Science Policy

Bioscience moving more towards asking what is going on in the cell?

Cells are autonomic systems that can repair and defend themselves – they function as automatic decision making systems.

Analogy is that a living cell looks like a complex city and we need to study the networks in systems biology which are really chemical information processing.

We have a convergence between bioscience, informatics and nanotechnology.

We see engineering and biology becoming unified and this presents challenges to develop models or even have theories to postulate and validate.

Synthetic biology is still a gleam in the eye of some scientists and others believe that it may rapidly advance.

The panelists each briefly discussed what their part of the world is focusing on with respect to investments in bioscience and related policy.

Australia moved science into industry and renamed it innovation science. They are focusing on biotechnology in the community, the economy and the world markets with four broad research arenas: proteomics, genomics, metabolomics and informatics.

The USA still has the competitive research fund and is focusing on the organism, cellular and sub-cellular levels and their interface.

The goal is to double the budget for the American Competitiveness program by 2016 in science and energy.

More accountability is required by government funding when giving dollars for research.

Agricultural biotechnology is underfunded.

The European Union is made up of 27 members with 8 associate states.

Their research policy is part of an agency that has a 7 year funding plan and consists of 53 Billion Euros.

It is centrally run but in addition all the individual countries have their own research funds.

They focus on agriculture and food, health and nanobiotechnology. Animal welfare is becoming an issue also.

With respect to metrology, a new program is being launched where the individual states will be putting in 250 Million Euros and the EU will match that Euro amount to do measurements on environmental and health issues.

They have a number of technology platforms such as plants, food, sustainable chemistry and a public-private partnership in medicine funded at the 2 Billion Euro level with half coming from industry in the hopes of finding new therapeutics.

There is a Euro Genetic Test that deals with references for human genetic testing.

Brazil spoke about having confidence in measurement.

When working with biological materials, what can be measured?

How do you assess what you have as a standard?

Is more different?

They have a special directorate for bioscience that covers micromolecular structure, biofuels and microorganisms that can hydrolyze sugars.

Standard references are needed, in all areas.

However, the openness of metrology may become a problem due to intellectual property concerns and the competitiveness of commercialization.

NMI Directors Roundtable

Each NMI Director gave a brief summary of the history of their institution and what they are currently working on in the area of bioscience.

All shared with us the funding levels for their measurement technology and standards research and in all cases, it is low given the mission of the NMI institutions and all that they are responsible for within bioscience.

New measurements of units are needed in bioscience but first we have to ask and decide what we need to measure and develop standards for in bioscience.

The USA's operation, NIST sits at the cross roads of all research and technology and has $10 M dollars annually to do standards and measurement technology research in the biosciences.

Canada operates a bit different with 20 institutes instead of just one just as NIST in the USA.

They are part of the NRC with 4,500 employees and an annual budget of 400 M dollars.

There is a national bioproducts program that focuses on chemical commodities and ethanol production.

Biofuels from marine algae, biomaterials and even bio-waste are being studied.

The EU has seven institutes and they are focused on building confidence in the measurement and standards as part of risk management.

They are promoting networking and reuniting resources to meet the ever growing challenges within biotechnology.

The United Kingdom does measurements and standards in human health, food safety, global climate change, environment and alternative fuels.

They are investing 10B pounds into university innovation and skills with an emphasis on synthetic biology and bioinformatics.

Korea expressed that they used the NIST model to set up KRISS in 1975 and are also working in many areas of biotechnology.

They too have expanded from phsyics and chemistry to include biology.

The Netherlands reported that research in biophysics is growing.

Their annual budget is $8 M dollars and they have 5000 employees.
They also receive $5 M from private industry.

They want to explore collaboration in areas of breath analysis and biofuels.

Plenary Session

Medicine – Lee Hood

There are a whole series of networks that make an organism work and the boundaries between networks and machines are fuzzy.
Biological networks process information.

There are two types of biological information – one is digital present in the genome and the second is how the environmental information impinges upon and modifies the digital information.

Dr. Hood is focusing on designing drugs that take the disease and make it well behaved.

System medicine believes that disease arises from diseased perturbed networks.

He is using biology to drive technology and computation. There is a need to create a cross discipline culture.

Measurements need to be global, quantitative and for all types of biological information.

He is using organ specific blood biomarkers to diagnose disease early and tract the stratification and progression.

He can also assess the use of drugs on an individual and assess toxicity, dose level response and wellness assessment.

The disease can be detected before clinical symptoms appear.

Therefore not only is systems medicine predictive of a disease but it can determine how to treat the disease based on network data.

Technical assistance to systems medicine over the next 10 years include:

High through put DNA sequencing
Discovery and validation of blood organ specific diagnostics by mass spectrometry.
Microfluidic protein chips
Single cell analysis
In vivo and in vitro molecular imaging to assess disease distribution and follow on therapy.

P4 Medicine
Predictive – probabilistic health history based on DNA sequence.
Personalized –deal with patients who are ______control
Preventative – need computation to develop database
Participatory – physician will be the integrator for the patient

There will be a digitalization of medicine in the next 10 years by analyzing single molecules, single cells and single individuals.

Healthcare costs will be reduced – cheaper medicine

Systems medicine will transform productivity and keep people active into their 90's.

P4 medicine will transform the health care industry.

Fundamentally new ideas need new organizational structures.

If you are going to invent the future then you need to set up strategic partnerships.

Lee Hood has set up three such partnerships by partnering to develop a P4 medical institute, bringing systems medicine to Georgetown University and with a country, Luxembourg.

Role of NIST is to validate and provide standards for organ specific blood proteins and measure biological complexity and correlate it with phenotypes.

This needs to be done on individuals and not on populations.

The challenge is protein capture.

Energy – Anna Palmisano

Anna presented an overview of the DOE alternative fuels program which focuses mainly on enzymatic fermentation of cellulosic feedstocks.

They are mainly looking at ethanol, diesel, hydrogen and co-products from fermentation.

The nation needs to have a regional and diverse feedstocks for bioenery production to achieve the 1 Billion tons by 2030 vision.

There are many challenges at all levels of production including the fact that lignin is recalcitrant and cellulose is mixed with hemicelluloses and ligin.

Right now the process is multi-stepped and cumbersome.

It is the DOE goal to have an integrated process instead of all the individual steps currently being utilized to produce ethanol from cellulosic materials.

She briefly described the Genomes to Life (GTL) Program which focuses on sub cellular, cellular and ecosystems.

There are 3 GTL Bioenergy Centers: one at LBNL, one at ORNL and one at Michigan-Wisconsin (Great Lakes).

All are focusing on overcoming the barriers in making ethanol production more effective and efficient such as how to overcome the recalcitrant property of lignin, finding a fundamental transformational process and sustainability of biofuels production from an agroeconomic orientation.

The challenges exist of finding ways to better understand plant cell walls; redesign plant cell walls to make biomass more amendable to bioprocessing; increasing the biomass yield significantly in an environmentally friendly way; and developing plant systems that require less water.

Recommendations for NIST:

Need the next generation DNA sequencing for complex grasses.
Need high through put genotyping.
Need innovative solutions for data management
Need improved biochemistry and thermochemical conversion to scale up demonstration.
There is a need for standards and benchmarks across the range of biomass to fuels.

There is also a need for improved analytical methods and sampling.

All this work has a socio-economic dynamic to it. We can optimize crops for local environments to estimate practical real world yield valuation.

New feedstocks are needed that won't compete with crops currently being utilized for food and fiber.

Stephen Weisburg – Environment

It is a difficult and cumbersome task to identify species in marine coastal waters by traditional methods.

A genetic bar coding method that could build a reference library would lower the current cost and probably increase the accuracy of the species identification.

Also needed are microarrays or low cost enzymatic assays that would tell which organisms are sensitive to which chemicals.

Invasive species identification, such as those organisms that are present in ballast water, is also needed at the genetic level to assess the potential threat of unwanted or pathogenic organisms.

Currently genomics are used in aquaculture and algal production of biofuels.

Aquaculture is in its infancy and currently it is being explored to reduce the pressures of overfishing in the oceans. However, contamination of natural stocks is a concern.

With respect to fish as food for human consumption, so much is imported from other countries and we do not have tests or assays in place to distinguish between fish fry and sushi grade fish or even to authenticate that the fish species is what you are really paying for and not some imitation. Seafood safety is another major area where rapid reliable diagnostics are needed.

Algae as biofuel is a good alternative since it is low in sulfur and some strains possess up to 50% of their body weight as pure oil.

However algae make more oil when they grow slow ore are in a starvation mode.

Genetic engineering is needed to improve growth rate of oil containing algae.

Bioremeditation can be used to treat contaminants in situ.

There is a strong relationship between population density and contamination as well as global climate change.

Challenges include: the method of validation, who will determine it and who does it; data interpretation; technology transfer to the user community; and environmental threats or perceived threats such as GMOs.

With respect to the method of validation, are we measuring the correct things? Have we identified the right sequence? Is it consistent across geographical separations? Is it temporally stable? Can we quantify it?

In transferring the technology we need to train the workforce and provide methods that are standardized and that require a certification process to ensure the local workers are properly trained.

Currently around 20% of the samples taken and analyzed have interference with PCR technologies.

Inhibition leads to underestimation and health officials won't accept false negatives in a warning system.

NIST's role should be to be a national leader in methods evaluation and methods standardization.

NIST should provide standard reference materials, specimen banking, data libraries and develop research applications.

All of these are similar to the NIST role in chemistry.

We need thresholds for interpreting data.

Discovery is moving faster than the linkage to legislation and regulation.

Manufacturing – James Thomas

Many people in the biotechnology manufacturing field do not know about NIST.

Oncology has the most unmet needs in our field.

Industry has a set of challenges such as more competitiveness, a more challenging reimbursement environment, and a more conservative regulatory environment.

Making biopharmaceutics and manufacturing them is a very complex and expensive system.

WE need effective and efficient production methods in designing the molecule, the process and then manufacturing the molecule.

Monoclonal antibiodies – heterogeneity can be influenced by the manufacturing process.

Challenges are: greater sensitivity, more specificity. Elimination of subjectivity and focus on critical quality attributes.

Trends in use of high end analytical tools are evolving such as the use of MS based analyses to determine the host fingerprint.

It is referred to as top down analysis and also done as a routine analysis for contaminants as well as for host cell protein measurements, molecule fragmentations and protein heterogeneity. The sensitivity of MS has increased dramatically since 2000.

How will bio-therapeutics be manufactured in the future?

There has been some work and some improvements in transgenic plants and animals as well as cell free systems and cell based systems. The best bet is cell based systems but this process is still 15 years out. Cho cells are the preferred current method of production.

There is a need to understand the entire organism's physiology and move towards more flexible manufacturing to get a greater amount of product produced per cell.

Manufacturing plants in the future will have greater flexibility, higher yield processes and better utilization of capital and significant reduction in operational costs.

There are opportunities for measurements and standards in the manufacturing operations such as: productivity, raw materials, product, quality, safety and the production environment – all within the plant.

James feels that we need to move from batch culture to repetitive feed batch or dynamic integrated bioprocessing.

Upstream parameters and monitoring of nutrients, physiological responses, etc. are important in a production scenario. Analytical capabilities such as on line HPLC, NIR MS, CSE, are being used to determine presence of virus, metabolite profiles and product varability.

Downstream purification, especially the amount that can be purified can be another bottleneck.

The industry is moving towards modular manufacturing or plug and play with disposable recyclable equipment and monitors such as pH and temperature probes.

Currently an analyzer designed for monitoring biological warfare threats is being employed in the manufacturing suites.

^{1}H NMR is used for all ingredients except for inorganics.

Potential for manufacturing technology improvements include:

Quick assessment of chemical modifications and their biological relevance

1. Merge characterization, release and online product quality to deliver PAT.
2. Improve measurements associated with creating, and quickly selecting high expressing clones.
3. HT tools for process development and formulation development that functions as scale down models
4. More continuous upstream and downstream processing with associated measurements and controls
5. Standard HTP methods for measuring microbes.
6. Powerful analytical tools and share standards for manufacturing.

Agriculture - Pam Ronald and Raoul Adamchak

Even though we have cheap and abundant food supply we have created negative environmental effects for some species, soil erosion, and run offs into our water supply, as well as harmful impact on human health such as Parkinson’s Disease, prostrate cancer and other diseases.

Twenty percent of the world’s supply of pesticides are utilized by farmers in less developed countries. There are 3 million cases of severe pesticide poisoning and 300,000 deaths annually.

Run off of pesticides and fertilizers get into ground water, aquifers and our streams and rivers.

Eutrophication occurs and eventually algae and sometimes toxic flagellates bloom causing fish kills.

In the USA 2-3 billion tons of soil is lost each year and 60% of the soils end up in water systems.

We can not continue current farming practices if the world population is expected to reach 9.2 billion by 2050.

To engage in sustainable agriculture, use of pesticides, and fertilizers must decrease; crop genetic diversity must increase,; harmful environmental inputs much decrease; soil fertility must increase while soil erosion decreases;and we must provide a healthy condition for farm workers while maintaining economic viability of farming and rural communities.

In addition, we need to protect the native species and reduce energy use in agriculture as well as recyle waste back into the farm practices.

Organic farming can deal with much of these items but it has to be comparable in yield and depends upon the crop being planted and the location or region.

Organic practices and inputs need to be evaluated on a case by case basis to determine if they meet standards for sustainable agriculture.

Organic farming has obstacles such as agricultural policies, research and education and extension practices.

Without additional yield increases, maintaining current per capita food consumption will require a doubling of the world's cropland area by 2050.

Genetic engineering can contribute to sustainable agriculture by providing resistance to pests and diseases as well as tolerance to environmental stress and provide increased nutritional content.

Examples were given of successful eradication of pests by cloning in BT genes to the cotton bollworm. Use of pesticides was decreased dramatically and the farmers yield of cotton increased by 80%.

Another example given was papaya ringspot virus that was destroying the entire crop in Oaha. Scientists cloned into the plant the PRSV coat protein and the crop rebounded. By 2003 90% of all papaya was transgenic.

Rice that was genetically modified to exist and grow in flood regions of Indochina is now used. This sub1 strain yield 1.2 tons per hectare more than conventional varieties and is a life saver for these third world villages.

Golden rice is another example of how increasing the nutritional value of a staple food for so many people has stopped the devastating blindness that occurs among children who are deficient in Vitamin A.

There is however great public concern on the lack of science base information, mistrust of government regulation and suspicion of providers of GE crops.

Need bar coding for genetically modified foods telling the consumer what has been modified.

There has not been one study that shows GE foods are not safe to eat – there is not scientific case for ruling out GE crops.

However each one should be considered on a case by case basis.

Risks are not dramatically different from the conventional hybridization technologies.

Measurement needs should focus on yields, pesticide use, fertilizer run off, soil erosion, farm incomes, monitor species diversity and energy use.