Amendment 0001

Special Notice 12-SN-0027, Special Program Announcement for 2012 Office of Naval Research: Research Opportunity: Synthetic Biology Tools for Sensing and Bioprocessing

The following provides answers to questions submitted in response to the Office of Naval Research Special Notice for Synthetic Biology Tools for Sensing and Bioprocessing:

Questions and Answers:

1) For "uncovering novel metabolic pathways," are you considering computational approaches?

Computational approaches that utilize only information about known enzymes/pathways are not of interest. This topic is meant to stimulate thinking about ways to avoid labor-intensive screening approaches as well as 'omic approaches that only consider homology to known enzymes/pathways or their close homologs . Projects that only do modeling or bioinformatics approaches in the absence of experimental testing/validation are also not of intrest. This topic is not meant to be focused on biomedically relevant products but rather on electrosynthesis, fuels or other high-value materials. How can I rapidly determine if I have an organism capable of unusual, perhaps previously unidentified metabolism lurking in my complex community?

2) For "information exchange between cells" are you interested in BOTH diffusible signals and the non-diffusible (electrical/magnetic/light)?

The topic reads "detection and/or production of chemical or non-chemical signals", so yes, either diffusible chemical or non-diffusible physical signals would be of interest. However, the tradeoff for using a diffusible signal which may be a rate-limiting step, would have to be some extraordinary gains in something else (e.g., amplification of signal, or ability to detect and analyte we can't currently detect). I am thinking about how to encode complex information and quickly distribute it to other cells (or within that same cell).

3) Please explain the living-systems-robotic hybrids.

This was the subject of a 2011 muri topic, for which the objectives were to try to elucidate and manipulate microbial signal reception and subsequent transmission to a non-living platform. This might involve characterization of microbial/cellular receptors for specific extracellular cues and mechanisms of chemotaxis; characterization of receptors/sensing of non-chemical cues (e.g., vibration, sound, magnetic or electric fields) and mechanisms of intracellular signal transduction; translation of microbially/cellularly received chemical/non-chemical cues into external signals interpretable by a non-living platform (e.g., flagellar motion or other mechanical oscilators, optical, electrical or magnetic outputs; signal processing (amplification/transduction) of microbial/cellular signals along with control algorithms to direct a device (e.g., robot) to carry out instructions – or – to allow feedback from a device to a microbial/cellular controller . The overall goal is to use living cells to interrogate their environments for multiple stimuli, process this information and then convey a set of outputs of instructions to control a device in a way that offers novel, smart interfaces for autonomous control. Success depends on the ability ot program cells to detect and process environmental information with minimal cross-talk and then to convert cellular outputs into signals interpretable by, and that provide actionable direction to, a silicon or organic-based device or system.

4) What does a 'cellular chemostat' imply.

Think about a cell within a reaction that monitors the progress of the reaction and adds nutrients, tweaks gene expression, destroys unwanted by-products, changes ph, etc.

5) Is this call open to companies as well as academics?

Yes, but, note that if the proposal is submitted by a company it must be awarded on a contract, which can take longer than making an award on a grant to a university. Note also that cost of an effort will be considered relative to its value - if working with a company offers a significant value or unique capability to the project that justifies the extra cost. Otherwise it may not fare well compared to other proposals.

6) For the sub-topic, "Develop microbial/multi-cellular catalysts that can utilize electrical current directly as an electron donor, and elucidate mechanisms of electron transport into these catalysts and their metabolic pathways", are you looking for researchers to define electron transfer pathways only, or to go a step further and demonstrate that parts from these pathways can be transferred to other chassis organisms or that this organism can serve as a chassis for genetic manipulation?

Yes to both parts of this question, if feasible. Note that focus here is on using electrical current as an electron donor for metabolism, not for microbial fuel cell applications.