the division of cancerous cells by forming clamps between DNA segments. We continue interpreting our results in terms of a molecular model, which includes the reaction kinetics and functional mechanism. Our work contributes to the understanding of energy dependent, non-equilibrium dynamics of biomolecules, which is a key feature of life.

**90-Plat**

**Photocontrol of Gene Expressions Systems Using Light-Induced Conformational Changes of Nucleic Acids**

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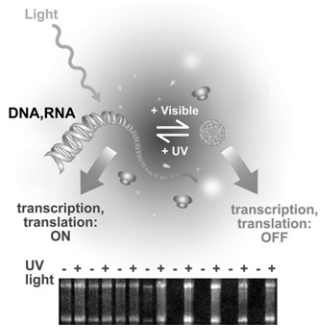
To understand non-trivial biological functions, it is crucial to develop minimal synthetic models that capture their basic features. Here, we demonstrate a sequence-independent, reversible control of transcription and gene expression using a photosensitive nucleic acid binder (pNAB). By introducing a pNAB whose affinity for nucleic acids is tuned by light, in vitro RNA production, EGFP translation, and GFP expression were successfully inhibited in the dark and recovered after a short illumination at 365 nm. Our results indicate that the accessibility of the protein machinery to one or several nucleic acid binding sites can be efficiently regulated by changing the conformational/condensation state of the nucleic acid (DNA conformation or mRNA aggregation), thus regulating gene activity in an efficient, reversible, and sequence-independent manner. The possibility offered by our approach to use light to trigger various gene expression systems in a system-independent way opens interesting perspectives to study gene expression dynamics as well as to develop photocontrolled biotechnological procedures.




Ref: A. Estévez-Torres, C. Crozatier, A. Diguet, T. Hara, H. Saito, K. Yoshikawa, D. Baigl, Proc. Natl. Acad. Sci. USA 2009, 106, 12219-12223.

**91-Plat**

**Long-Range Electronic Couplings Observed in DNA By SR-EPR**

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DNA can self-assemble into a wide variety of pre-programmed 2-dimensional and 3-dimensional structures. This property, combined with the ability to conduct charge, makes DNA an attractive material for the fabrication of nanoscale circuitry, sensors, and catalysts. Fermi's Golden Rule, an equation governing the rate of charge transfer, describes the ease with which DNA conducts electrons or ''holes'' (positive charges). However, the predictive power of Fermi's Golden Rule is limited by the difficulty of independently measuring the terms that appear in this equation. One of these terms, the square of the electronic coupling matrix element, is proportional to the scalar exchange coupling between the charge donor and acceptor. Using a nitroxide radical and the paramagnetic Dy(III) ion as surrogates for donor and acceptor, we have measured scalar exchange couplings and their distance dependence in a family of DNA duplexes via saturation-recovery electron paramagnetic resonance (SR-EPR). Scalar exchange couplings are observed at distances as great as 5.6 nm. The decay in the scalar exchange coupling parallels the decay in electron transfer rates recently measured in DNA. The SR-EPR methodology is general and provides a new tool for determining the electronic coupling matrix element in Fermi's Golden Rule. The knowledge gained from these measurements may prove useful in designing DNA-based electronic devices.

**92-Plat**

**Overcharging Below the Nanoscale: Multivalent Cations Reverse the Ion Selectivity of a Biological Channel**

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We report charge inversion within a nanoscopic biological protein ion channel in salts of multivalent ions. The presence of positive divalent and trivalent counterions reverses the cationic selectivity of the bacterial porin OmpF into anionic. We discuss the conditions under which charge inversion can be inferred from the change of sign of the measured quantity, the channel zero current potential. By comparing experimental results in protein channels whose charge has been modified after site-directed mutagenesis, the predictions of current theories of charge inversion are critically examined. It is emphasized that charge inversion does not necessarily increase with the bare surface charge density of the interface and that even this concept of surface charge density may become meaningless in some biological ion channels. Thus, any theory based on electrostatic correlations or chemical binding should explicitly take into account the particular structure of the charged interface.

**93-Plat**

**Optical Proteomics Combining Nonlinear Electrokinetics and Coherent Two-Dimensional Infrared Spectroscopy**

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We have previously demonstrated that multidimensional optical spectroscopy (EVV 2DIR) can conveniently and easily quantify tryptophan (W), tyrosine (Y), phenylalanine (F) and the total methyl ($CH_3$) content of a protein , but more independent variables need to be quantified in order to uniquely identify a higher proportion of the proteome. Bioinformatics analysis shows that only a small number of amino acids need be quantified to uniquely identify a substantial proportion of the human proteome. For example, if the approximate mass ($\pm$ 10%) of a protein is also known as well as the W, F, Y and $CH_3$ content, then the number of proteins uniquely identified increases from 2% to 15% of the entries in the human protein database (Ensemble release 44) containing 33100 proteins.

In this paper, we demonstrate a comprehensive protein identification and characterisation strategy based on the combination and principles of nonlinear electrokinetics together with EVV-2DIR spectroscopy.

A complex mixture is spatially resolved via Capillary Zone Electrophoresis (CZE) and the electrophoretic mobilities of the resulting fractions are analysed in a manner that facilitates the assignment of values to a substantial range of physicochemical properties such as the molecular weight and surface charge densities to each fraction with an accuracy larger than 80%[4]. The two analysis methods are joined up with a specially-devised CZE-EVV interface platform which enables the preservation of the spatial resolution of the fractions and facilitates upstream optical interrogation of each individual fraction[5].

**94-Plat**

**Denatured-State Conformation As Regulator of Amyloid Assembly Pathways?**

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Deposits of insoluble protein fibrils with cross beta-sheet structure are the hallmark feature of numerous human disorders, including Alzheimer's disease and type II diabetes. Using correlated dynamic light scattering (DLS) and atomic force microscopy (AFM) we investigated amyloid formation with hen egg white lysozyme at acidic pH values. We found that there was a pronounced transition in the aggregation behavior at low *vs* near physiological salt concentrations. At low salt concentrations ($<$ 100 mM), DLS indicated the near simultaneous nucleation of three distinct aggregate populations. For elevated salt concentrations, only a single aggregate peak nucleated. AFM imaging shortly after nucleation further indicated distinct aggregate morphologies and sizes. Low salt concentrations yielded polymeric aggregates of varying dimensions but consistent with the three aggregate peaks observed in DLS. Aggregation near physiological salt concentrations, in contrast, yielded oligomeric intermediates that nucleated into protofibril strands. It is commonly accepted that amyloid fibril growth by native proteins requires a partially denatured conformation. We wondered, however, whether these changes in aggregation behavior could be related to *differences* in the conformation of denatured lysozyme monomers. Using DLS to measure lysozyme's diffusivity, we found that lysozyme assumes a noticeably more extended conformation at low vs. high salt concentrations. These latter measurements were carefully corrected for the effects of protein interaction and variable solution viscosity on protein diffusivity. ANS fluorescence measurements revealed a similar trend towards increased solution exposure of lysozyme monomers at low salt concentrations compared to high salt concentrations. These observations suggest that amyloid fibril assembly pathways might depend on the conformation of the denatured state from which they grow. This has potentially significant implications for our understanding of amyloid fibril formation in general and how to control the emergence of toxic intermediates, in particular.