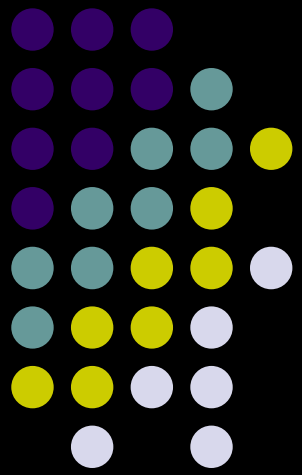
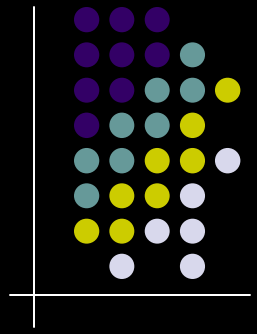
Assessing Biosecurity Concerns Related to Synthetic Biology

Update by the NSABB Working Group on Synthetic Genomics

David Relman, WG Chair



Topics



- Charge to WG
- Roundtable on Synthetic Biology
- Overview of Synthetic Biology
- Working Group Preliminary Findings
- Working Group Preliminary Recommendations

WG Charge

- Identify any biosecurity or dual use concerns that may be associated with synthetic biology and that would not be adequately addressed by the dual use research oversight framework proposed by the NSABB

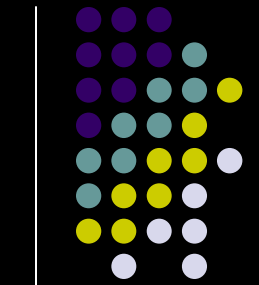
Working Group Members

- David Relman (Chair)
- Susan Ehrlich
- Claire Fraser-Liggett
- John Gordon
- Mike Imperiale
- Adel Mahmoud
- Harvey Rubin
- Tom Shenk
- Ken Cole (DoD)
- Dan Drell (DoE)
- Jose Fernandez (DHHS)
- Maria Giovanni (NIH)
- Wendy Hall (DHS)
- Sue Haseltine (DoI)
- Caird Rexroad (USDA)
- Jenifer Smith (FBI)
- Scott Steele (EOP/OSTP)
- Ron Walters (Intelligence)
- Rob Weyant (CDC)

Roundtable on Synthetic Biology

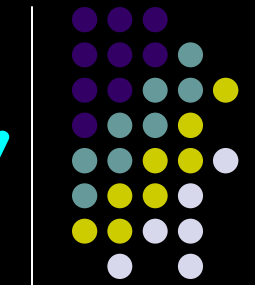
- October 2007
- Hosted by:
  - NSABB WG on Synthetic Genomics
  - NIH RAC Biosafety WG (addressing an NSABB recommendation accepted by USG)
- To explore:
  - State of the science in "synthetic biology"
  - Current capabilities for predicting function
  - Risk assessment and risk management in a context of uncertainty

Roundtable on Synthetic Biology



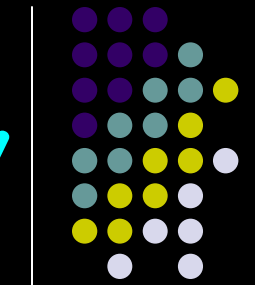
- Session I: State of the Science
- Speakers
  - Roger Brent
    Director and President
    Molecular Sciences Institute, Berkeley, CA
  - Steven Benner
    Distinguished Fellow
    Foundation for Applied Molecular Evolution, Gainesville, FL
  - Ron Weiss
    Professor of Electrical Engineering
    Princeton University
  - Steen Rasmussen
    Team Leader for Self-Organizing Systems
    Los Alamos National Laboratory

Roundtable on Synthetic Biology



- Questions to Speakers
  - How they define "synthetic biology", what makes it unique from other scientific approaches;
  - Goals and experimental approaches in synthetic biology;
  - Current capabilities and applications associated with synthetic biology;
  - How these capabilities go beyond what is achievable using recombinant DNA or other related technologies;
  - Major milestones to date in synthetic biology and the current challenges;
  - Future directions and goals;
  - How close we are to predicting the detailed behavior of a cell based on its component parts;
  - How close we are to designing biological systems and novel organisms with predictable functions; and
  - Whether their synthetic biology research routinely undergoes biosafety review.

Roundtable on Synthetic Biology



- Session II: Predicting Function
- Speakers:
  - Bill Goldman
    Professor of Molecular Microbiology
    Washington U School of Medicine
  - Jim Musser
    Co-Director and Executive VP
    Methodist Hospital Research Institute
  - Marc Kirschner
    Chair, Systems Biology
    Harvard Medical School
  - Owen White
    Director of Bioinformatics, Institute for Genome Sciences
    U Maryland School of Medicine

Roundtable on Synthetic Biology

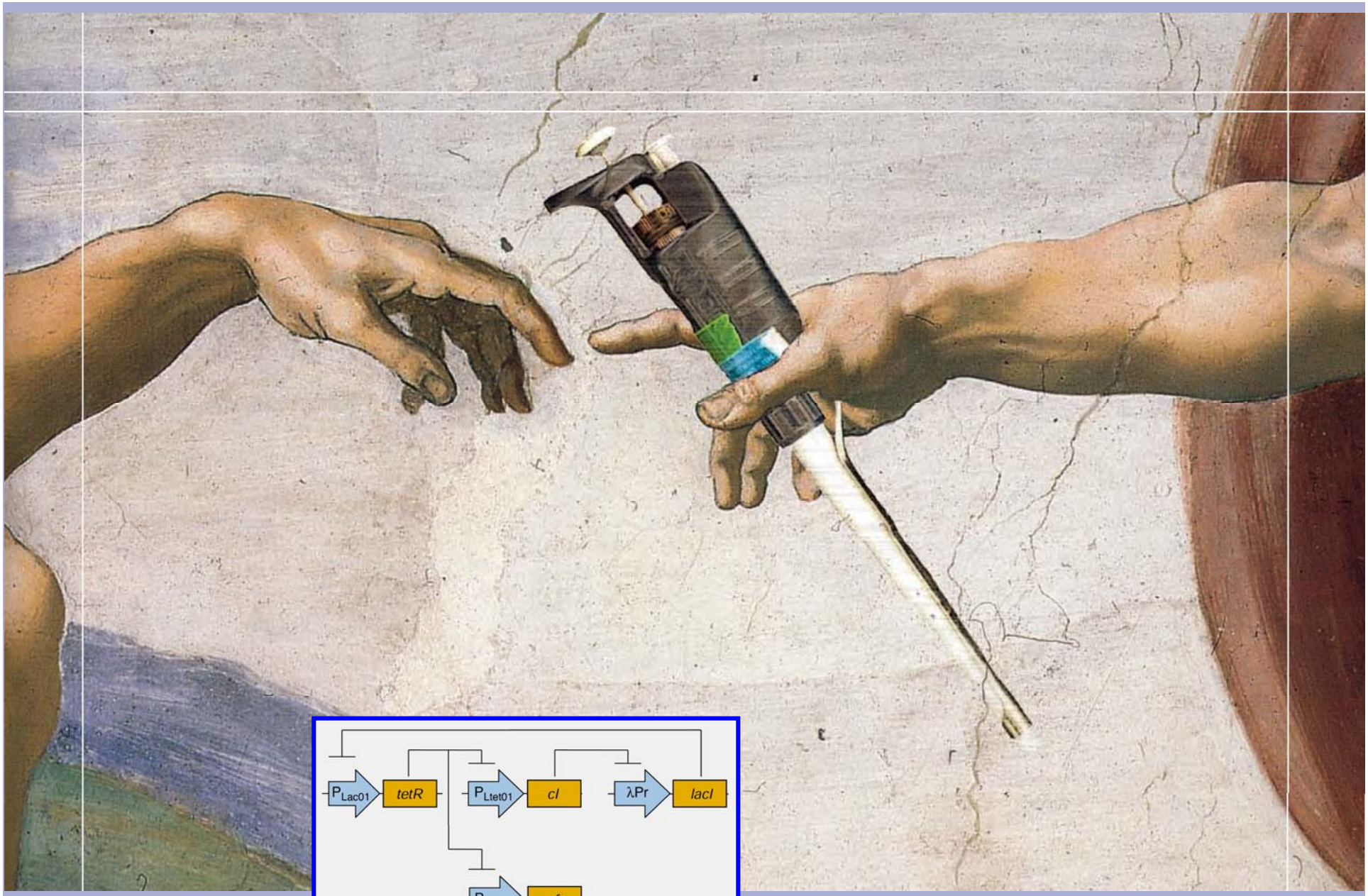
- Questions to Speakers
  - How accurately can virulence or other pathogenic properties be predicted on the basis of sequence alone? Can the predictions be generalized;
  - What kinds of genes/sequences are sufficient for establishing virulence in a heterologous, avirulent organism;
  - What factors determine the evolutionary distance across which virulence might be genetically transferred? Does current understanding of lateral gene transfer help us predict the degree to which virulence can be manipulated or created *de novo;*
  - Major challenges and unmet needs that hinder recognition and prediction of virulence;
  - Considerations for predicting function within systems;
  - What properties of an organism are most successfully predicted from genetic sequence;
  - Degree to which current knowledge allows construction of entirely new organisms with predictable behaviors ;
  - Capabilities, limitations, current uses of tools or approaches for predicting function from sequence.

Roundtable on Synthetic Biology

- Session III: Risk Assessment and Risk Management in a Context of Uncertainty
- Panelists:
  - Rocco Casagrande
    Managing Director
    Gryphon Scientific
  - Larry McCray
    Research Associate, Emerging Technologies
    MIT

Roundtable on Synthetic Biology

- Discussion Questions
  - Are there novel or distinct biosafety risks or challenges associated with "synthetic biology"?
  - To what degree are the biosafety risks of synthetic biology currently being addressed?
  - For recombinant DNA research, the initial risk assessment is based on properties of the parental organism. For the more novel synthetic organisms, a parental organism may not be obvious and/or the biological properties of the new organism may be largely unknown. How to approach risk assessment and management in such cases?
  - Can one engineer biological containment into synthetic systems/organisms (e.g, use of unnatural genetic code or amino acids, self-destruct mechanisms, other safeguards)?
  - Are there any existing risk assessment tools that would be applicable to the biosafety risk assessment process in the context of synthetic biology?



Alan Moses, Berkeley Science Review

From: Elowitz, Leibler; Nature 403:335, 2000

What is Synthetic Biology?

- Life, altered by humans
- Novel functionalities
- Unnatural components
- Natural parts, unnatural assembly
- Artificial systems that mimic properties of natural organisms; allow quantitative predictions of behavior
- Approach: emphasis on design and testing via simulation, before fabrication, design-based biological engineering
- Goal: predictive biological understanding

What is Synthetic Biology?

- Many definitions, uses, stated goals--no clear consensus
- For the purposes of the WG, "Synthetic Biology" refers to the design and construction of novel organisms (viruses, microbes, plants, animals, etc) with predictable properties--with varying degrees of reliance on a master "blueprint" from Nature. It encompasses:
  - Design of novel biological "circuits" and components, and construction of organisms (both free-living and dependent) based on properties of components; as well as
  - Re-design and synthesis of existing, natural organisms for specific purposes

What is Synthetic Biology? Approaches

- Design and synthesis of a new organism with predictable properties using basic functional (genetic) components ("building blocks")…**"Bottom-up approach"**
- Design and/or synthesis starting with an extant organism or blueprint…**"Top-down approach"**
  - "the re-design of existing, natural biological systems for specific purposes" [syntheticbiology.org]
  - Synthetic genomics
- Blends of the two
- Degree to which entire genome is synthetic varies…

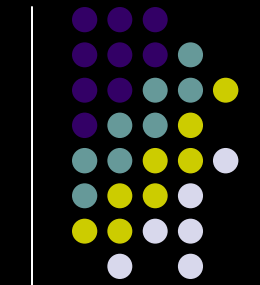
Working Group Deliberations

- What are the biosecurity/DURC risks associated with synthetic biology?
- Are these risks novel as compared to those identified for synthetic genomics or rDNA?
- Are the biosecurity risks adequately addressed by the oversight framework for dual use research recommended by the NSABB or are additional measures necessary?
- If additional biosecurity measures are warranted, what should they be?

Preliminary Observations and Findings

- Multiplicity of definitions, goals, and approaches in synthetic biology
- Recurring theme:
  - There remain significant limitations to our current ability to custom design novel organisms with defined properties, such as pathogens, in a predictable manner, either by *de novo* synthesis or by re-engineering extant organisms

Preliminary Observations and Findings



- The practice of synthetic biology presupposes an ability to predict biological properties from sequence or structure.
- Biological function exists at many levels (genetic sequence, molecular structure, cellular physiology, organ histology). It continues to elude efforts at formal derivation.
- Further work, experimental and theoretical, is needed (and can be expected) for improved predictive capabilities

Preliminary Observations and Findings

- Risk assessment is problematic and difficult, especially for organisms that share few similarities with extant organisms.
- In light of this uncertainty, it is important to conduct synthetic biology research under appropriate biosafety conditions

Preliminary Observations and Findings

- Biosafety risks presented by synthetic biology may not be recognized by all practitioners
  - Despite the term synthetic **biology**, not all practitioners consider that their work is biological in nature. Many think of themselves as **engineers** or **chemists** and so they may not be considering the biological and public health implications of their work.
  - In addition, many practitioners have backgrounds that are not rooted in the life sciences. Consequently, their training may not have included or emphasized principles and practices of biological risk assessment and biocontainment.
- Raising awareness within the disparate scientific communities that engage in synthetic biology about the possible biosafety risks and need for responsible conduct of research is critical. The biosafety outreach and education effort must recognize that the synthetic biology community is not confined to the life sciences.

Preliminary Observations and Findings

- The biosecurity or dual use research risks associated with synthetic biology should be considered on the basis of experimental aim and approach.
  - "Bottom-up" approach, without reliance on an extant organism, is still in its infancy, and does not pose any significant biosecurity or dual use research concerns at the present time that would not be addressed by the proposed oversight system. However, this work is advancing quickly and deserves re-visiting at regular intervals.

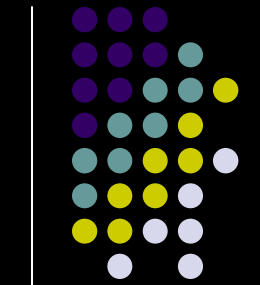
Preliminary Observations and Findings

- The design, construction, and use of new biological parts, devices, and systems ("top-down" approach) is a well-developed and ongoing endeavor. Re-engineering of extant organisms or viruses using methods in molecular biology is well-established. This work may be considered dual use research of concern, but it should also be adequately addressed by the oversight paradigm previously proposed by the NSABB.
- With all of these approaches, the science and technology is evolving quickly. It behooves us to re-visit both the biosecurity and the biosafety issues on a regular basis.

Preliminary Observations and Findings

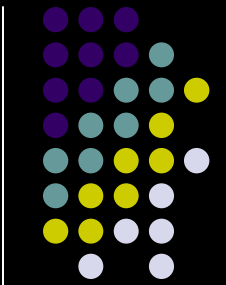
- As synthetic biology techniques become easier and less expensive, the range of practitioners will continue to expand to include not only scientists and engineers, but hobbyists.
- It is unlikely that traditional research/biosafety oversight practices will adequately address the less traditional users.

Preliminary Observations and Findings



- The increasing dissemination of synthetic biology technology creates challenges for education and oversight.
  - Clearly, students at all levels need to be educated about the importance of working safely and responsibly. At the same time, we must be mindful to avoid the unintended effects of stifling opportunities and excitement about science among students.
  - Education efforts and biosafety oversight requirements need to be tailored to the audience.

Preliminary Observations and Findings



- The goals, potential benefits and risks, and current limitations of synthetic biology are not uniformly understood within the scientific community and the general public.
  - More effective and extensive dialogue within and across the disparate scientific communities engaged in synthetic biology would be useful in this regard, especially regarding the need to address biosafety in the conduct of synthetic biology research.
  - More effective outreach to the general public would foster a more realistic understanding of synthetic biology and its goals and current limitations.

Preliminary Recommendations

- The proposed system of oversight for dual use research of concern should be adequate for addressing the potential for deliberate misuse of synthetic biology, at the present time
  - No current need for special biosecurity oversight of synthetic biology

Preliminary Recommendations

- Synthetic biology should be subject to institutional biosafety review and oversight
  - Once the NIH completes the development of biosafety guidance for synthetic biology, the USG should launch a biosafety outreach and education program targeted to the research communities that are most likely to undertake work under the umbrella of synthetic biology
  - Focus should be raising awareness about the potential biological, dual use, and public health implications of their work, as well as the need for considering and addressing any biosafety risks during the conduct of the research

Preliminary Recommendations

- Extend the oversight of dual use research of concern beyond the boundaries of the life sciences
  - Synthetic biology is just one example of an area of science that may pose some dual use concerns and whose practitioners are trained in multiple disparate scientific disciplines
  - Research that is highly relevant to the life sciences or that has implications for public health is currently, and will increasingly, be conducted outside of the life sciences

Preliminary Recommendations

- Oversight of dual use research of concern should be uniform and comprehensive; extend the oversight of dual use research of concern beyond federally funded research
  - Dual use research of concern is as likely to be conducted in the private and voluntary sectors as it is in federal labs and in federally funded labs in academia

Preliminary Recommendations

- USG should include advances in synthetic biology and mechanisms of virulence or pathogenicity, in "tech-watch" or "science-watch" endeavors
  - The USG should convene workshops to assess or re-assess the biosecurity implications of work in synthetic biology and other fields that enhance our ability to engineer new virulence capabilities in organisms. It will be important to assess whether new research avenues and technologies are adequately addressed by the extant biosecurity/dual use research oversight system.