Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Posters: Systems and Synthetic Biology

1261-Pos
Crowding-Induced Spatial Organization of Gene Expression in Cell-Sized Vesicles
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E. coli cells, which are commonly used to study gene expression, show membraneless organization of gene expression components within the cell. Cell-free expression systems are also widely used to study gene expression, but a major limitation is the lack of a means to spatially organize DNA plasmids and ribosomes to mimic the cellular environment. In this work, we used computer simulations to guide experimental efforts to control the spatial organization of DNA and ribosomes in cell-sized vesicles using macromolecular crowding. Using Brownian dynamics simulations of coarse-grained models of DNA plasmids and crowders, we showed that plasmids remain uniformly distributed at low levels of crowding but become strongly adsorbed at confining surfaces at high levels of crowding. These effects are due to entropic depletion interactions resulting from the presence of crowding molecules. We validated the simulation results experimentally by using fluorescently-labelled DNA plasmids and ribosomes in cell-sized vesicles at different concentrations of the macromolecular crowder Ficoll-70. Large crowder concentrations resulted in preferential localization of plasmids at the walls of the vesicle, while ribosomes remained uniformly distributed throughout the vesicle. We then used kinetic Monte Carlo simulations to study how protein production was affected by crowding-induced changes in spatial organization and diffusion. The localization of DNA to the wall resulted in lower protein abundance and a decrease in translational efficiency with an increase in system size. Experimentally, we tracked the dynamics of transcription and translation in crowded vesicles using a coupled mRNA/protein reporter technique. These results were consistent with results from simulations. We thus used computer simulations to design a cell-free experimental platform capable of spatial organization of gene expression components. This platform can be used to better understand the spatial control of gene expression in cells.

1262-Pos
Optogenetic Control of Non-Apoptotic Cell Death
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We introduce optogenetic tools (designated LiPOP) that enable photoswitchable necroptosis and pyroptosis in live cells with varying kinetics. The LiPOP tools allow us to reconstruct the key molecular steps involved in these two non-apoptotic cell death pathways by harnessing the power of light. We further demonstrate the use of LiPOP, by itself or coupled with bioluminescence, to achieve optochemical killing of bacteria and cancer cells in vivo. LiPOPs set the stage for triggering necroptotic and pyroptotic cell death both in vitro and in vivo and will likely find use in studying the role of nonapoptotic cell death pathways within the tumor microenvironment.

1263-Pos
Engineering Adaptive Gene Circuits in Bacteria Mastering Game Playing by Reinforcement Learning
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Learning to solve problems is central to artificial and living intelligent systems. Although physical and chemical systems mimicking neural connectivity have been shown to solve complex problems, no living system with a synthetic genetic construction has ever been reported to learn complex algorithms such as playing board games — a classic benchmark for artificial intelligence. Engineering a synthetic genetic system in living cells able to learn and play even the simplest board games, such as tic-tac-toe, has remained elusive because it requires not only a set of gene circuits implementing the needed decision algorithms but also an adaptive memory system that can predictably adjust their strength through learning. We will report that engineered *Escherichia coli* encoding a library of new genetic switches — we call memregulons — that act as both memory systems and logic gates, can learn to produce predictable gene regulation. As the memregulon devices allow the design of gene circuits with predictable behaviour, we use them to implement in living cells a computational algorithm allowing the bacteria to master playing tic-tac-toe by using reinforcement learning. Learning is achieved by persistently modifying the relative expression of memregulons by applying external chemicals after each training game is won or lost, leading to new decisions. Bacteria learn by playing against other players or other bacteria in an unsupervised manner and the same library allows them to learn other types of games or algorithms.

1264-Pos
Modeling and Manipulating Antibody Response Against Influenza and Coronavirus Spike Proteins and Exploring their Role in Directing Spike Evolution
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The antibody repertoire possesses near limitless diversity, enabling the adaptive immune system to accommodate essentially any antigen. However, this diversity explores the antigenic space unequally, allowing some pathogens like the influenza virus to impose complex immunodominance hierarchies that distract antibody responses away from key sites of virus vulnerability. We developed a computational model of affinity maturation to map the patterns of immunodominance that evolve upon immunization with natural and engineered displays of hemagglutinin (HA) - the influenza spike, which mediates entry to the host cell and is the main vaccine antigen. Based on this knowledge, we designed immunization protocols that subvert immune distraction and focus serum antibody responses upon a functionally conserved, but immunologically recessive, target of human broadly neutralizing antibodies. These antibodies would confer universal immunity to influenza. We tested in silico predictions by vaccinating transgenic mice in which antibody diversity was humanized to mirror clinically relevant humoral output.
We further used 3d coarse-grained computational models to estimate the antibody pressure on the seasonal flu H1N1 and sarbecovirus subgenus spikes. Analyzing publically available sequences, we found that antibody pressure, through the geometrical organization of spikes on viral surface, shaped their mutability. Studying the mutability patterns of SARS-CoV-2 and the 2009 H1N1 pandemic spikes, we found that they are not predominantly shaped by antibody pressure. However, for SARS-CoV-2, we find that over time, it acquired, at low frequency, several mutations at antibody-accessible positions, which could indicate possible escape. Hence, we offer a geometry-based approach to estimate and assess whether a pandemic virus is changing its mutational pattern to that indicative of a circulating virus.

1265-Pos
Cell Cycle Dependence of P53 Dynamics during the DNA Damage Response
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The transcription factor p53 regulates the cellular response to numerous stresses. A major activating stress for p53 is DNA damage, which can arise from several sources including chemotherapeutic drugs, gamma irradiation, and UV light. Once activated, it generates several downstream effects, including DNA repair, cell cycle arrest, and apoptosis. With the development of single-cell, time-lapse fluorescence microscopy technique, recent studies have shown that the dynamics of the tumor suppressor p53 encode information about stresses to which a cell responds and are decoded differentially to regulate appropriate responses, including cell cycle progression. Although it is known that distinct DNA damage repair pathways are activated when cells are damaged in different cell cycle phases, the dependence of p53 dynamics on cell cycle phase and how this relationship shapes p53-mediated cell fate decisions are poorly understood. In this study, we used long-term time-lapse fluorescence microscopy to track p53 dynamics as a function of cell cycle phase in individual cells in