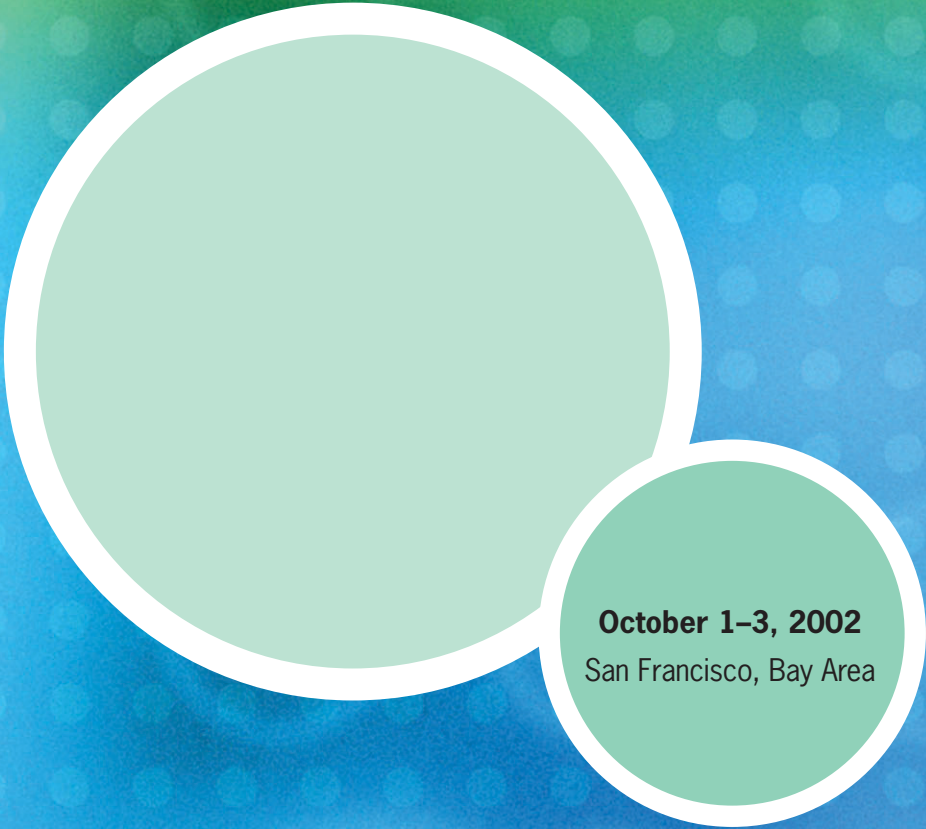


BioFutures by Design

A GBN WorldView Learning Journey

Meeting Report

by Brian Sager



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BioFutures by Design

A GBN WorldView Meeting Report

BioFutures—emerging developments in biotechnology and their convergence with other technologies—has been a learning priority for GBN throughout the past year. This focus reflects our assumption that business executives need to become more familiar with both the science and the technologies underlying this promising industry. As part of our ongoing exploration, BioFutures by Design, A GBN WorldView Meeting, took place in the San Francisco Bay Area, October 1–3, 2002. The participants represented the biotechnology and chemical industries, federal and state governments, and technology companies with products ranging from computers to photographic film.

Such widespread interest in biotechnology is hardly surprising: although the industry is still relatively young, it is evolving and growing rapidly. Whereas most of the activity and attention was initially focused on the “Cure” space (drug development) and the “Comprehend” space (primary research like the human genome project), many of the most exciting developments are occurring in the “Create” space—the intentional design of new products and processes that use biology as an engineering tool. The purpose of this meeting was to provide a behind-the-scenes look at the companies and individuals at the forefront of biotechnology and especially those in the “Create” space that are extending biotechnology’s opportunities far beyond human healthcare. And we also wanted to consider the new legal, ethical, and regulatory challenges that will arise—and influence the rate and shape of innovation—as bioengineering impacts a wider range of industries.

And these challenges are significant: a fundamental lack of biotech knowledge in the business community; a decline in the quality of basic science education; high scientific and financial barriers to entry; a confusing patchwork of regulations—outdated, inconsistent, and in some countries, non-existent; significant economic and policy issues, many of which overlap with deep ethical concerns; and inadequate institutional capacity to engage and resolve such issues. On the other hand, the opportunities afforded by increasing convergence of science and technology are enormous. As we strive to balance the potential risks and rewards of the biofuture, we will also generate a more informed and robust public debate and innovations in business and governance.

BioFutures: An Overview

On the evening of October 1, Meeting Director Brian Sager kicked off the session with a global overview of the biotechnology industry. Brian—a GBN consultant, scientist, and biotech entrepreneur—pointed out that more than 4,000 companies are currently engaged in biotechnology, generating revenues in excess of \$35 billion dollars. While most of these firms are small and privately held, their distribution is rapidly globalizing. Both Europe and North America are home to approximately 1,800 companies, with the U.S. still accounting for the preponderance of industry revenues. Growth is particularly aggressive in Asia, especially Shanghai, due in part to the lack of regulation.

Overall, the business of biotech is increasingly robust, despite volatile market valuations and persistent barriers to entry and success that range from financing to regulation. On the other hand, advances in the underlying science are accelerating and converging at an unprecedented level, creating many opportunities. This is already evident in the large number of experimental drugs being tested. But more importantly, as biology becomes predictive, new theoretical, industrial, environmental, computing, and engineering applications are emerging that cut across—and may eventually transform—established industries.

Perspectives on BioFutures: Round-Table Discussion

A round-table discussion followed featuring Brian Sager; GBN Network member Rob Carlson, a physicist and visiting scholar in the Comparative History of Ideas (CHID) Program, University of Washington; and GBN consultant Steve Weber, professor of political economy at U.C. Berkeley. The initial discussion and subsequent Q&A identified more issues than answers around such topics as barriers to entry, regulation, economic and policy concerns, and prevailing myths.

Entry Barriers to Bioscience

- The cost of doing biological science has fallen, in particular the costs of reagents and instrumentation. That means the cost of making biological products is getting closer to that of growing plants and away from classic industrial manufacturing costs.
- Human ingenuity is randomly distributed. If tools are cheap and widely distributed and many new products and processes are created without regulation, can society tolerate this innovation? Are we capable of adapting to unexpected errors, especially if they impact our global ecology? Many people and institutions operate as passive recipients of biotechnology—is this appropriate? Sustainable?
- What is the source for biological innovation? Who is creating this innovation and why? Is their motivation intellectual (scientists) or financial (companies)? Is their motivation productive and idealistic or destructive and malicious? Is the source of innovation centralized or decentralized?
- Are the capital requirements driven by venture funding models or by entrepreneurs operating on a shoestring?

Bio-Regulation

- Who's regulating when and how a product can come to market? What judgment criteria are used? How rapidly does this adapt to changing conditions? The pace of progress would suggest that it would be difficult to regulate an industrial bio-product until it is too late to do so. How will people make appropriate choices?
- As to FDA regulation, we cannot abdicate our personal responsibility to institutions. FDA approval suggests safety and efficacy for new drugs, but this is far from a guarantee.
- A lack of global authority suggests a lack of regulatory harmony and there will always be islands of rebellion. For example, China is developing a strong biotechnology industry without any regulatory oversight. How will that impact China and the rest of the world?

Economic and Policy Issues

- In terms of a bio-economic structure, where is the rate-limiting step in the system? Who can manipulate the bio-markets? For example, as bio-created products become abundant, do they become more or less valuable?
- Will the venture model survive? The capital required for innovation in certain biological products and processes is less than traditionally anticipated. While our capabilities and cost curves have not yet flattened out, when they do reach this level, what impact will it have on sources of innovation?
- Raw materials, tools, and techniques exist to biologically construct many new things, yet we do not breed or modify humans because, as a society, we do not feel comfortable doing so. But different people may draw different ethical lines—if so, how can we reach appropriate policy decisions?

Myth-Busting

- Science is an art, improvisational and opportunistic. This makes a discussion about ethics almost beside the point: the work will happen anyway, somewhere.
- Even under the best of circumstances, the product development time for new drugs is long, and testing—even FDA approval—is not as rigorous as it should be. There also is a lack of rigorous testing for industrial products, and their development time is far shorter.

Governmental regulation is, at best, a creaking patchwork of haphazard attempts to balance between potential risk and potential promise. Further, scientists are not willing to police themselves.

This lively and wide-ranging discussion set the stage for two Learning Journeys that took place the following day.

Learning Journeys

GBN Learning Journeys are designed to get busy managers and executives out of their offices and into the companies and organizations that are creating the future. In this way, individuals can freely test and challenge their own assumptions through personal experience. On October 2, two different Learning Journeys took participants to a variety of sites around the San Francisco Bay Area. The underlying themes of the day's travels were threefold:

- Empowering Design/The Evolution of Scale: The entrepreneurial path of biotech firms, from start-up to global company, including the role of strategic collaborations, partnerships and alliances, and intellectual property issues.
- The Impact of Design/The Potential of Biotechnologies and the Bio-economy: Will biotech emerge as a discrete sector, or will the wide array of new technologies be a driver of transformation throughout many industries?
- The Nature of Design/The Nature of Knowledge: From the end of the distinction of “human” DNA to the integration of sensory perception and consciousness, what are the ethical and cultural barriers and paths along the way to the full expression of our biological potential?

Summaries of each Learning Journey follow.

Learning Journey 1: Risks and Rewards

Genencor (Palo Alto, CA)

Genencor creates biocatalytic proteins and biomaterials for a wide variety of applications in the healthcare, agriculture, and industrial/consumer markets. Since its founding in 1982, Genencor has grown to become a leading biotechnology company, with more than 250 products, \$325 million in year 2001 revenues, and more than 3,400 owned and licensed patents and applications.

During the visit, Genencor demonstrated the broad potential of biotechnology to contribute to both human therapeutics and to industrial applications in the factory. They provided a detailed overview of their technology platforms and products, which range from industrial applications (laundry detergents) to healthcare applications (dermatology creams. The group was also taken on a well-organized tour of the bio-fermentation facilities (which were very similar to those of a brewery!) This fermentation equipment acts as an ecosystem for microorganism populations—the microorganisms are actually nanoscale factories. One of Genencor's oldest and most successful products is the enzyme that is used in Tide detergent that finds and “eats” the dirt on laundry.

Genencor's early growth was concentrated in industrial applications. Throughout the '90s Genencor acquired core competencies in protein engineering, expression technology, enzyme substrate interaction and partnering. In the industrial sector, Genencor continues to fuel the chemical industry's move into the biochemical arena; specifically, the company is currently extending its core competencies into the difficult problems of malignant melanoma and solid tumors by concentrating on proteins with an innovative delivery system. Specifically, Genencor is developing enzymes capable of finding and treating a tumor; a material is injected that the enzyme then transitions to a toxic substance at the tumor's surface. The result is an efficient, efficacious treatment system.

At the conclusion of our visit we asked our Genencor hosts to describe the biofuture they envision. In addition to cures for many common diseases and immunotherapeutics, they mentioned silicon biotechnology, the interface between silicon and the biological world. Silicon acts to stabilize an enzyme; retrofitting these materials with biosensors provides the potential to monitor an entire enzyme interaction.

Stanford Law School (Stanford, CA)

At Stanford, the group met with Professor Henry Greely to discuss his views on the legal framework for current and potential biotechnology applications. Professor Greely is co-director of the Stanford Program in Genomics, Ethics and Society; director of the Stanford Program in Law, Science and Technology; and a member of Stanford's Bio-X Leadership Council. He has taught at the law school since 1985 and is considered one of the nation's leading experts on legal and ethical issues associated with biotechnology. A graduate of Yale Law School, Greely clerked for the U.S. Court of Appeals (5th Circuit) and for Justice Potter Stewart of the U.S. Supreme Court, worked at the Departments of Defense and Energy, and for the Los Angeles firm of Tuttle & Taylor.

According to Professor Greely's conservative viewpoint, the current legal framework is sufficient to deal with the biotechnology industry, even as it continues to grow and evolve. He started the conversation by stating that the things we worry about won't happen and the things we don't worry about will in fact be the challenges. He identified insurance discrimination as one of the challenges for society in this biotech era. Although many of us are aware of the potential rise of healthcare discrimination and a "biologic" divide, the implications for individual employees are not being widely discussed. For example, Professor Greely described what may happen when an employee is identified as having a genetic deficiency that may make a portion of his or her work duties high risk. Although an employer cannot legally ban the individual from the work, the employer can make the employee sign an agreement that waives all rights to sue the employer if they choose to continue the high-risk activity.

Rolltronics (Menlo Park, CA)

Rolltronics Corporation, a Silicon Valley technology company, is developing roll-to-roll (R2R) manufacturing processes for the production of electronic devices with dramatically lower costs and improved product features: thin, light, flexible, durable, affordable, faster to prototype and faster to market. R2R processing employs techniques such as those used for printing newspapers, coating food packaging, or making photographic film, and allows manufacturers to obtain more output with less expensive equipment, while simultaneously saving on materials, energy, and labor costs.

At Rolltronics, the group met with founder and CEO Michael Sauvante who provided an overview of the company, its products, and its strategic direction. The company is focused on components for ultra-high-density memory, ultra-light batteries, and integrated circuits on thin plastic films. Integrated circuit applications include RFID tags, biometric sensors, digital x-ray detector plates, and flat panel and flexible displays, including organic LEDs and electronic paper. Future R&D will incorporate new device technologies such as plastic electronics and nanoelectronics. Increasingly, Rolltronics' main focus will be on technology development through the pilot manufacturing stage and specialty (relatively low-volume) production. Such high-volume production of mature products will typically involve joint ventures or licensing with partners, who will incorporate these components into consumer products or other devices for which they have marketing, sales, and delivery channels.

Sauvante also described the entrepreneurial beginnings of Rolltronics. Many in the industry fear that the current infrastructure will break down as new technologies lead to completely different manufacturing platforms. Rolltronics challenges that view; it is an interesting example of an entrepreneurial organization that is doing cutting-edge work with an old technology (R2R) and infrastructure. At the same time, Rolltronics is reinventing itself for the biosensor era. Although many of the developments at Rolltronics

are in early stages, the Learning Journey group was able to imagine applications of embedded biosensors inside a polymer substrate for use in a treatment delivery system or diagnostic.

Alta BioPharma (San Francisco, CA)

Alta BioPharma was formed to invest primarily in private later-stage life sciences companies with novel products and technologies capable of capturing large new markets. It invests in product and platform biopharmaceutical companies as well as medical technology companies. It typically acts as lead investor, seeding companies with \$8–\$12 million over the course of its involvement. Alta BioPharma ranks fifth highest in venture capital biotech investments (\$204 million in the past 90 days).

The group met with Dan Janney, one of the firm's lead partners. He gave an overview of the fund and described its philosophy and approach to venture investments in biotechnology and life-science related companies. The group was struck by the firm's traditional approach to biotechnology, as well as the formal, very conservative environment in which this approach is practiced.

Janney described what Alta BioPharma looks for in potential investment targets: an innovative technology or science, an entrepreneurial spark, a strong management team, good scientists, and finally market potential. The GBN group assumed that either the technology or science would be considered most important, and was surprised to hear a more traditional "business school" answer: the management team matters most.

The Learning Journey group asked Janney why the biotech era isn't growing more rapidly. He responded that the FDA has forced moderate growth. Although regulation is a constraint, once a product is approved, the FDA becomes your "best friend." Most frustrating, however, is the disconnect between the FDA's lack of knowledge about the new biotech era and the challenges faced by regulatory bodies with each new product. This was a fitting point on which to end our visit in preparation for a conversation with the EPA.

Environmental Protection Agency, #9 Agricultural Initiative (San Francisco, CA)

At our final site, the Environmental Protection Agency, the group met with officials who monitor biotechnology uses in agriculture. These six people, who represented different functions within the agency, were very open to sharing and discussing the challenges associated with regulation in the biotech era.

The EPA was established during the Nixon administration in response to a river fire outside Cleveland. Its original charter was to protect human health and the environment and many of the statutes still in play today were developed at that time as a means of codifying the "public will." The EPA's focus turned to hazardous waste in the 1980s and the agency continues to study the risk-benefit balance of man-made impacts on the environment. From its inception, however, the organization has been inherently reactive and it is struggling to become proactive and effective in the age of genetically modified species.

Even so, the GBN group reached the consensus that the EPA is both understaffed and underprepared for the biofuture. The EPA is not having strategic conversations with the right constituents, and outdated systems and processes from the insecticide/herbicide era are still being used to assess the risk of biotechnology in agricultural contexts. Further, since information ages quickly, there is a significant disconnect between the EPA's knowledge of biotechnology and the cutting-edge R&D work underway.

As we enter a world of new species, society is also struggling with what is "good" and "bad." One of the questions the EPA posed to our group was: Is it bad to introduce new species to an ecosystem? Suddenly

an ecosystem becomes a zoo. Where and how do we draw the lines? And what role can and should the EPA play in that debate?

Learning Journey 2: From the Quantum to the Koran

Hyseq Pharmaceuticals, Inc. (Sunnyvale, CA)

Hyseq Pharmaceuticals is engaged in research and development of novel biopharmaceutical products from its collection of proprietary genes discovered using its high-throughput screening-by-hybridization platform. Hyseq's screening-by-hybridization platform provides a significant advantage in discovering novel, rarely expressed genes, and assembly of one of the most important proprietary databases of full-length human gene sequences. Hyseq is expanding and accelerating its research activities to further elucidate the role of novel genes in its proprietary database. Hyseq's database includes genes which encode a number of therapeutically important classes of molecules, including chemokines, growth factors, stem cell factors, interferons, integrins, proteases, hormones, receptors, and other potential protein therapeutics or drug targets.

At Hyseq, the group met with CEO Ted Love. Love's long and distinguished research career has included running research and development efforts at Genentech, the first biotechnology company. Love spent much of the meeting discussing several innovative deal structures with which Hyseq has been able to advance its strategic objectives. After stating that his job as a CEO was to "providing a return to the shareholders," he elaborated on his approach to the company's business. For example, to settle litigation with Affymetrix, one of its competitors, Hyseq formed two joint ventures with Affymetrix, Callida (90 percent owned by Hyseq, 10 percent of Affymetrix), and Nmer (held within Callida). Love also described three research and development collaborations with Deltagen, Kirin, and Amgen. Deltagen (Menlo Park, CA) is focused on "knocking out" specific genes in the mouse genome and looking for structural or functional changes in genetically engineered mice. Kirin Pharmaceuticals (Japan) is seeking to identify certain developmentally regulated genes that may be potential drug targets. Amgen is developing a thrombolytic (blood clot dissolving) drug, and Hyseq will be paying for the clinical trial costs associated with testing this drug in return for 50 percent ownership of sales revenues.

Love noted that, unlike the headlines in recent press, the number of genes in the human genome was far from certain, with the true number ranging from 40,000 to 60,000, depending upon the definition of a gene. Love added that Hyseq has 10,000 patents to DNA sequences of unknown function that may be genes or fragments of genes, and thus "controls" 15–25 percent of the human genome. Love's continuous references to intellectual property rights emphasized for the group the critical and controversial nature of gene patenting."

Islamic Cultural Center of Northern California (Oakland, CA)

The Learning Journey participants next met with Dr. Hamid Mavani, the religious director of the Islamic Cultural Center, to discuss Islam's views on biotechnology. He explained that Islam has not separated science from religion and that these areas are still bound together by ethics. Further, biotechnology is not new to Islamic literature, in that Islamic religious scholars have for some time been grappling with medical advances ranging from in vitro fertilization (IVF) to organ transplantation. To guide the use of biotechnology and other medical technologies by those of the Islamic faith, religious leaders and Islamic jurists employ the Koran to deal with new issues.

Islam considers the Koran to be the literal and timeless word of God, and looks to Islamic jurists for rulings on how particular issues should be viewed. Many biological advances in medicine can be of benefit to Muslims. Dr. Mavani has published *A Guide to Islamic Medical Ethics* which surveys common rulings pertaining to a range of issues, including euthanasia (prohibited), transplantation (permitted), abortion (generally prohibited, save for medical emergencies), blood transfusions (permitted), and scientific experimentation (permitted unless experimentation leads to harm).

When the Koran does not speak to a particular issue, the next most important framework is the “doctrine of the best public interest.” In particular, the Islamic faith holds that followers should avoid hurting themselves or others and that “everything in religion should be easy,” meaning that faithfully adherence to doctrine should be pragmatic and not burdensome.

One of the interesting questions raised by this visit: Will religious institutions have more influence on biotechnology innovation than government regulators?

Molecular Sciences Institute (Berkeley, CA)

The Molecular Sciences Institute is dedicated to the advancement of basic biological research in a multidisciplinary academic environment. The Institute believes that the key challenge for biological sciences this decade will be to accumulate, organize, rigorously analyze, and evaluate the complex data that will result from genome sequencing. It is committed to developing technologies to accumulate higher-value types of data than those coming from conventional genomics; generate intellectual, mathematical, and computational frameworks to aid our thinking about complex biological processes; and synthesize data and frameworks to allow us to make testable predictions about the behaviors of living systems. The goal of the institute is to weave the scientific disciplines of physics, engineering, computer science, and mathematics as integral components with biology, genetics, and chemistry in this new “post-genomic” biological paradigm.

The Institute’s research focus is on the “Alpha Project,” the development of an accurate computer simulation and the quantitative modeling of a complex biological process. The subject of the Alpha Project is the mating, pheromone-induced, shape-change pathway found in yeast. In this “pheromone response,” single, genetically haploid yeast cells of one of two potential mating types (a- and alpha-) exchange chemical pheromones that induce them to change their shape and grow towards one another, after which they fuse into a diploid cell. At a molecular level, more than 20 discrete proteins and genes are involved in the pheromone signal transduction and shape change pathway, so this process is relatively complex. Accordingly, many biological and biochemical variables are being incorporated into the simulation, including the concentration and rate of diffusion of each mating pheromone, the binding constants of the pheromones to different proteins, the binding constants of different proteins with one another, the diffusion rates of specific proteins within the cells, and the formation of any of a variety of complexes of multiple proteins at different times.

The computer modeling is not based upon differential equations, but rather, stochastic, random elements. The major source of variability in the biological response is the position of each haploid cell in its respective cell cycle when it is exposed to pheromones from the other cell (each cell is on an independent “clock”).

Computer models are checked against experimental data for accuracy. In particular, genes involved in the pheromone response are tagged with fluorescent proteins, so their level of genetic expression can be correlated to the light levels arising from each cell, as viewed by fluorescence microscopy. The institute estimates it will take five years to create the next level of accuracy in the pheromone response computer model, and hopes that the resulting model can be applied across multiple different biological pathways, ushering in a new era of quantitative biology.

U.C. Berkeley Chemistry Lab (Berkeley, CA)

During our visit here, Dr. Mark Kubinec surveyed the range of paradigms for computing. He first spoke about silicon chip-based computing, which provides a simple binary system in which logical states are represented by ones (“on”) and zeros (“off”) that are physically manifested as differential voltage levels in a silicon device.

He then discussed DNA-based computers, which are an example of a topological/spatial-computing paradigm. This paradigm is best applied to the “NP”-complete class of problems (e.g., the classic “traveling salesperson” problem, in which a salesperson tries to optimize her path through a set of cities, visiting each only once). These types of NP-complete problems become exponentially more difficult to solve as the number of potential elements in the answers linearly increases. For a 100-city problem there are so many possible combinations in the answer set, a modern silicon-based supercomputer would require a great deal of time to reach a solution. The inherent parallelism of DNA computers allows this problem to be chemically solved in a test tube within the span of an afternoon.

With DNA computers, specific pieces of DNA sequences are assigned unique meanings (e.g., AGGTCCA = San Diego). Each DNA sequence would represent one city, and the DNA sequences are then mixed together in solution. The key to fast computation is the literal mixing of all possible answers, in molecular form, in the test tube. After mixing, the DNA fragments are ligated (glued) together, and amplified (using “polymerase chain reaction”) to form a randomly generated set of all possible answers. The amplified strands are then physically separated (filtered) according to their total DNA sequence length to purify only the set of answers representing a specific length (e.g., all solutions for exactly 12 cities means the fragments should be 12 “city units” long). These DNA strands are then chemically analyzed to determine the ordering of their sequence, which is used to map out the order of the cities represented by each DNA fragment. While powerful, DNA computing is only useful for a certain class of computational problems, which can leverage the inherent high parallelism of chemical reactions comprised of molecular interactions.

Dr. Kubinec concluded with an overview of quantum computing. Similar to silicon-based computers, quantum computers rely on a binary system of ones and zeros. Different from silicon-based computers, quantum computers represent these ones and zeros not by voltage levels but by differential energy states in the nuclei of specific atoms. Two specific logical gates can be formed in this manner, satisfying the theoretical requirement for an effective computing system. Quantum computers rely on the superimposition principle, in which a quantum entity can be in two states simultaneously (e.g., “spin up” and “spin down”), until measured. Since superimposition spans all possible quantum states in the nucleus of an atom, one can make one query for the answer to a specific question, since all the possible answers to that question are present all at once. Using quantum computers, computational problems that would take a million years for a silicon-based supercomputer to solve can be answered in one week. The reason is that in a silicon-based computer, “n” states imply $n/2$ operations are required for an answer. In a quantum computer, only the square root of n divided by two operations are required for an answer.

These computers are at an early stage of development: Dr. Kubinec built the first two-bit quantum computer two years ago, and the best quantum computer to date is only a five-bit system. This is because each bit is represented by a discrete and uniquely identifiable atom in a single molecule, and most atoms in a molecule cannot be uniquely identified. So the bottleneck in quantum computing is the creation of molecules whose atoms are all uniquely identifiable.

SurroMed (Mountain View, CA)

SurroMed is building a technology-based therapeutics company whose distinctive competence is biomarker-enabled drug discovery and development. It is applying proprietary technologies for biomarker discovery in clinical research studies to better understand drug mechanisms in action, discover root causes

of disease, and discern the molecular basis of patient-to-patient variations in disease presentation, progression, and response to treatment. SurroMed currently has 70 employees, \$73 million in private equity funding, and sufficient cash reserves to survive for two years at its current burn rate. The company recently shut down its Singapore facility and transferred all those employees to the Singapore Research Institute.

The company's CFO and legal counsel gave an overview of its business strategy and operations. SurroMed is developing a capability for biomarker-enabled drug development, where these biomarkers serve as surrogate markers for gauging the effects of particular medicines. Biomarkers range from simple metabolites in the blood, such as carbohydrates, steroids, lipids, and blood glucose levels, to more complex proteins such as insulin, to organelles such as the CD4 cells used to gauge immune system function, to the clinical history of patients (blood pressure, temperature, weight levels, feelings of wellness).

SurroMed is integrating the data, each at different levels of biological organization, into a central database, where bioanalysis can be performed *in silico*, that is, through data mining and pattern analyses. For example, the company is using microfluidics and microvolume laser-scanning cytometry to perform differential proteomics and physiomics (also called "metabolomics") on a variety of tissues from specific patients. This approach allows the rapid profiling of thousand of biomolecules per sample with high throughput. In this manner, the physiological responses of specific patients to a drug can be rapidly assessed, and the patients classified into categories like "strong responder," "average responder," or "non-responder." This will help guide and accelerate clinical testing plans for drug development.

SurroMed has also formed Nanoplex Technologies, a spin-out company. Nanoplex currently has 11 employees and is located inside SurroMed. The company focuses on both biological and non-biological applications of its "nanobarcode" technology, where nanoparticles can be synthesized with discrete and unique identifier tags. For biological applications, these nanoparticles can be used to tag small biological molecules during analysis of patient tissue and in fluid sampling. For non-biological applications, these nanoparticles can be used to tag parts for inventory management, and to ensure the authenticity of paper currency and clothing by use of an anti-counterfeit, nanoparticle reader system. For example, the company is currently in discussions with Levi Strauss to partner in embedding denim pants with nanoparticles. This is a very clear example of convergence between biotechnology, nanotechnology, and the textile industry.

Burning Questions

Enroute back to Trader Vic's for dinner the Learning Journey groups pondered a number of burning questions posed by the day's experience. Would the benefits of biotech outweigh the risks? Will we be one species or many, as physicist Freeman Dyson ask? Why is there such a disconnect between the real science and theory? Some voiced disappointment on how far we seem to be from harnessing biotech to have a significant impact on helping humanity. And we wondered who needs to have the relevant conversation on achieving adaptive governance structures. We imagined governance by network!

Insights and Implications

On the final morning both Learning Journey groups came together for a round-table discussion on their experiences and insights during the learning journeys. Denise Caruso, journalist and founder of Hybrid Vigor (<http://hybridvigor.org>), a non-profit institute dedicated to stimulating unconventional, interdisciplinary, and systemic thinking about a broad range of social and scientific problems, joined the plenary group and shared insights on the balance between risk and promise for the biotechnology industry. Each participant was also asked to share his or her deepest concerns and hopes for our collective biofuture. Highlights from this discussion are summarized below:

Deepest Concerns for Our Biofutures

Environmental

- Unanticipated, positive feedback between biotechnology products and the environment could lead to ecological disruption, from which we may not be able to recover.
- We may be tinkering with biological systems we do not truly understand, and so we may have unforeseen consequences.
- Accidental disasters at these outer edges are far more dangerous than common human errors.

Public Health

- Biotechnology advances may impede or even eliminate the privacy of individual patients as they seek treatment.
- Government institutions either need to lead or get out of the way. If we cannot do research in the U.S., it will go overseas where the work may be unregulated.

Social

- A lack of understanding and fear of biotechnology may stand in the way of useful advancement; this is amplified by a lack of communication from the sources of innovation.
- If biotechnology companies overpromise and underdeliver, they may lose the opportunity to positively impact both society and the framework in which they are perceived. This is especially true regarding fair and equal access to medical advances.
- People who are not informed about biotechnology will not be able to enrich the conversation about its uses, potential, and appropriate regulation; this includes government institutions as well as the executive, legislative, and judicial branches of government. Since the technical knowledge gap is high, especially for certain regulatory authorities, it is hard to have a meaningful dialog about governance.
- We are ineffective at dealing with the long-term issues associated with biotechnology (e.g., an attention span greater than one election cycle). We are good at being first, but not at considering the long view.
- Certain religious groups may impede the development of potentially useful technologies such as stem cells and GMOs for food. Most religious and ethical groups in fact are polarizing the issues rather than engaging in respectful dialog.

Deepest Hopes for Our Biofutures

Environmental

- Sustaining a high population on the earth via minimally invasive, ecologically sound green products and processes.
- Biotechnology can create a set of tools for sustained development, including waste management and cheap, distributed energy.

Public Health

- Biotechnology products may help to prevent human disease; humans have an innate ability to adapt, and to improvise around obstacles, and this capability will help us best use biotechnology in an effective and helpful manner.
- There may be a re-definition of what it means to be human, which is an incredible possibility,
- There may be a democratization process for health care, in which individuals will gain control over their health with new levels of depth and understanding

Social

- Human beings need to listen to each other; fundamentalism must be avoided in discussions of the use and progress of biotechnology
- Many participants were happy to see relatively slower progress in biotechnology than they had anticipated: this may provide enough time to deal with emerging issues and effectively grapple with them.

The meeting concluded with a small-group brainstorming session, followed by a large-group discussion, focused on the ways in which biotechnology might impact the broader economy as well as specific industries. The four principal themes explored during this session are summarized below:

Exploring the Impact of Convergent Biotechnology

In what unexpected ways can biofutures impact non-healthcare-related industries?

- Lower cost, lower energy manufacturing processes
- Biotechnology-based waste management tools
- Distributed, renewable manufacturing infrastructure

What are the greatest risks of biofutures to non-healthcare related industries?

- Quality control issues—how can one precisely control inherently complex biological production?
- Variable manufacturing yields, especially batch variability issues
- Product liability risks, including those influenced by potential consumer backlash

What are the greatest rewards of biofutures for non-healthcare related industries?

- Greater ranges of specifically designed, low-cost biomaterials-based products and components
- Flexibility in the location and structure of manufacturing
- Green production processes that minimize pollutants and reduce waste in the air, water, and soil

How might non-healthcare-related industries prepare to take advantage of these opportunities and manage the associated risks?

- Strategic alliances and product development collaborations between companies that have a deep understanding of a specific vertical market and a biotechnology company that can provide a new source of innovation in that market
- Joint ventures between biotechnology companies and more tradition industrial partners
- Widespread corporate participation in both evolving standards boards for particular products and in formulating regulation and public policy surrounding the use of specific biologically derived manufacturing processes and industrial products.

Balancing Risk and Benefit

In what ways can biofutures influence risk assessment and management?

- A new, developing ability to manage and deal with deep uncertainty—this will trickle into other areas of science and technology.
- The personal nature of risk and benefit makes these issues more visceral and intimate

What are the greatest risks of ignoring these risks?

- Biological catastrophes
- Economic catastrophes
- “Poisoning of the well” for rational progress, as the social contract and the public trust may be betrayed
- Social disruption, “bioanarchy”

What are the greatest rewards of resolving these issues?

- Smooth progress via informed decisions
- Enabling dialog that has a positive, rippling effect in society—providing greater understanding to more people
- Participation in active discussion will lead to shared acceptance of the consequences, including the double-edged nature of risk and benefit

Evolving Governance

In what unexpected ways can biofutures influence governance?

- A shift towards individualized decision-making and control, especially through decentralization and/or cooperation through non-government organizations
- Alternative regulatory agencies such as patient and consumer advocacy groups as well as the evolution of existing agencies
- Re-examination and redefinition of ethical issues and frameworks incorporated into the formulation of public policy and decision-making

What are the greatest risks of biofutures to governance?

- Distribution of biotechnology in a flawed healthcare system, in which there is unbalanced control of the distribution channels
- Genetic discrimination
- Epidemics and other unexpected bio-disasters that impact society and shape government policy in unanticipated ways (e.g., a “new, more infectious form of HIV transferred through casual, non-sexual contact”)

What are the greatest rewards of biofutures to governance?

- A smarter focus on risk rather than on artificial, black-and-white ethics
- More investment in biotechnology will lead to a greater public benefit, especially through a lowering of the healthcare cost burden, so more resources can be allocated to other areas
- A healthcare-focused culture, in which public health is a central agenda item, leading to a more humanitarian focus for governments worldwide

Concluding Remarks: The Big Challenges Ahead

As the meeting concluded, the participants discussed in plenary how our global society might best prepare for the opportunities of our biofuture and manage the associated risks. Two principle approaches emerged.

First, we need to encourage a national dialog on scenarios around biotechnology to raise public awareness and promote education at both the scientific and public policy levels. The current level of literacy is simply not adequate to meet the challenges ahead. Second, we need to create a set of new, adaptive governance structures, both within governments and within companies to address the full range of business, regulatory, and ethical issues that will certain arise and interact.

Ultimately, such a proactive and inclusive stance to our biofuture may better able us to balance and address the risks and effectively take advantage of the tremendous opportunities for both businesses and society.

