Synthetic Genomics
Options for Governance

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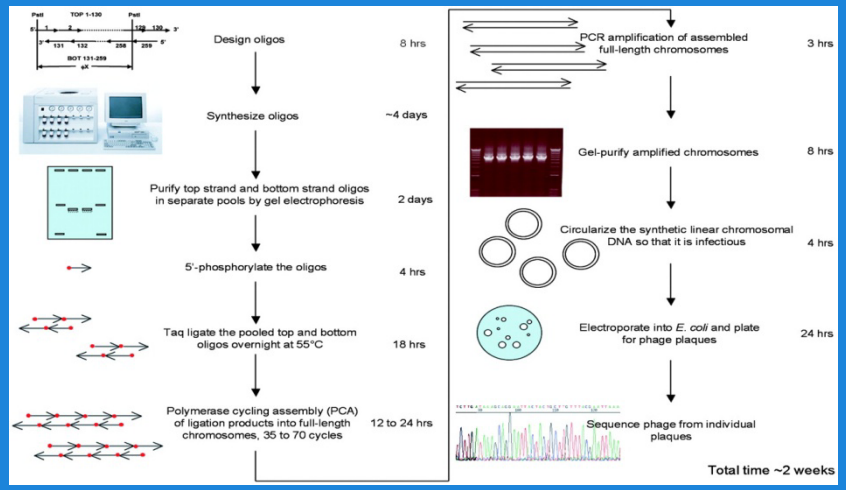
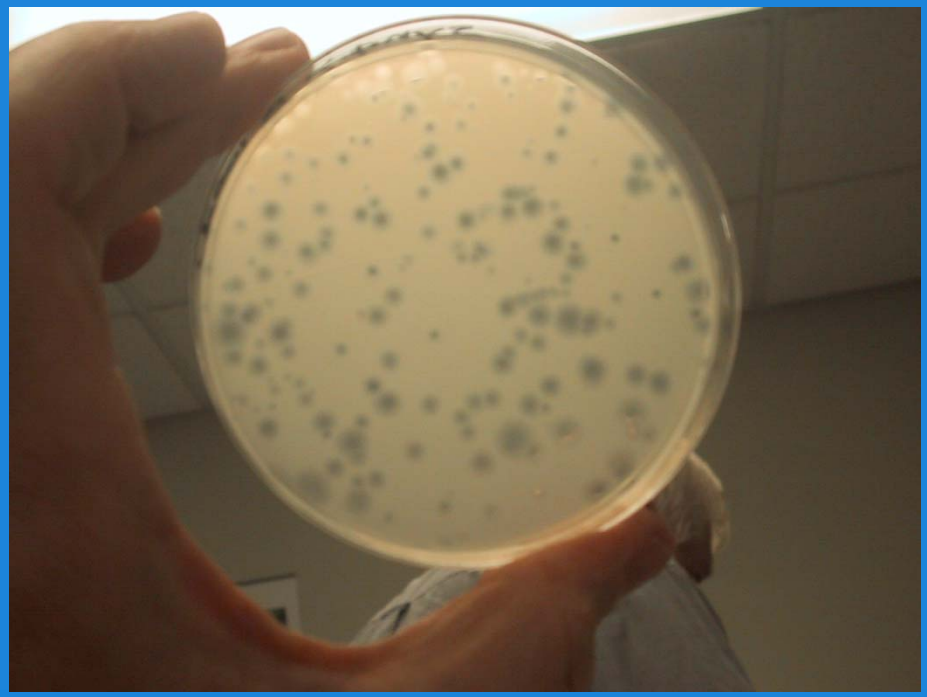
Synthetic genomics at JCVI

- ΦX174 synthesis





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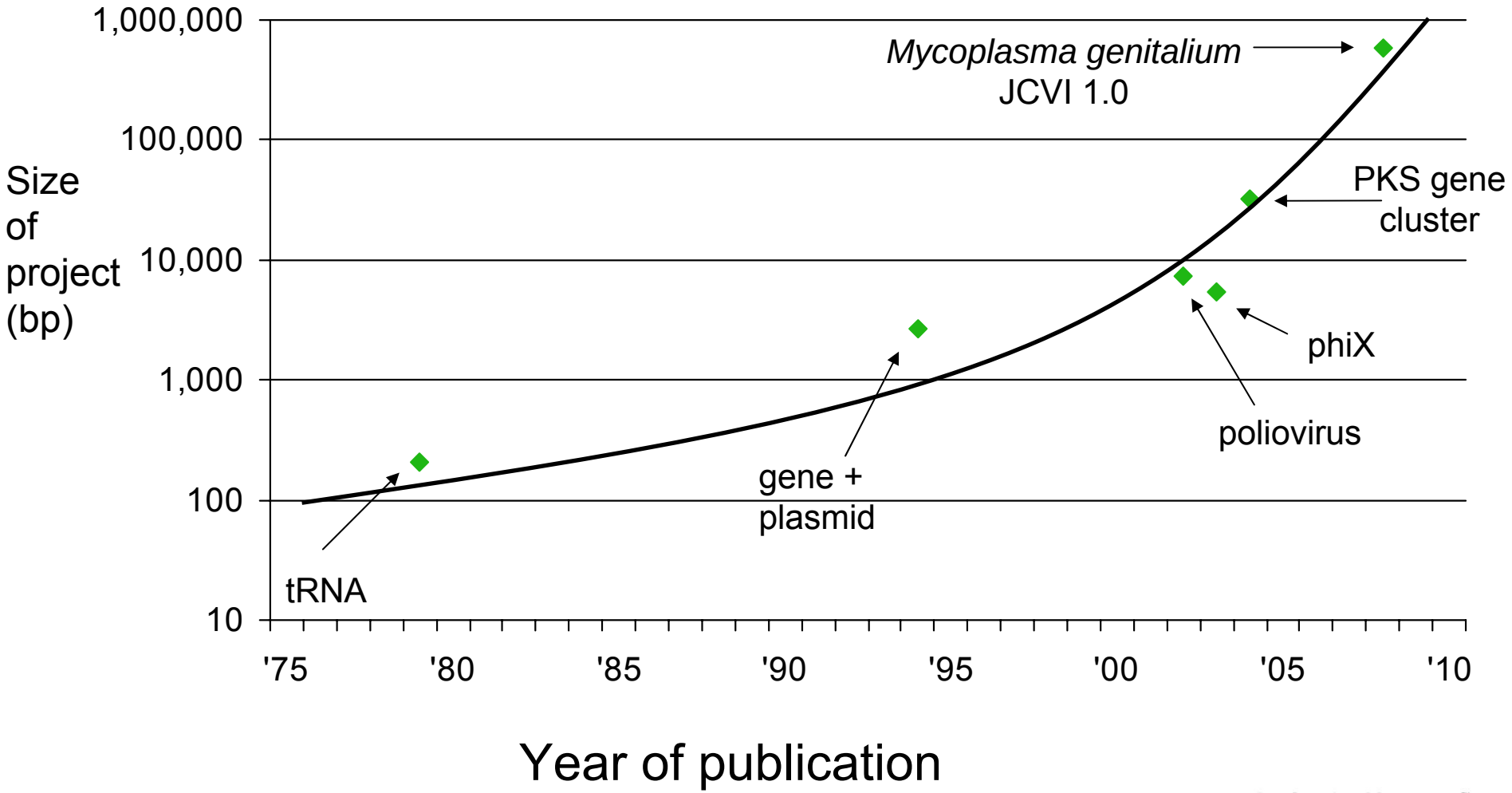
External Events Influence How a Technology is Perceived



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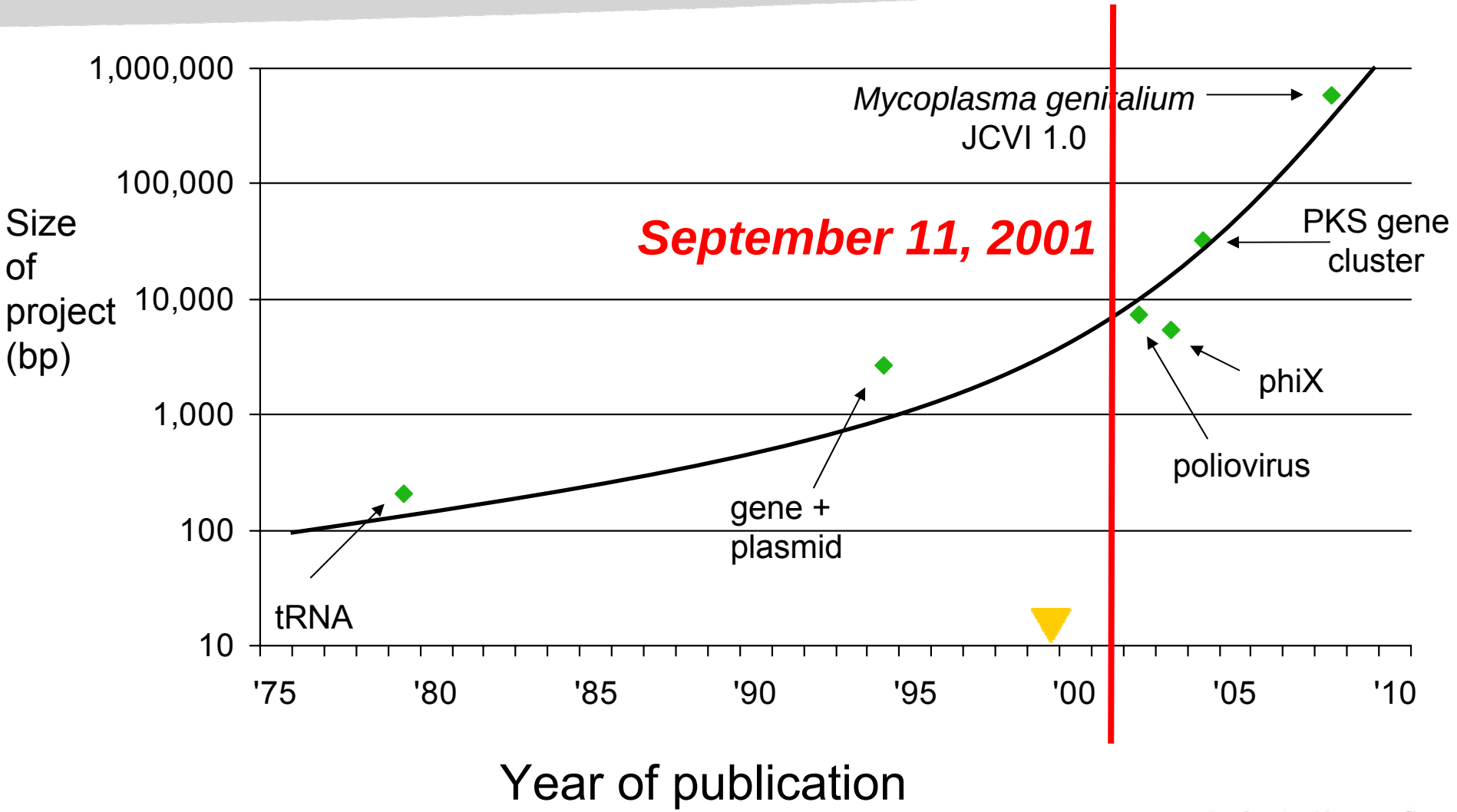

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Governance Concerns Related to Synthetic Genomics

- Along with the promise of benefits, *all* new technologies raise societal concerns
- Five key societal concerns:
  - Bioterrorism
  - Laboratory Safety
  - Harm to the Environment
  - Distribution of Benefits
  - Ethical and Religious Concerns

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Bioterrorism

- Societal concerns
  - New way to obtain pathogens
  - Construction of a pathogen with increased resistance to known treatments or increased virulence
- What is different about synthetic genomics?
  - Can no longer limit access by physical means alone
  - Most pathogens easier to obtain by other means
    - *Except a few viruses*: 1918 influenza, Smallpox, Ebola

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Laboratory Safety

- Societal concerns
  - Concern is for risks to users from specific microbes
    - No concern for harm to users from synthetic DNA itself
- What is different about synthetic genomics?
  - Speed and scale
  - Researchers new to the field

SYNTHETIC GENOMICS | *Options for Governance*

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October 2007

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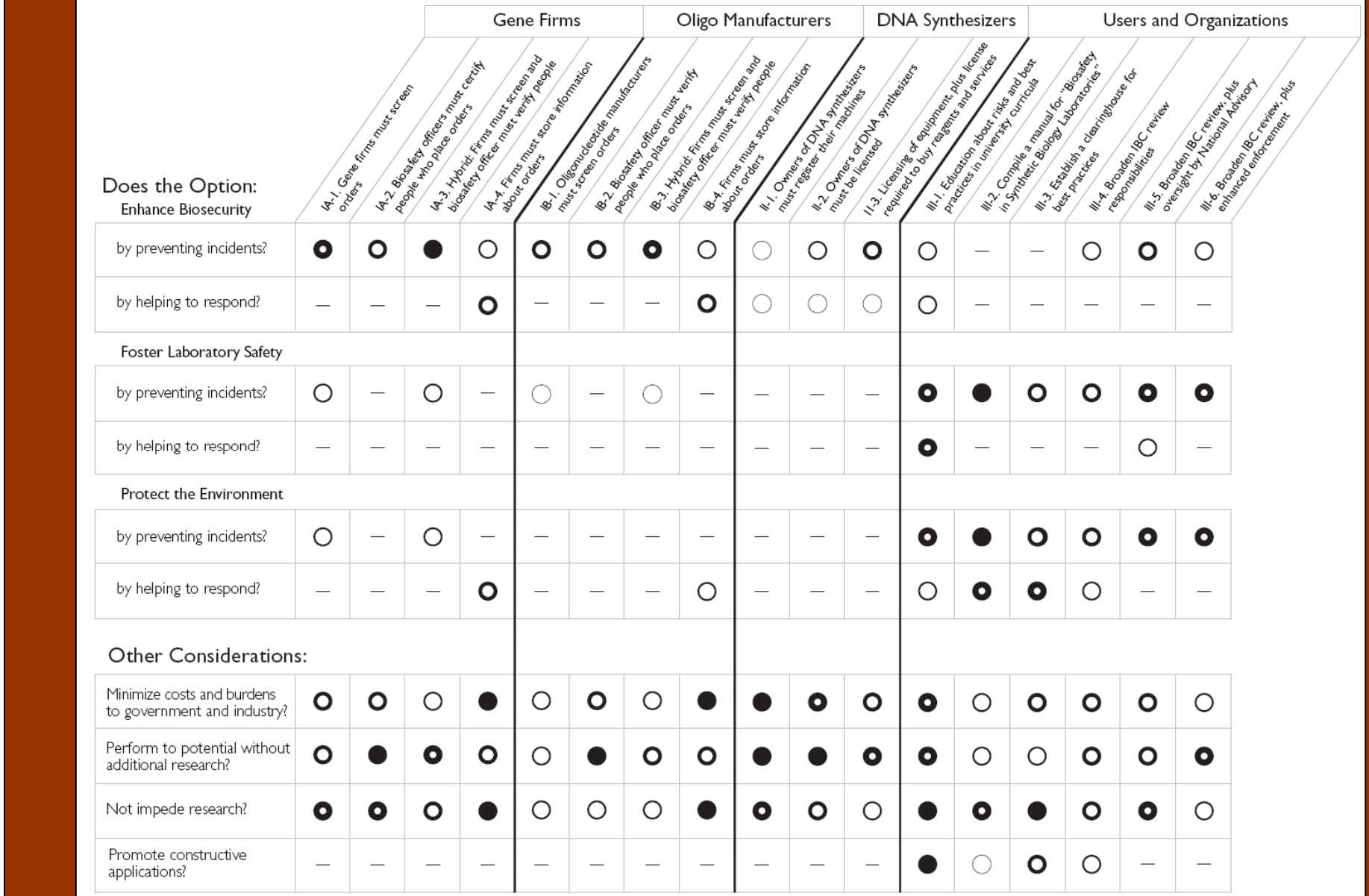
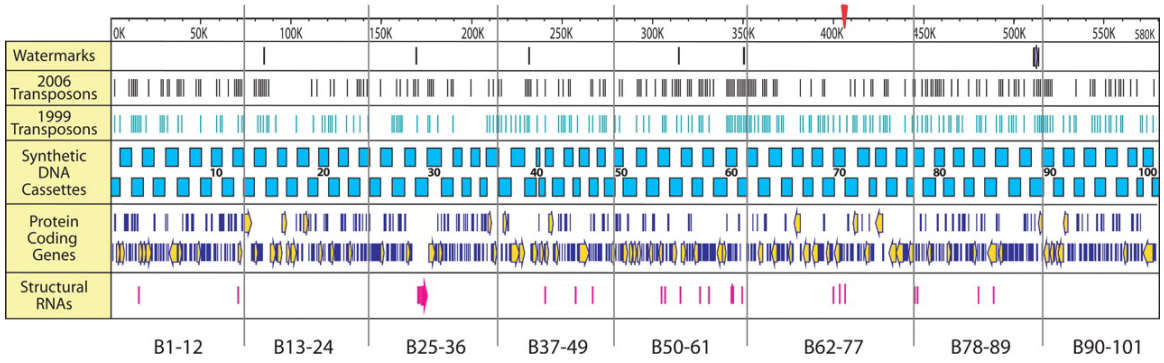
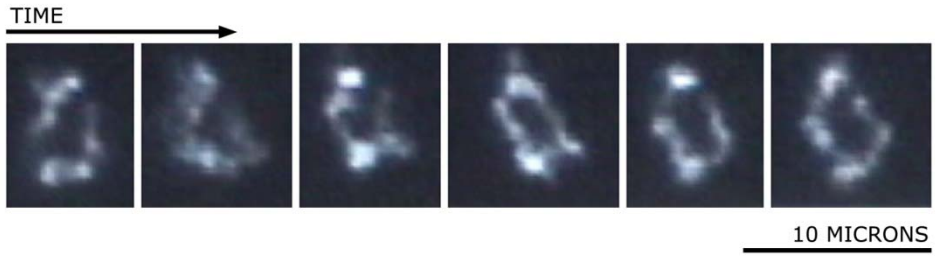

Gene Firms
Oligo Manufacturers
DNA Synthesizers
Users and Organizations
IA-1. Gene firms must screen orders
IA-2. Biosafety officers must certify people who place orders
IA-3. Hybrid: Firms must screen and biosafety officer must verify people
IA-4. Firms must store information about orders
IB-1. Oligonucleotide manufacturers must screen orders
IB-2. Biosafety officer must verify people who place orders
IB-3. Hybrid: Firms must screen and biosafety officer must verify people
IB-4. Firms must store information about orders
II-1. Owners of DNA synthesizers must register their machines
II-2. Owners of DNA synthesizers must be licensed
II-3. Licensing of equipment, plus license required to buy reagents and services
III-1. Education about risks and best practices in university curricula
III-2. Compile a manual for "Biosafety in Synthetic Biology Laboratories"
III-3. Establish a clearinghouse for best practices
III-4. Broaden IBC review responsibilities
III-5. Broaden IBC review, plus oversight by National Advisory
III-6. Broaden IBC review, plus enhanced enforcement
Does the Option:
Enhance Biosecurity
by preventing incidents?
by helping to respond?
Foster Laboratory Safety
by preventing incidents?
by helping to respond?
Protect the Environment
by preventing incidents?
by helping to respond?
Other Considerations:
Minimize costs and burdens to government and industry?
Perform to potential without additional research?
Not impede research?
Promote constructive applications?

A synthetic chromosome





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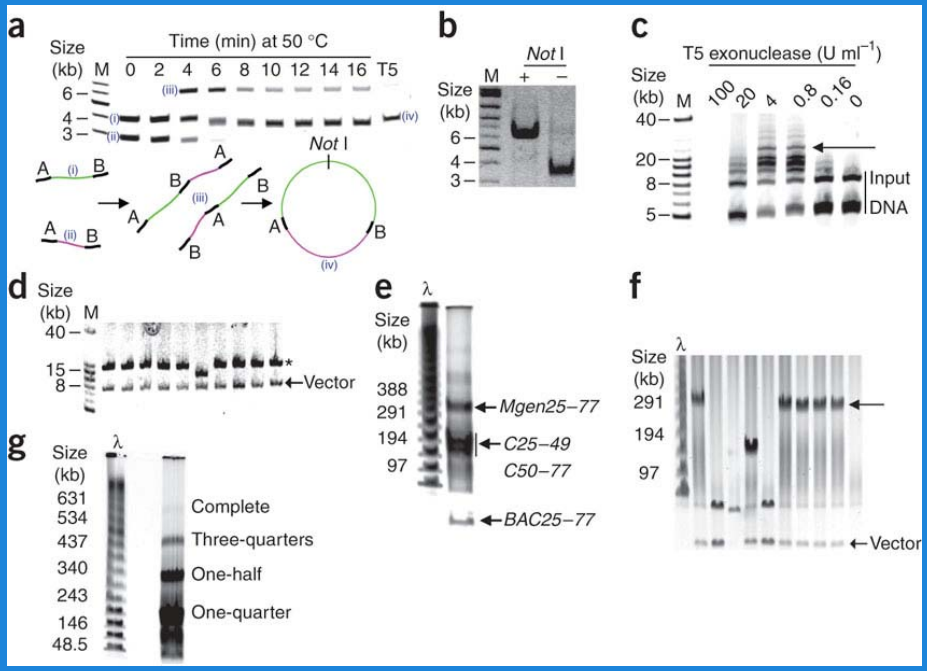
Synthetic genomics at JCVI

- Enzymatic assembly of multi-kilobase molecules



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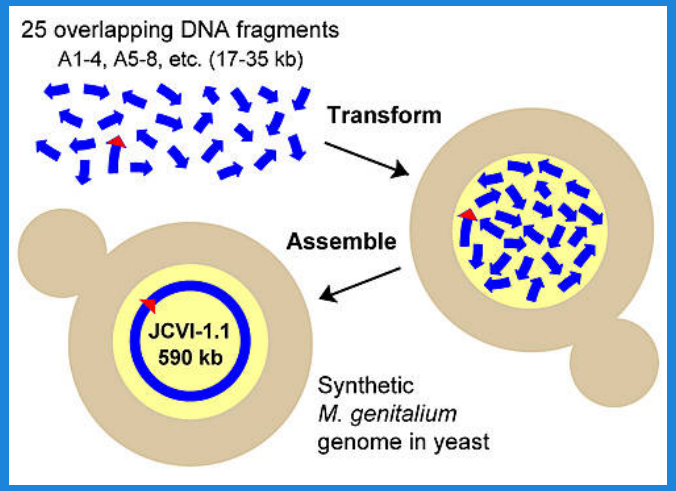
Synthetic genomics at JCVI

- One-step assembly of *M. genitalium* genome



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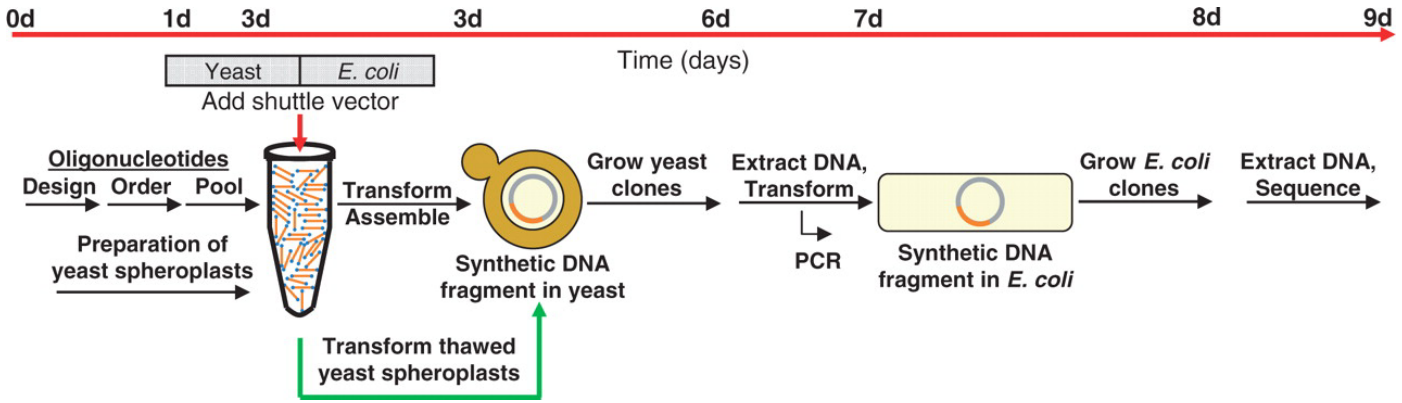
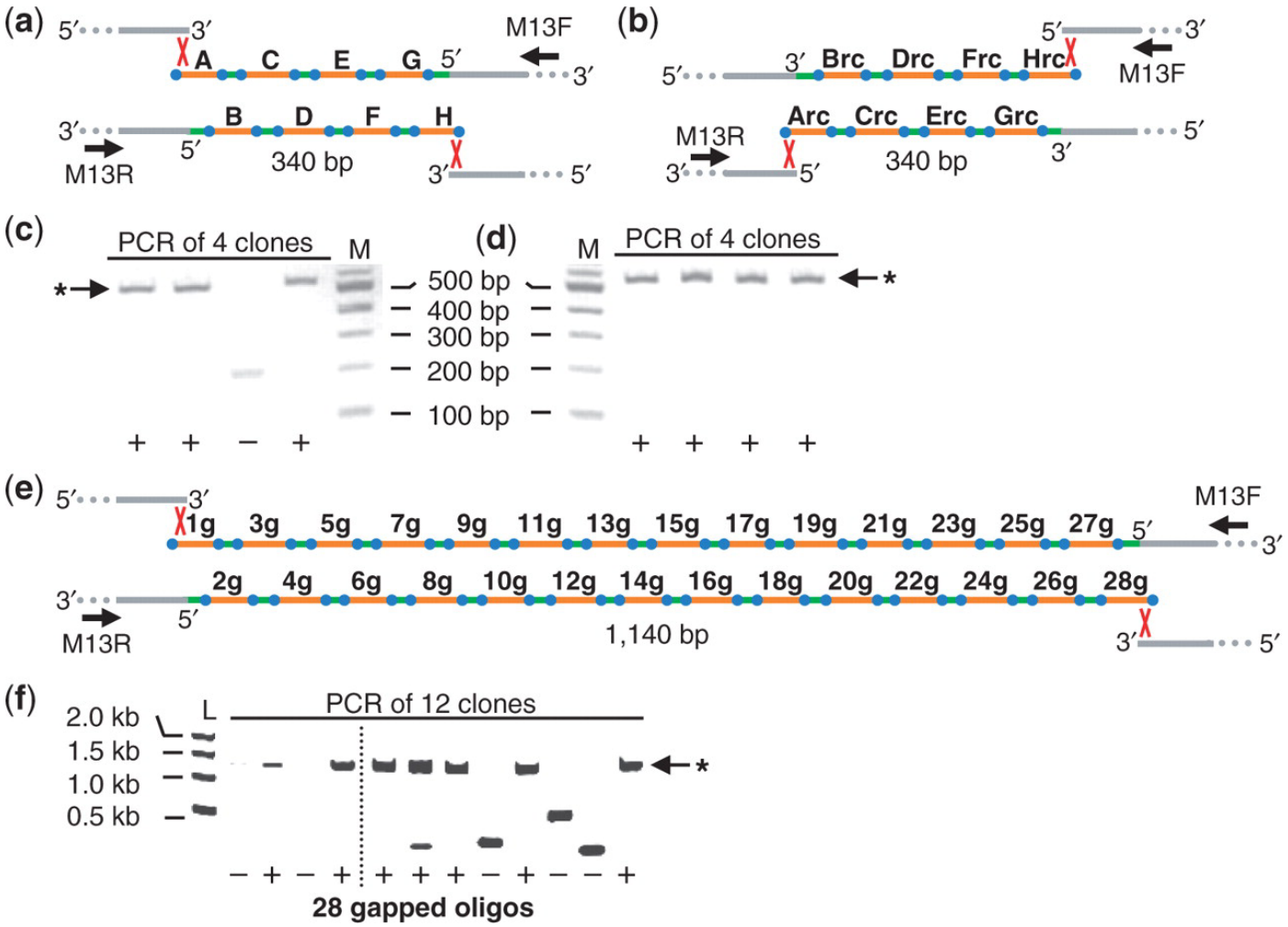
Schematic overview and timeline for the assembly of overlapping ssDNA oligonucleotides (orange lines with blue circles) into a linear dsDNA yeast/E. coli shuttle vector (pRS313; grey) within the nucleus of a yeast cell



Gibson, D. G. Nucl. Acids Res. 2009 37:6984-6990; doi:10.1093/nar/gkp687

Nucleic Acids Research

Twenty base-pair overlaps are sufficient for oligonucleotide assembly in yeast



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Nucleic Acids Research

Societal Concerns Related to Synthetic Genomics

- Five key societal concerns:
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  - Harm to the Environment
  - Distribution of Benefits
  - Ethical and Religious Concerns

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Harm to the Environment

- Societal concerns
  - No concern for harm from synthetic DNA itself
  - Only concern is whether specific engineered organisms pose risks to the environment
  - Part of larger societal debate about rDNA since the mid-1970s (starting with Asilomar)
- What is different about synthetic genomics?
  - Speed, scale, power of the technology

Distribution of Benefits

- Societal concerns
  - Intellectual property concerns
    - Patents, open source
  - “Concentration” within a small number of firms
- What is different about synthetic genomics?
  - Maybe little; raised for every emerging technology
  - However, the synthetic biology community itself is divided on this issue

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Ethical and Religious Concerns

- Societal concerns
  - Hubris (“playing God”)
  - Concerns about changing the relationship of humans to nature
- What is different about synthetic genomics?
  - Construction of a free-living organism from chemicals adds a new concern to the list

Stakeholders

- Citizens
- Consumers
- Businesses
- Scientists
- Policymakers
- Governments
- Do-it-yourself community

And their representative groups

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Regulation and governance of synthetic genomics

- Changes to NIH guidelines?
- Changes to Coordinated Framework?
- Changes to TSCA?
- Changes in patent review (domestic and international)?

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Where we are today…

- The technology is improving and the user base is expanding
- Applications are beginning to appear and many new ones are being developed
- Societal impacts are being scrutinized
- Governance options are being seriously considered…
  - By the research community itself, the developing industry, and by governments

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