for energy efficiency? Experimental data shows that at its replication speed limit, E. coli produces 4 mass equivalents of non-ribosomal proteins for every mass equivalent of ribosomes. The model shows that this ratio is expected if the bacterial fitness function is the energy efficiency of fast-growing cells. We conclude that a principal evolutionary driving force for bacteria is the energy efficiency of the fastest growing cells.

1570-Pos Board B521
Morusin from Cortex Mori Inhibits Invasive Growth in Human Hepatoma SK-Hep1 Cells
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Morusin, a preylated flavonoid, is extracted from Cortex Mori, which is used in traditional Chinese medicine. In addition, morusin has been demonstrated to induce apoptotic effect in some cancers such as liver cancer, but other anti-cancer action is not well understood. In our preliminary study, we found Cortex Mori ethanolic extract and morusin exhibited cytotoxicity and antimigration effects in SK-Hep1 cells. Moreover, 5, 10, and 15 μM of morusin reduced cell mobility, migration and invasion by analysis wound healing assay and boyden chamber assay in SK-Hep1 cells. Accordingly, cell migration, and adhesion as well as angiogenesis require the formation of a leading pseudopodium, angiogenesis growth factor. Our results showed morusin significantly inhibited lamellipodia and filopodia formation, cell-matrix adhesion and angiogenesis. Furthermore, morusin can also inhibit growth factors and focal adhesion kinase (FAK) phosphorylation, and integrins and VEGF expression. By zymography assay and western blot assay, morusin inhibited MMP2 and MMP9 activation expression. Finally, we also found morusin inhibited c-Met and EGFR activation, and down stream activation decreased ERK, Akt, NF-κB, FAK, and Stat3. In conclusion, our data demonstrated morusin can reduce invasive growth of malignant liver through signaling inhibition.

1571-Pos Board B522
Noise Treatment in Models of Genetic Switches
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Mathematical modeling plays a key role in understanding and characterization of critical chemical processes underlying the dynamics of cellular decision-making. Deterministic modeling of relevant processes in complex genetic