the other hand, in the case of T2DM, chronic glucose and lipid over accumulations cause β-cell dysfunctions. The physiological parameters used in clinics such as plasma insulin concentrations, however, seem to be insufficient for the understanding the dynamics of each β-cells. In numerous cases, during many years of subclinical periods, they don't have insulin deficiency on their early stages. For the universal understanding of such complex backgrounds, we apply a simple physical model. The model consists of L^2 lattice array of β-cells which are electrically coupled with each other and they interact with brain, liver, muscles and fats. We consider the blood glucose level as an external stress and assume that each of β-cells has its own threshold of damage. For the given blood glucose level, the β-cells with low-threshold are damaged more easily. As the extra loads of the dysfunctional β-cells are transferred to the normal β-cells, they are damaged more easily. Considering the load sharing, we numerically simulate overall β-cell dysfunction as different normal β-cell numbers. Regarding the activities of K_{ATP} channel as the β-cell function, we obtained increasing patterns of the blood glucose level in the body and the decreasing patterns of β-cell membrane bursting and insulin secretions of each β-cells.

3858-Pos

Noise Can Induce Steady-State Bimodality in Positive Feedback Loops Without Cooperativity

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Positive feedback is a common network motif in gene regulatory networks that is widely recognized to lead to bistability and, as a consequence, to hysteresis and switch-like responses. A non-linear, cooperative promoter response provides the necessary ingredient to generate bistability in deterministic descriptions of positive feedback. Using a synthetic system, we show experimentally that positive feedback is capable of inducing a bimodal, switch-like response with non-cooperative feedback, even when the underlying deterministic dynamics do not admit bistability. In accordance with theoretical models, the bimodal response requires the promoter within the feedback loop to be noisy, with infrequent, large bursts of expression. In addition, the transcription factor (TF) involved in the feedback loop has to be short-lived. Using a stochastic model and experimentally measured in vivo parameters of the promoter response in the absence of feedback, we can quantitatively describe the feedback response. We also find that multiple TF binding sites in a promoter can be important for the bimodal response not because of molecular cooperativity in TF binding, but because of increased noise in the promoter. Because many promoters possess multiple binding sites and many TFs are unstable, positive feedback loops in many gene regulatory networks may exhibit bimodal responses, but not necessarily because of deterministic bistability as is commonly thought.

Vibrational Spectroscopy

3859-Pos

Micro-Spectroscopy of Biomolecules and Cells at Variable Pressure in a Micro-Capillary

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Combining Raman microscopy with a micro-capillary compartment enables spectroscopic studies of small amounts of biological material at variable pressure. We present experiments over the pressure range from atmospheric pressure to 4 kBar in a micro-capillary that use less than 100 nanoliters of sample. We investigate pressure dependent structural changes in DMPC and POPC lipid systems through measurements of the Raman spectrum in the CH2 stretch band and fingerprint regions. The micro-capillary also allows to enclose living cells and to optically interrogate them through a microscope. This is illustrated through Raman spectroscopy and direct optical imaging of individual red blood cells at variable pressure.

3860-Pos

Raman Spectroscopic Signatures of the Metabolic States of Escherichia Coli Cells and their Dependence on Antibiotics Treatment

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The metabolic states of Escherichia coli (E. coli) cells were characterized with laser tweezers Raman spectroscopy and the cellular response to the antibiotics Cefazolin and Penicillin/Streptomycin were correlated to spectroscopic changes.
The Raman spectra of *E. coli* cells were measured at different time points in the bacterial growth curve, which revealed several spectral features applicable for identification of the bacterial cell's growth phase. The time dependent behavior of Raman peak intensities allowed us to identify four groups of Raman peaks with similar intensity time trends, displaying specificity to the same bio-molecule. The intensity of Raman peaks associated with DNA increased over time in contrast to protein specific Raman peaks, which decreased at different rates. In addition, the intensity of the adenine ring-breathing mode increased initially and decreased after approximately 10h. A separation of Raman spectra specific to different metabolic states of E. coli cells was visualized with principal component analysis (PCA).
The exposure of bacterial cells to Cefazolin and Penicillin/Streptomycin at the end of the exponential growth phase, resulted in differences in the time dependence of several Raman intensities. In addition, a shift of the spectral position of the adenine ring-breathing mode, associated with normal growth, was not observed for either of the two antibiotic drug exposures. The time dependence of the amide I Raman band intensity changed for Penicillin/Streptomycin exposure compared to normal growth, but not for Cefazolin treatment. This suggests that Raman spectroscopic markers of cellular response may differ between antibiotics or drug classes.

3861-Pos

Data Processing in FTIR Imaging of Cells and Tissues: Towards Protein Secondary Structure Imaging

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IR spectroscopic images were recorded using an Equinox Bruker FTIR spectrometer coupled to a Hyperion 3000 imaging system equipped with a mercury cadmium telluride (MCT)-based focal plane array (FPA) detector of 64×64 pixels (Bruker Optik, Ettlingen, Germany). Images containing 4096 IR spectra at 8 cm-1 spectral resolution were acquired by coadding 256 interferograms in about 5 minutes. All the data processing was carried out by the program ''Kinetics'' running under MatLab. The ''Kinetics'' software, previously used for FTIR spectrum processing and analysis, was extended for the processing of FPA-acquired FTIR data. Different types of images can be generated, either based on the absorbance at 1 wavenumber or the ratio of the absorbances at 2 wavenumbers or more advanced combination of the data. We show here that protein secondary structure content evaluated as described in [1] sheds light on the molecular determinants that allow the differentiation between sub-structures in tissues. Similarly we shall illustrate heterogeneity in prostate cancer cells (PC-3) in culture based on secondary structure imaging.
References
[1] Goormaghtigh,E., J.M.Ruysschaert, and V.Raussens. Evaluation of the information content in infrared spectra for protein secondary structure determination, Biophys.J. 90 (2006) 2946-2957.

3862-Pos

Inter-Residue Coupling of Model PPII Helices using 13c Isotopic Labeling

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Characterization of poly-proline II (PPII) conformation on a site-specific basis has importance in developing a model for structure and stability in these systems. Coupling of selected residues for a series of related peptides having predominantly PPII conformations were measured using VCD and IR spectra of selected variants that were doubly labeled with ^{13}C on the amide C=O. The characteristics of the ^{13}C=O component of the amide I'IR band and their sensitivity to the local structure of the peptide are compared to predictions based on DFT level calculations for related structures and used to determine coupling between C=O groups along the backbone of this helical structure. Doubly labeled peptides have spectral shifts reflecting the mass change in addition to coupling between residues. In the PPII case the coupling is relatively weak, yet by combining IR and VCD along with DFT level calculations, we have been able to determine its coupling constants. Comparison of PPII structures with ''random coils'' can be done by comparing all Proline, mixed Ala-Pro and Lys-rich sequences. The shifts and couplings reflect the computations in all cases. The distinct vibrational coupling patterns of the labeled sites based on this structure are also well matched by *ab initio* DFT-level calculations of their IR and VCD spectral patterns.