White paper
Herbert M. Sauro (University of Washington)

Research interests:

I am interested in how biological cells work. Over the last 80 years we have amassed enough knowledge of the parts and connections between parts in cells to be in a position to try and understand the operating principles by which cellular networks operate. With understanding comes the power to reengineer. My earliest work focused on developing and using what was originally coined metabolic control analysis but more accurately should be called biochemical control analysis (BCA). This is an extremely rich theoretical approach that allows us to understand how the whole depends on the individual parts. From it a number of basic principles of operation have emerged. Since then my work diverged somewhat into standards and software development with work on SBML (Systems Biology Markup Language) and now more recently SBOL (Systems Biology Open Language). Even more recently my lab has been interested in the evolutionary robustness of synthetic circuits. My first interest is however understanding how cells work and together with my NSF funded postdoc Kyung Kim and a few undergraduates we again have been working on a number of projects related to understanding networks. The most relevant here is the importance of noise in cellular networks. BCA is a deterministic theory and as originally developed has nothing to say about noise. However, we know that noise is an ever present phenomena in cells and as such our theories should take it into account. What is most exciting about noise is that it could be used as a second signaling channel in addition to the 'DC' signal we are most familiar with. It is possible to use chemical networks to manipulate and possibly compute with noise, thus an entirely new way to carry out computation in parallel might be envisioned. As a result we have been attempting to extend BCA to the stochastic regime and have reported some results in recent publications. However, our understand of how noise can be used and controlled in biochemical network is still extremely naïve.

Main challenges and state of the art:

My personal list of challenges includes the following, split into more philosophical and practical challenges:

Philosophical:

1. A recognition by the US scientific community in particular that theory is an important part of any scientific endeavor. Without theory, all we have is data and perhaps well drawn cartoons.
2. A recognition that biology should be seen by the community as an engineering substrate just as much as silicon or steel.
3. The development of a robust synthetic biology engineering discipline.
4. There will undoubtedly be early successes but the real potential of synthetic biology can **only** be achieved by thinking long term.

Scientific and Technical:

1. Very cheap DNA synthesis, i.e. 1 or 2 cents a base
2. Good debugging tools
3. An attempt to define a set or reusable golden parts, that is, highly characterized biological parts to see whether true predictive biology is even possible. Obviously nature can do it, so I presume we can too.
4. Understanding how context affects biological components, related to point 3.
5. Understanding noise in biochemical networks and exploring noise as a distinct computational medium.

Important directions of research:

Important directions of research include:

- Cheap DNA synthesis
- Better and more diverse monitoring tools at the molecular level. Should have good bandwidth and be able monitor, where possible, in real time, *cf.* recent pH detector
- A better theoretical understanding of how noise propagates through cellular networks.
- Use of evolution to help in design
- Standards in synthetic biology to enable rapid and error free exchange of designs between labs, hosting of design and part repositories, publication of designs and part specification data.