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Authors
Zhu, Songning
Digman, Michelle A
Thompson, Jamie
et al.

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Posters: Novel Techniques for Systems and Synthetic Biology

2016-Pos

A novel electrical device demonstrates localized stimulation triggers cell-type-specific proliferation in biofilms

Colin J. Comerci[1], Alan L. Gillman[2], Leticia Galera-Laporta[1], Edgar Gutierrez[3], Alex Groisman[3], Joseph Larkin[4], Jordi Garcia-Ojalvo[5], Gurol M. Suel[3].
[1]School of Biological Sciences, University of California San Diego, La Jolla, CA, USA, [2]Department of Molecular Biology, University of California San Diego, La Jolla, CA, USA, [3]University of California San Diego, La Jolla, CA, USA, [4]Biological Physics, Boston University, Boston, MA, USA, [5]Universitat Pompeu Fabra, Barcelona, Spain.

Biological systems ranging from bacteria to mammals utilize electrochemical signaling. While artificial electrochemical signals have been utilized to characterize neural tissue responses, the effects of such stimuli on non-neural systems remain unclear. To pursue this question, we developed a novel experimental platform that combines a microfluidic chip with a multi-electrode array (MiCMA) to enable localized electrochemical stimulation of bacterial biofilms. The device also allows simultaneous measurement of the physiological response within the biofilm with single-cell resolution. We find that stimulation of an electrode locally changes the ratio of the two major cell types comprising *Bacillus subtilis* biofilms, namely motile and extracellular matrix-producing cells. Specifically, stimulation promotes the proliferation of motile cells, but not matrix cells, even though these two cell types are genetically identical and reside in the same microenvironment. Our work thus reveals that an electronic interface can selectively target bacterial cell types, enabling control of biofilm composition and development.

2017-Pos

IVF bovine oocyte classification and selection

Songning Zhu[1], Michelle A. Digman[1], Jamie Thompson[2], Fernando Campos-Chillon[2].
[1]Department of Biomedical Engineering, University of California Irvine, Irvine, CA, USA, [2]College of Agriculture, Food and Environmental Sciences, California Polytechnic State University, San Luis Obispo, CA, USA.

The current technology for in vitro fertilization (IVF) has a long history of merely 40 years. The addition of all live births from either fresh or frozen oocytes transferred from a single oocyte collection is known as the IVF productivity rate. The ability to select the best quality eggs is the key to minimizing the number of oocytes generated, procedural cycles for potential failed attempts, and lowering cost and maximize efficiencies. The current standard for egg selection is based on defined morphological criteria. Technicians usually look for an identifiable pattern such as cytoplasm, perivitelline space, zona pellucida, size, etc. Concomitantly oocyte is also screened using genetic analysis that enhances selectivity. However, the same selection procedure is not possible for oocytes. It also has been shown that eggs with similar morphology performance might have drastically different metabolism. Here we proposed a solution where we focus on developing advanced non-invasive imaging methods to map the energy metabolism of oocytes using fluorescent lifetime imaging (FLIM). Combining multiphoton excitation, hyperspectral imaging, and machine learning approach to minimize instrumenting costs, minimize laser exposure to the bovine oocyte, and maximize predictably results for oocyte selection whether fresh or frozen. Hyperspectral imaging (HI) offers the capability of collecting intensity of autofluorescence signals from the oocytes with less laser exposure minimizing the risk of photo-toxicity. Using the phasor approach to HI enables the use of multiparametric analysis of the emission in the range of 350-500 nm range (in the range of emission of metabolic cofactors in oocytes). Complete profiling of the entire egg in three-dimensional space shows its morphological and metabolic features is then generated, showing significant differences for super-stimulation with follicle stimulating hormone, in-vitro maturation, IVF, and in-vitro culture produced oocytes.

2018-Pos

Biological nanopore control of synthesis: Single-molecule reaction and characterization

Chao-Nan Yang, Yi-Lun Ying, Yi-Tao Long.
Nanjing University, Nanjing, China.

In contemporary biopolymer synthesis, conservative synthesis of monomers to polymers has been achieved by using organocatalyst. However, the high-efficiency conversion in biopolymer synthesis is rare, due to the difficulties in precisely monitoring and controlling the reaction immediates[1,2]. Here, we report a novel molecular machine for controllable single-biomolecule synthesis with biological protein nanopore (NP-Synth.), which combines the advantages of manipulating reaction sites at atomically level and real-time recording of the reaction trajectories. Driven by the applied voltage, the two reactant molecules from the reducing phase successively enters into the nanopore confinement. The catalytical site inside the nanopore facilitates the rapid conjugation of these two molecules. The nanopore confinement here directs the orientation of the reactive group of the reactant for directly driving the synthesis. Following the real-time current traces, the reaction process is optimized by adjusting the length of the reactant and the applied potential. This work shows that the NP-Synth. can produce, by combining well-defined protein nanopore, ordered biopolymers that were previously inaccessible to organic chemistry.

2019-Pos

Mapping functional regions of essential bacterial proteins with dominant-negative protein fragments

Andrew Savinov[1], Andres Fernandez[2,3], Stanley Fields[4,5].
[1]Department of Biology, Massachusetts Institute of Technology, Cambridge, MA, USA, [2]Molecular and Cellular Biology, University of Washington, Seattle, WA, USA, [3]Fred Hutchinson Cancer Research Center, Seattle, WA, [4]Department of Genome Sciences, University of Washington, Seattle, WA, USA, [5]Department of Medicine, University of Washington, Seattle, WA, USA.

Fragments of native proteins can act as dominant negative inhibitors, representing a substantial stress for cells. Massively-parallel measurements of growth inhibition by protein fragments have been used to discover peptide inhibitors and map protein interaction sites. However, the underlying principles governing fragment-based inhibition have thus far remained unclear. Here, we adapt a high-throughput inhibitory fragment assay for use in *Escherichia coli*, applying it to a set of ten essential proteins. This approach yielded single amino acid resolution maps of inhibitory activity, with peaks localized to functionally important interaction sites, including oligomerization interfaces and folding contacts. Leveraging these data, we perform a systematic analysis to uncover principles of fragment-based inhibition. We determine a robust negative correlation between susceptibility to inhibition and cellular protein concentration, demonstrating that inhibitory fragments likely act primarily by titrating native protein interactions. We also characterize a series of trade-offs related to fragment length, showing that shorter peptides allow higher-resolution mapping but suffer from lower activity. We employ an unsupervised statistical analysis to show that the inhibitory activities of protein fragments are largely driven not by generic properties such as charge, hydrophobicity, and secondary structure, but by the more specific characteristics of their bespoke macromolecular interactions. AlphaFold computational modeling of peptide complexes with one protein shows that the inhibitory activity of peptides is associated with their predicted ability to form native-like interactions. Overall, this work demonstrates fundamental characteristics of inhibitory protein fragment function and provides a foundation for understanding and controlling protein interactions *in vivo*.

2020-Pos

The role of RNA condensation in reducing gene expression noise

Alexander J. Mayer[1], Marcus Roper[1], Amy S. Gladfelter[2], Grace McLaughlin[2].
[1]Mathematics, University of California Los Angeles, Los Angeles, CA, USA, [2]Biology, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.

Biomolecular condensates have been shown to play a fundamental role in localizing biochemistry in a cell. RNA is a common constituent with proteins and can determine biophysical properties. Functions of biomolecular condensates are varied including activating, inhibiting, and localizing reactions. Recently it has been proposed that condensates can buffer noise to diminish cell to cell variability. Here we introduce a phenomenological model in which phase separation of mRNAs into RNP droplets can regulate the abundance of the protein these mRNA encode and markedly decreases expression noise. We place particular emphasis on how this mechanism can facilitate efficient transcription by reducing noise even in the limit of infrequent bursts of transcription, by exploiting the physics of concentration dependent, deterministic phase separation threshold. We investigate two biologically relevant scenarios in which phase separation acts to either ''buffer'' noise by storing mRNA in inert droplets, or ''filter'' phase