SynCTI Seminar Series

NUS Synthetic Biology for Clinical and Technological Innovation (SynCTI)

The CRISPR revolution

Dr Chase Beisel
Department of Chemical and Biomolecular Engineering
North Carolina State University, U.S.

CRISPR has become synonymous with disruptive genome-editing technologies that are revolutionizing basic research, biotechnology, medicine, and agriculture. One critical aspect of CRISPR often overlooked in this fanfare is that it was not invented; instead, CRISPR is naturally part of adaptive immune systems in bacteria and archaea called CRISPR-Cas systems. These systems have proven remarkably diverse and stand in stark contrast to small handful of proteins currently used as technologies. In this talk, I will describe the unique properties of CRISPR-Cas systems and how these properties directly lend to genome editing and many other uses. I will also describe my group's ongoing efforts to explore the functional diversity of these systems and how they can be harnessed for applications in bacterial strain engineering and programmable-spectrum antimicrobials. Through these advances, we aim to understand the functional diversity of these versatile immune systems and further advance the reach and impact of the ensuing revolutionary technologies.

Credentials of *Pseudomonas putida* as a Real (not metaphoric) Cell Factory

Professor Victor de Lorenzo
Laboratory of Environmental Molecular Microbiology
National Center for Biotechnology, Madrid

Although bacterial cytoplasm is not compartmentalized this does not mean that cellular components are randomly organized or free to diffuse. Many studies have shown that proteins are located at particular regions of bacterial cells. We have investigated the subcellular localization of the molecular machineries that run the whole gene expression flow of *Pseudomonas putida*. Based on fluorescent protein fusions to subunits of RNA polymerase (RNAP) and ribosomes, microscopy and image analysis showed RNAP co-localized in 3D with chromosomal DNA, while ribosomal proteins were only abundant outside of the nucleoid. We have developed a genetic approach for exploring the intracellular micro-granularity of *P. putida's* cytoplasm based on the *Pm* promoter and its regulator XylS by following the expression noise of *Pm-gfp* fusions in single cells. Using mathematical modelling and computational simulations, we determined the kinetic properties of the system and used them as a baseline code to interpret promoter activity in terms of upstream regulator variability. Transcriptional noise was predicted to depend on the intracellular physical distance between regulator source (where XylS is produced) and the target promoter which can be modified by obstacles in the way. This approach allowed deconvolution of cytometry data into mechanistic information on gene expression flow and provided a basis for selecting a given noise level in engineered regulatory nodes, such as in synthetic biology constructs. It is thus possible that the macromolecules involved in the flow of genetic information have a fixed 3D distribution in *P. putida* in order to optimize the catabolic ability of the corresponding enzymes. New approaches to examine the potential of *P. putida* as chemical microfactories will be discussed.

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Hosted by A/P Matthew Chang

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