

the enzyme activity (i.e., positive feedback). If fluctuations are absent, the system can be described by PDEs with delay. Spatiotemporal patterns such as traveling waves or spirals as well as uniform oscillations are observed.

In this work, we investigate effects of fluctuations in such systems. There are two major sources of fluctuations: conformation of each enzyme fluctuates individually and thus disperses time to finish the cycle (intramolecular fluctuations); stochastic interactions between molecules vary waiting time to start the next cycle (intermolecular fluctuations). Intermolecular fluctuations may in some cases enhance synchronization of the enzymes, while intramolecular fluctuations merely disturb it. We show that the combination of these two types of fluctuations may determine the dominant spatiotemporal pattern. Relevance to oscillatory patterns observed *in vivo* is also discussed.

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Proteome-Wide Fluctuation Analysis Of *S.cerevisiae*

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We measured over 40,000 single live yeast *S. cerevisiae* cells to determine the concentration and diffusion constants of more than 4100 proteins. These proteins account for more than 75% of the yeast proteome. We used Fluorescence Correlation Spectroscopy (FCS), Photon Counting Histograms (PCH), and Brightness & Number analysis (B&N) to analyze the intensity fluctuations of single molecules fused to GFP. The data was collected using a commercial FCS setup attached to a confocal microscope (ConfoCor3 and LSM 510 META, Carl Zeiss Jena GmbH, Germany) controlled by custom software.

The cells were imaged in transmitted light. We acquired fluorescence images, using the avalanche photo diodes of the FCS setup. This allows us to determine the localization of proteins, the cell cycle as well as cell health.

We developed a software package to automate the measurements and data analysis. We use the Open Microscopy Environment (OME) to organize our images, fluctuation measurements, and analysis results.

We calculated the protein copy number per cell, and compare the noise in concentration levels between different proteins in respect to localization and biochemical pathway.

We find that the diffusion coefficient for GFP is identical in nucleus and cytosol. But interestingly, most of the proteins localized in the nucleus diffuse slower than proteins localized in the cytoplasm.

We will present our data and compare them to information gathered with different methods like flow-cytometry and mass-spectroscopy. We will discuss conclusions derived by complementing our data with information collected in public databases like *Saccharomyces* Genome Database (www.yeastgenome.org), Yeast GFP Fusion Localization Database (yeastgfp.ucsf.edu), and the General Repository for Interaction Datasets (www.thebiogrid.org).

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Macroscopic Singularity In Morphogen Gradient And Bioelectric Field Of Growth Control

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In embryogenesis, every physiological system is developed through a growth control system mediated by organizers and growth control boundaries. The growth control signal transduction is embedded in various physiological functions. Many physiological processes are regulated through growth control mechanisms such as hypertrophy, hyperplasia, atrophy, apoptosis and signal transduction pathways involving growth control genes such as proto-oncogenes. A model of growth control system suggests that a growth control system originates from a network of organizers which distribute at extreme points of structural surface (or interface) curvature. Organizers and growth control boundaries are macroscopic singularities (i.e. discontinuity and abrupt transition) of morphogen gradient field and bioelectric field. Small, nonspecific perturbations around singular points - organizers can have long lasting systemic effect. This offers an efficient way of manipulating the system. The growth control model further suggests that singular points - organizers and separators - boundaries in growth control form an undifferentiated, interconnected cellular network that regulates growth and physiology both during and after embryogenesis. Stem cells are important components of this undifferentiated network. Acupuncture points and meridians originate from organizers and growth control boundaries respectively. The model of growth control system has met the gold standard of science - the following predictions of the model have been independently confirmed: 1. Organizers have high electric conductance, high electric current density and high density of gap junctions. 2. Growth control boundaries have high electric conductance and high density of gap junctions. 3. Singularity has important role in morphogenesis. 4. Morphogens and organizers partially retain their regulatory function after embryogenesis. 5. Nonspecific stimulation at acupoints - potential organizers in adult causes extensive growth control effects.

Singularity provides a potentially efficient way of manipulating the growth control, stem cells and physiological systems.

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Isotopomeric ^{13}C Labeling of Amino Acids Reveal Compartmentation in *Saccharomyces uvarum*

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The first step in the synthesis of the aspartic acid (Asp) methionine (Met) and threonine (Thr) can occur in close relatives of *Saccharomyces cerevisiae* such as *S. uvarum* via mitochondrial aspartate aminotransferase (AAT1) or its cytosolic homologue AAT2. Also the amination of cytosolic pyruvate in the production of alanine (Ala) in these species can occur in both compartments using cytosolic (ALT2) or mitochondrial alanine aminotransferase. The aim of this work was to reveal the compartmentation of the synthesis of these amino acids during respiratory growth using isotopomeric data derived from the ^{13}C labeling of proteinogenic amino acids. *S. uvarum* was grown under steady-state growth conditions and fed with a mixture of either $^{13}\text{C}[1,2]$ or $^{13}\text{C}[2]$ labeled acetate and unlabeled glucose at two dilution rates. Absolute and conditional labeling patterns were measured using ^{13}C NMR and compared with simulated isotopomer distributions within a least squares optimization routine that adjusted the flux parameters. Biomass composition was used to further constrain the fluxes. A software tool was created to automate the composition of the weakly non-linear isotopomer balance equations for all metabolites in the system, thus allowing us to easily test variations of any metabolic network. We properly account for symmetric and prochiral metabolites. The resulting equations are solved without the need for matrix calculations within the optimization routine making this approach a candidate for speeding up the simulation of large metabolic systems. The results of this optimization reaffirm that the precursor for Asp, Met, and Thr is mitochondrial oxaloacetate and that mitochondrial putative alanine transaminase (ALT1) is functional in the synthesis of alanine.

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Time recoder system of protozoa

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Unicellular animals might be cleverer than previously thought. Anticipating events are higher functions performed by the brains of higher animals; their evolutionary origins and the way they self-organize, however, remain open questions. Here we show that *Physarum polycephalum* and *Blepharisma japonicum* can anticipate the timing of periodic events. The organisms move rapidly under favourable conditions, but stops moving when transferred to less-favourable conditions. They exposed to low-temperature conditions, presented in several times consecutive pulses at constant intervals, reduced their locomotive speed in response to each episode. When subsequently subjected to favourable conditions, they spontaneously reduced their locomotive speed at the time point when the next unfavourable episode would have occurred. This implied anticipation of impending environmental change. After this behaviour had been evoked several times, the locomotion returned to normal. We explored the mechanisms underlying these behaviours from a dynamical systems perspective. We have developed a dynamical systems model that reproduces the experimentally observed phenomena. Poly-rhythmic amoeboid movement in *Physarum* has previously been reported by two independent research groups. Oscillations were observed with a series of different periods (600, 240, 30, 10, 2, 0.5, and 0.05 minutes), and the overall activity showed a 1/f-type power spectrum in the Fourier analysis. These results imply that there are oscillations with a series of frequencies and that the frequency distribution is wide and continuous. This is the most fundamental assumption used in the mathematical modeling. Our results hint at the cellular origins of primitive intelligence and imply that simple dynamics might be sufficient to explain its emergence.

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Single-cell Analyses of the *Escherichia Coli* Proteome with Single-molecule Sensitivity

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Genetically identical organisms do not have the same gene expression. This stochastic difference in gene expression, also known as noise, can be the