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Viewpoint

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The First Annual Winter q-bio Meeting: Quantitative Biology on the Hawaiian Islands

Arthur Prindle[†] and Brynne C. Stanton*[,‡]

[†]Department of Bioengineering, University of California, San Diego, San Diego, California, United States

[‡]Synthetic Biology Center, Department of Biological Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts, United States

Technology is driving revolutionary changes in biology. Over the past decade, scientists and engineers have begun to define the path forward in the genomic era. Systems biology has arisen as the deduction of interaction networks from -omics data generated in the wake of remarkable technological achievements. Likewise, DNA synthesis technologies are driving the development of Synthetic Biology, whereby engineered circuitry and even entire genomes can be reconstituted from chemical building blocks. These two emerging areas have catalyzed the growth of Quantitative biology (q-bio), whereby the central goal is the deduction of quantitative principles that can be used to construct predictive models for biological phenomena.

The Winter q-bio meeting brought together scientists and engineers interested in all areas of q-bio. The focus for the meeting this year was synthetic biology, with about half of the invited speakers being renowned leaders in this area. It was held February 18−21, 2013 on Oahu, at the Hilton Hawaiian Village resort in the heart of the famous Waikiki beach. Each year, the meeting will take place on the Hawaiian Islands and focus on topics within q-bio.

The meeting was a tremendous success, and gathered over 300 attendees from 17 different countries in its first year. A towel in every welcome bag signified a different type of meeting, one where prominent experts and students alike were invited to interact and talk about science in a laid back setting. Local bars, restaurants, and beaches made great conversation spots for graduate students, postdocs, professors, editors, industrial collaborators, and program officers throughout the conference. On Wednesday night, conference attendees strolled down the beach to an outdoor banquet at the Moana Surfrider, a beautiful colonial hotel founded in 1901 as one of the first in Waikiki.

However, the real attraction was the impressive speaker lineup, which kept attendees indoors throughout much of the week. We will attempt to describe some snapshots of work presented at the meeting below (full list of invited speakers in Table 1 and on the Web site: w-qbio.org).

The meeting kicked off with an exciting talk given by Jim Collins (Boston University) on interspecies antibiotic tolerance and the evolution of bioengineering at the molecular level. Collins described the complementary approaches of systems and synthetic biology using a "boombox" illustration. Systems biology seeks to take apart the boombox to identify its components and their interactions, while synthetic biology attempts to put together individual components to assemble modules that approach boombox-like function. Collins also described exciting recent efforts toward cholera prevention through the use of engineered probiotic bacteria in yogurt.

The synthetic biology focus continued with an exceptional talk from J. Craig Venter (J. Craig Venter Institute) where he spoke of "digitizing biology" and likened life to a DNA software system. Such an analogy is supported by the finding that DNA can be transformed into a cell to modify the original species and is based on his seminal work where the chemically synthesized *Mycoplasma mycoides* genome (which serves as the software) was transplanted into *Mycoplasma capricolum* cells. The resulting cells were phenotypically identical to the *M. mycoides* donor strain, indicating that the phenotype of a single cell is dictated by the software of another cell. This work underscores the sufficiency of genomic DNA and demonstrates that phenotype is wholly specified by the genome.

Venter's talk also focused on "biological teleportation" and "digital-biological conversion" − sending DNA as digital information and converting it back into biology for use in rapid vaccine production. The endeavors currently underway by Venter and his team will likely have a dramatic and lasting impact on human health in the near future.

Representing another excellent talk focused on synthetic biology and human health, Martin Fussenegger (ETH Zürich) showcased how synthetic biology approaches can serve as a powerful tool to treat human disease and demonstrated how drug- and gene-based therapies can be combined to treat metabolic disorders, such as the metabolic syndrome. The metabolic syndrome is a combination of disorders and risk factors including hypertension, hyperglycemia, obesity and dyslipidemia that show a little-understood interdependent pathophysiology.[1] Fussenegger described how the licensed antihypertensive drug guanabenz was triggering a synthetic signaling cascade that controlled expression of insulin- and satiety-stimulating peptide hormones which attenuated all symptoms in a mouse model of the metabolic syndrome.

Tim Gardner (Amyris Inc.) delivered a unique perspective on synthetic biology by recounting his journey from academic research to industrial biotechnology. Summarizing years of strain optimization in a plot of historical data, Gardner illustrated a dramatic hinge point at which research productivity nearly doubles.[2] What key biological insight could account for this? Not biology per se, but rather biological practice: reduce error bars! Gardner described how eliminating failures of quality allowed incremental improvements to rise above measurement noise. The message was well-received and

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Table 1. Invited Speakers and Organizing Committee at the First Annual Winter q-bio Meeting[a]

Invited Speakers	
Jim Collins	Biomedical Engineering, Boston University
Mary Dunlop	Engineering and Mathematical Sciences, The University of Vermont
Johan Elf	Molecular Biotechnology, Uppsala University
Michael Elowitz	Biology, Bioengineering, Applied Physics, California Institute of Technology
Timothy Elston	Pharmacology, UNC Chapel Hill School of Medicine
James E. Ferrell	Biochemistry, Chemical and Systems Biology, Stanford University
Martin Fussenegger	Biotechnology and Bioengineering, ETH Zurich
Timothy Gardner	Amyris
Leon Glass	Physiology, McGill University
Terry Hwa	Physics, University of California, San Diego
Roy Kishony	Systems Biology, Harvard Medical School
Galit Lahav	Systems Biology, Harvard Medical School
Andre Levchenko	Biomedical Engineering, Johns Hopkins University
Wendell Lim	Cellular and Molecular Pharmacology, Biochemistry and Biophysics, University of California, San Francisco
Mariko Okada	Laboratory for Cellular Systems Modeling, RIKEN RCAI
Bernhard Palsson	Bioengineering, University of California, San Diego
Kit Pogliano	Biological Sciences, University of California, San Diego
Gurol Suel	Biological Sciences, University of California, San Diego
Chao Tang	Theoretical Biology, Peking University
John Tyson	Biological Sciences, Virginia Tech
J. Craig Venter	The J. Craig Venter Institute
Chris Voigt	Bioengineering, Massachusetts Institute of Technology
Ruth Williams	Mathematics, University of California, San Diego
Ned S. Wingreen	Molecular Biology, Princeton University
Organizing Committee	
Bill Ditto	Physics, University of Hawaii, Manoa
Jeff Hasty	Biology, Bioengineering, and BioCircuits Institite, University of California, San Diego
William Hlavacek	Biology, University of New Mexico and Theoretical Biology and Biophysics, Los Alamos National Laboratory
Alex Hoffmann	Biochemistry, University of California, San Diego
Brian Munsky	Center for Nonlinear Studies, Los Alamos National Laboratory
Lev Tsimring	BioCircuits Institute, University of California, San Diego

[a]The full list of invited speakers, contributed talks, and poster presentations is available on the website (w-qbio.org).

concluded to applause with a quotation by Sydney Brenner, "Data should obey the CAP principle: it should be complete, it should be accurate, and it should be permanent. Otherwise there is no progress."[3]

Other highlights of the synthetic biology-driven talks included work by Mary Dunlop (University of Vermont) on feedback control for microbial biofuel production and another by Wendell Lim (UCSF) on dissecting and engineering cell signaling networks. Poster awards were also given to Lukasz Bugaj (UC Berkeley) for his work on optogenetic control of protein clustering and Anupama Thubagere (Caltech) for her work on spatial localization of chemical reactions in DNA origami.

In addition to the synthetic biology focus, other talks centered upon systems biology approaches. Galit Lahav's (Harvard Medical School) talk, titled "Dynamics Matter", was aptly renamed to, "Of course Dynamics Matter" and focused on p53 dynamics in response to various forms of stresses. Sophisticated single cell studies examined the behavior of cells over time, after applying diverse forms of stresses, to uncover how cells transfer information through dynamics. She revealed that UV- and γ-irradiation prompted different dynamic behaviors and gave way to graded or digital-like p53 responses, respectively.[4] Further work revealed that p53 dynamics control cell fate, whereby a sustained p53 response forced cells into senescence, and a pulsing p53 response rendered cells that are capable of dividing and growing normally.[5] In the future, this work will be applied more broadly to understand the molecular mechanisms utilized at the cellular level to decode p53 dynamics.

Also related to understanding dynamic behaviors, Michael Elowitz (Caltech) described the single-cell gene expression dynamics of B. subtilis involved in sporulation. To precisely time a sporulation event several generations ahead, the cell must solve what Elowitz terms the water bucket problem, a task akin to filling a hole-filled bucket smoothly to the brim. The complication lies in the fact that the dilution rate depends on the concentration of the timer molecule, meaning that choosing a fixed production rate would require the cell to anticipate its growth conditions several generations in advance. His elegantly described solution involves a polyphasic positive feedback strategy analogous to infrequent compounding in finance: each cell cycle, add a pulse of timer molecule proportional to the current concentration.[6]

Roy Kishony (Harvard Medical School) opened with a simple yet confounding (and tongue-tying) question for antimicrobial medicine: how do we kill bugs with drugs without creating bug−drug resistance? To tackle this problem, Kishony led us on an exciting journey of microbial evolution in what he calls evolutionary medicine. Devices such as his OMG (Observatory of Microbial Growth) produced beautiful spatial evolutionary lineages in response to increasing antibiotic concentrations. In clinical experiments, he tracked the path of a human outbreak by analyzing mutations over time, a form of

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molecular "clock".[7] Kishony proposed an exciting and unexpected solution to the bug−drug problem: suppressive (anti-synergy) drug combinations that disfavor the development of resistance to any individual drug.[8]

In an exciting double feature on the cell cycle, John Tyson (Virginia Tech) described early theoretical work that predicted how checkpoints might operate as bistable switches. Importantly, this motif yields irreversible progression that ensures that the cell cycle only proceeds in one direction.[9] These predictions have prompted many experimental studies on bistability in cell-cycle checkpoints and continue to be validated in ongoing work.[10] James Ferrell (Stanford) explored questions of spatial and temporal synchronization during early cell division in frog embryos. How can this incredibly large egg divide synchronously in under 10 min when diffusive signal propagation would take 2 h? Using in vitro cell cycling by egg extracts, he devised an elegant experimental method to measure division signal propagation. We all watched as green foci formed and vanished along the axis of a long tube, undergoing what Ferrell described as trigger waves. In essence, while diffusion slows as signal spreads, trigger waves remain fast since each new trigger point replenishes the signal as it switches.

Other highlights of the quantitative biology of natural systems included work by Kit Pogliano (UCSD) on microbial warfare-inspired drug development and Mariko Okada (RIKEN RCAI) on NF-kB immune signaling. Additionally, Bernhard Palsson (UCSD) gave a fascinating talk centered upon genome scale modeling, and touched on how such models could be applied toward synthetic biology. His group is currently applying these models to further understand genotype-phenotype relationships.

The research highlighted here covers only a fraction of the high caliber work presented at the First Annual Winter q-bio Meeting. In addition to the invited speakers, over 50 contributed talks and a lively poster session sustained the high energy level high throughout the conference. The meeting was a forum to share cutting edge research in quantitative biology, with leaders spanning systems and synthetic biology coming together to engage in lively and creative discussions under a single roof. Moving forward, the Winter q-bio Meeting will continue to grow and develop as a venue for the development of academia−industry partnerships and cross-disciplinary collaborations within quantitative biology.

AUTHOR INFORMATION

Corresponding Author

*E-mail: bcstanton@gmail.com.

Author Contributions

Both authors contributed equally.

Notes

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