

Lessons from Current Technologies: Gene Drives

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**Novel and Exceptional Technology &
Research Advisory Committee (NExTRAC)**

NIH

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Question/Topic 1

Overview of the technology,
including potential applications in
next 5-10 years.

What is a gene drive?

A gene drive is a process of inheritance by which a gene is guaranteed to pass from one generation to the next, and ultimately throughout a population.



EVOLUTION Made to Order

Plant Breeding and Technological Innovation
in Twentieth-Century America

HELEN ANNE CURRY

(2016)

- ❖ Speeding up
evolution
- ❖ Controlling
evolution and
heredity
- ❖ Evolution on
demand
- ❖ Directed
innovation

An overview of genetic technologies

Curry sorts early genetic technologies in America into three periods:

- ❖ X-ray radiation in the 1920s and 1930s
- ❖ Colchicine in the 1930s and 1940s
- ❖ Radioisotopes and other nuclear technologies from 1945 to 1960

An overview of genetic technologies

- ❖ 1965: “Genetic engineering” used in reference to manipulations of viruses and bacteria.
- ❖ mid-1980s: recombinant DNA techniques—the transgenic methods now associated with the notion of genetic engineering—appear.



CRISPR-Cas 9

**Clustered
Regularly
Interspaced
Short
Palindromic
Repeats**

**(Doudna and
Charpentier,
Science 2012)**

(from Harvard Magazine 2016)

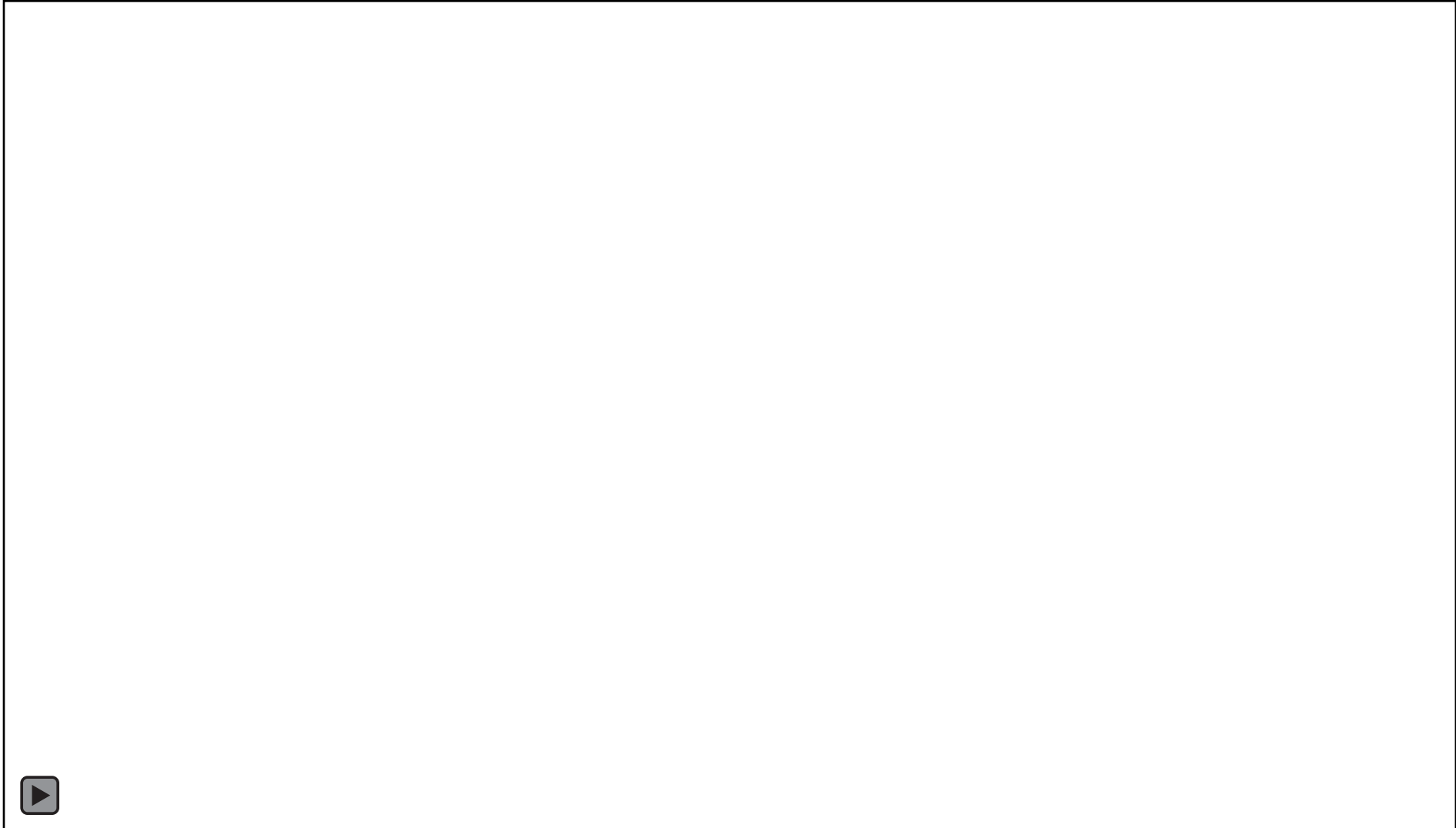
Global CRISPR-based gene drive



Global CRISPR-based gene drive

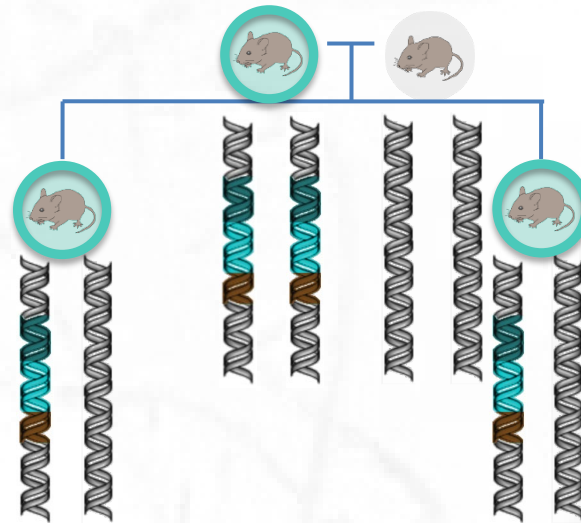


Global CRISPR-based gene drive



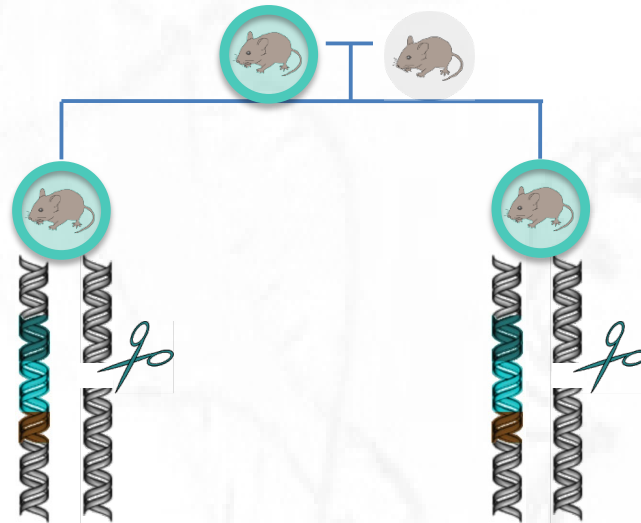
Esvelt KM, Smidler AL, Catteruccia F, Church GM (2014) *eLife*

Global CRISPR-based gene drive



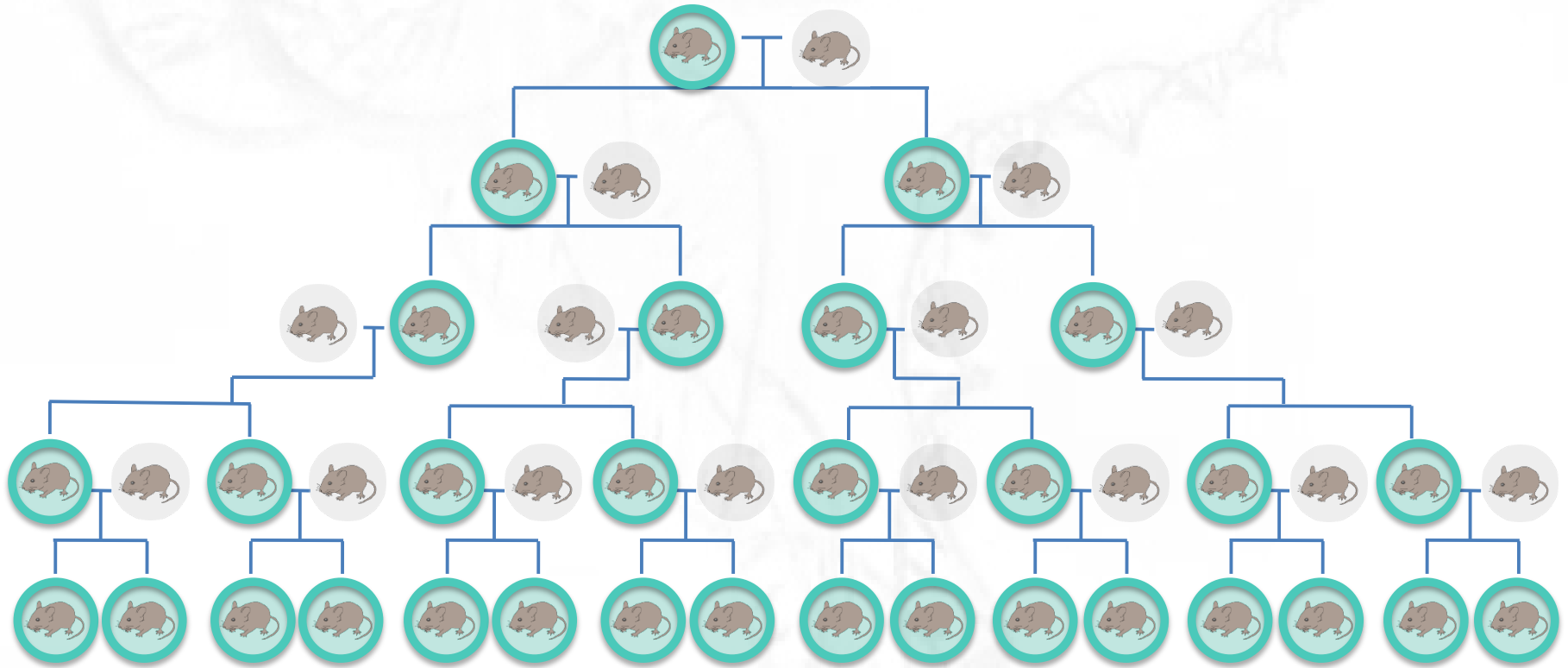
Esvelt KM, Smidler AL, Catteruccia F, Church GM (2014) *eLife*
Oye K, Esvelt K et al. (2014) *Science*

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Global CRISPR-based gene drive



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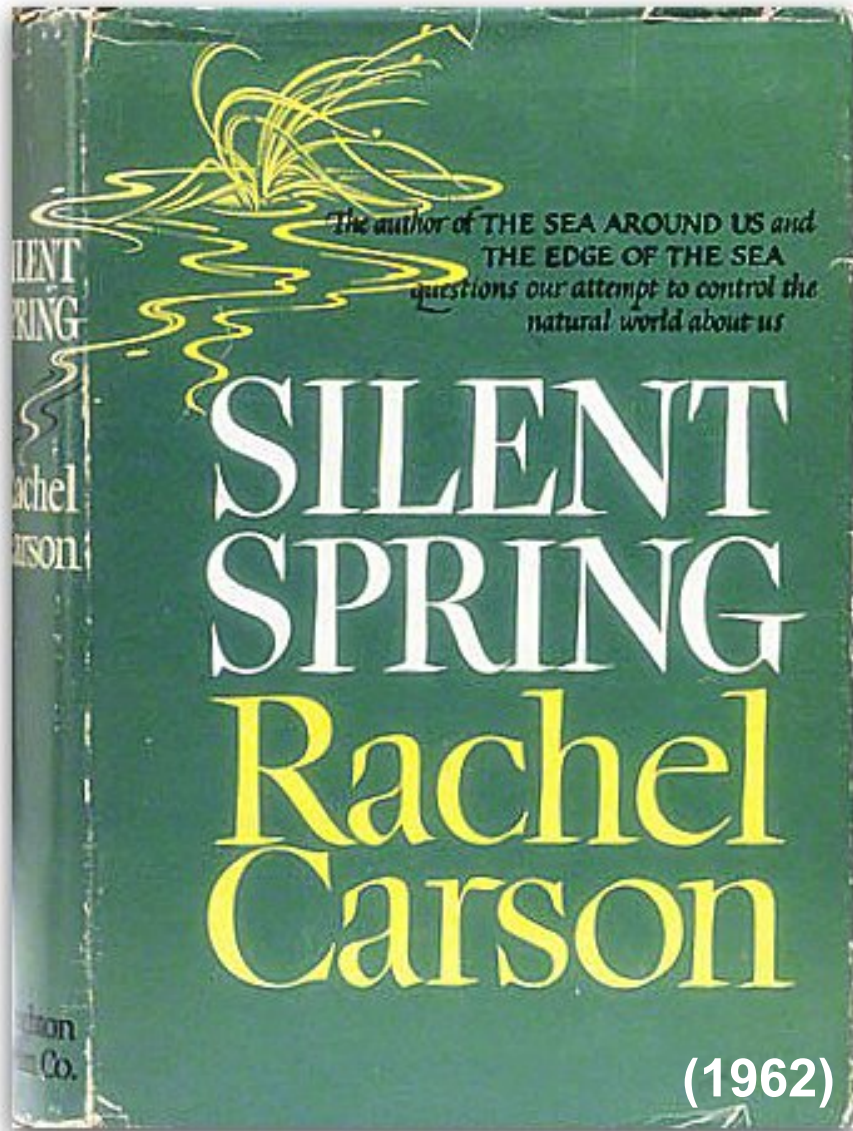
Facts about gene drives

- ❖ Occur in many species
- ❖ Spread and persist
- ❖ Sexual reproduction required
- ❖ Short generation time

Question/Topic 2

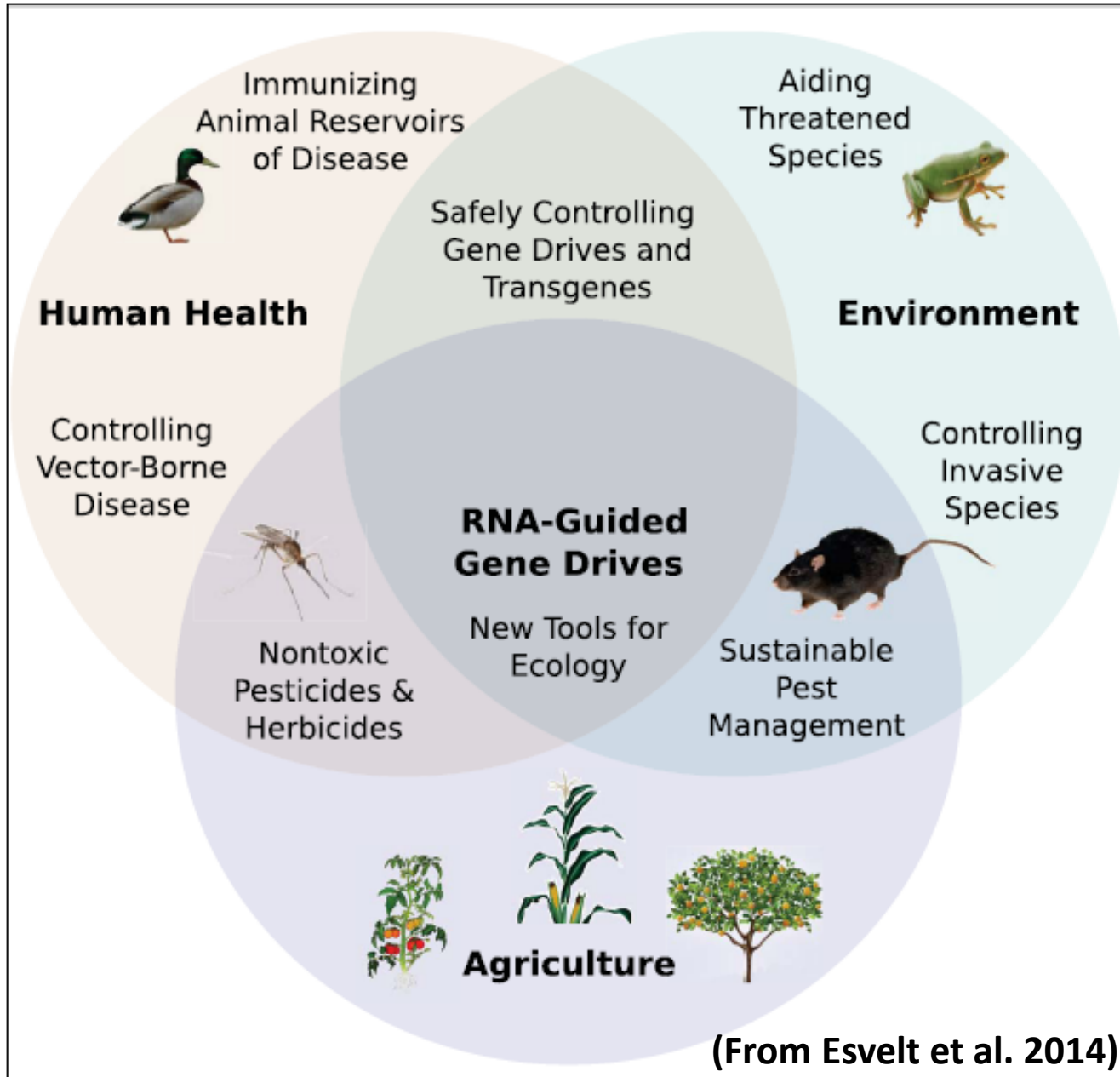
What features of the technology make it scientifically transformative/something new?

Are these features specific to the technology or are there some features common to all technologies/crosscutting issues?



Some of the most fascinating of the new methods [for controlling insect pests] are those that seek to turn the strength of a species against itself - to use the drive of an insect's life forces to destroy it.

Proposals to use gene drives



SCIENCE

Gene Drives Offer New Hope Against Diseases and Crop Pests

By NICHOLAS WADE DEC. 21, 2015



A woman in Tanzania under a mosquito bed net to avoid malaria.

DAILY COMMENT

COULD GENETICALLY MODIFIED MOSQUITOES SAVE HAWAII'S ENDANGERED BIRDS?



By Michael Specter, SEPTEMBER 9, 2016



Question/Topic 3

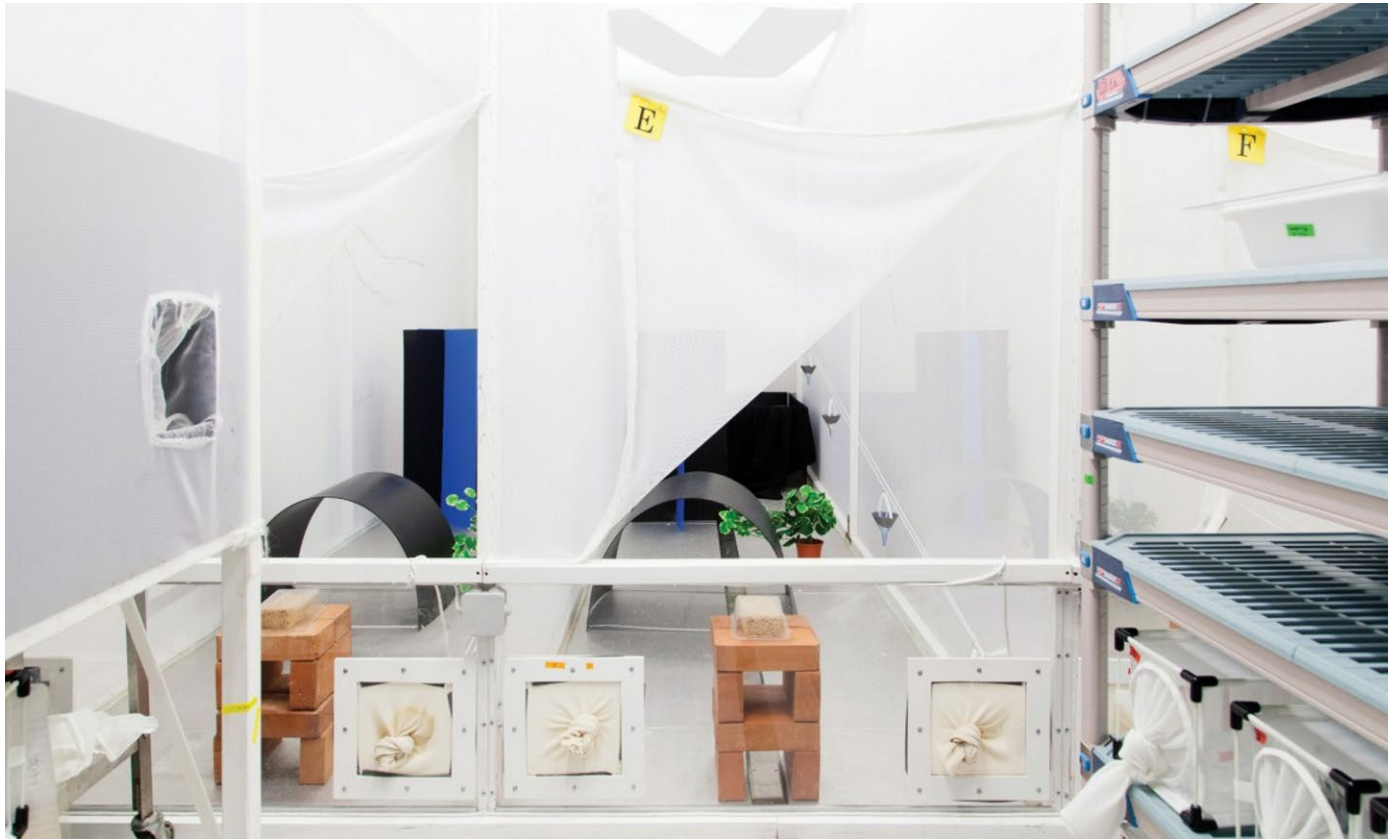
What is impactful, what is exciting,
what are the challenges?

Are these features specific to the
technology or are there some
features common to all
technologies/crosscutting issues?

The Extinction Invention

A genetic technology that can kill off mosquito species could eradicate malaria. But is it too risky to ever use?

by Antonio Regalado April 13, 2016



Room-size insect cages at the Polo d'Innovazione Genomica, in Perugia, Italy, mimic the outdoors for studying mating behavior of self-destructing mosquitoes.

How might we think about
answering the question:
Should we alter nature with gene
drives?

The National Academies of
SCIENCES • ENGINEERING • MEDICINE
BOARD ON LIFE SCIENCES

Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values

June 8, 2016

Public Release Event

Join the conversation:

#GeneDriveStudy



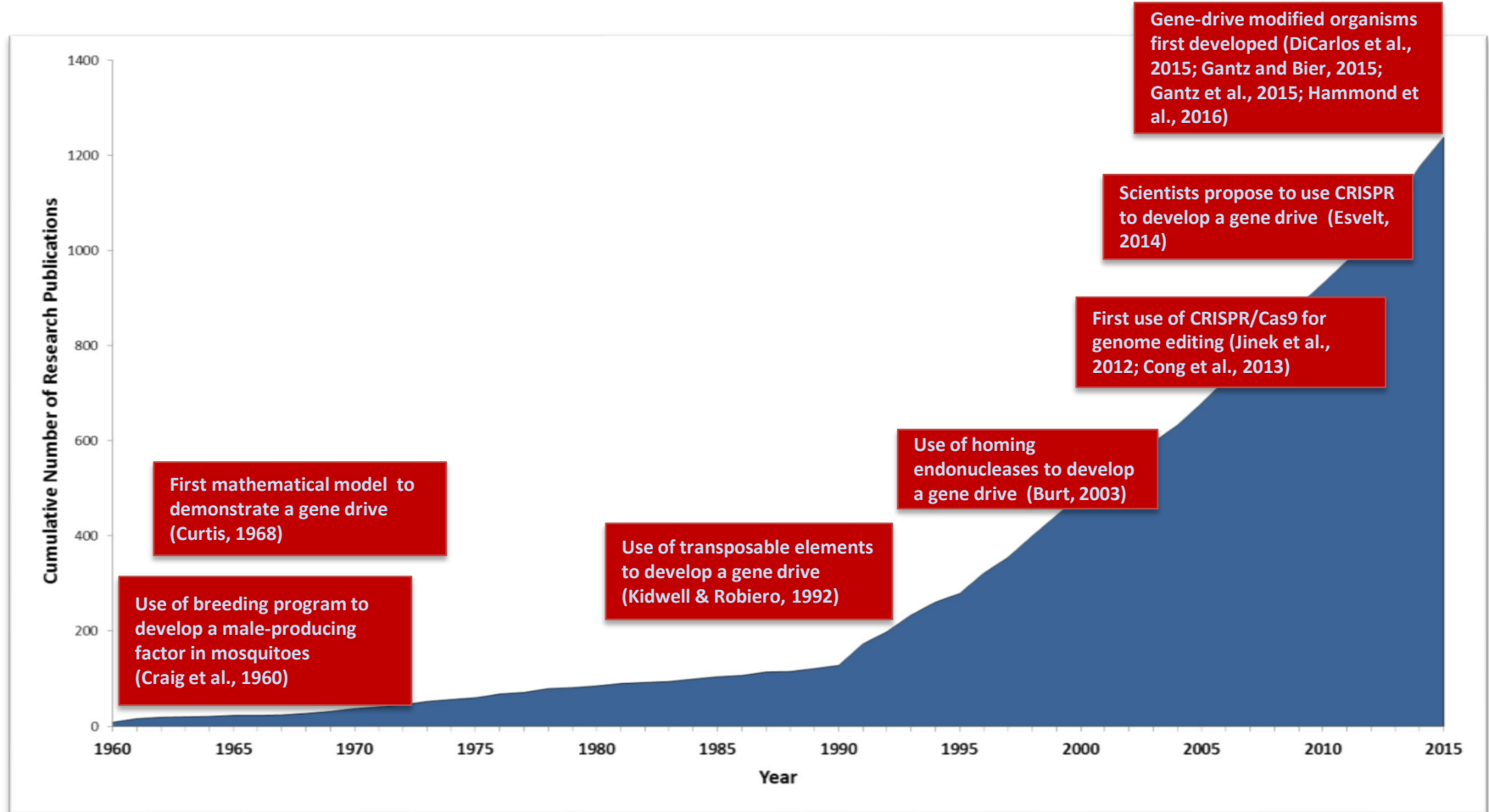
nas-sites.org/gene-drives



Motivations for the Study

Recent increase in the pace of the field

Cumulative number of gene drive research publications (1960 – 2015)



State of the science

- ❖ Insufficient evidence to support the release of gene-drive modified organisms into the environment.
- ❖ But benefits of gene drives for basic and applied research are significant and justify proceeding with laboratory research and controlled field trials.

**Use phased testing to evaluate
gene-edited organisms before
release**

**Stepwise, iterative approach to
guide scientific evaluation and
support evidence-based
decision making**



(February, 2019)

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Goats and Soda STORIES OF LIFE IN A CHANGING WORLD

EXCLUSIVE

Scientists Release Controversial Genetically Modified Mosquitoes In High-Security Lab

February 20, 2019 · 5:00 AM ET

Heard on [Morning Edition](#)



ROB STEIN



Guard against unintended release or persistence



Can we control gene drives in the field?

Managing gene drives using localization technology

- ❖ Split, precision, threshold drives
- ❖ Other safeguards: drug-inducibility, nutrient dependency



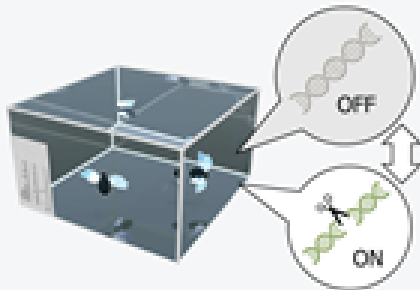
Defense Advanced Research Projects Agency > Program Information

Safe Genes

(Safe Genes Workshop, Monday, May 6, 2019)

Dr. Renee Wegrzyn

Control of Gene Editing



Enable temporal, spatial, and reversible control of gene editors

Countermeasures and Prophylaxis



Inhibit unwanted gene editing activity

Genetic Remediation

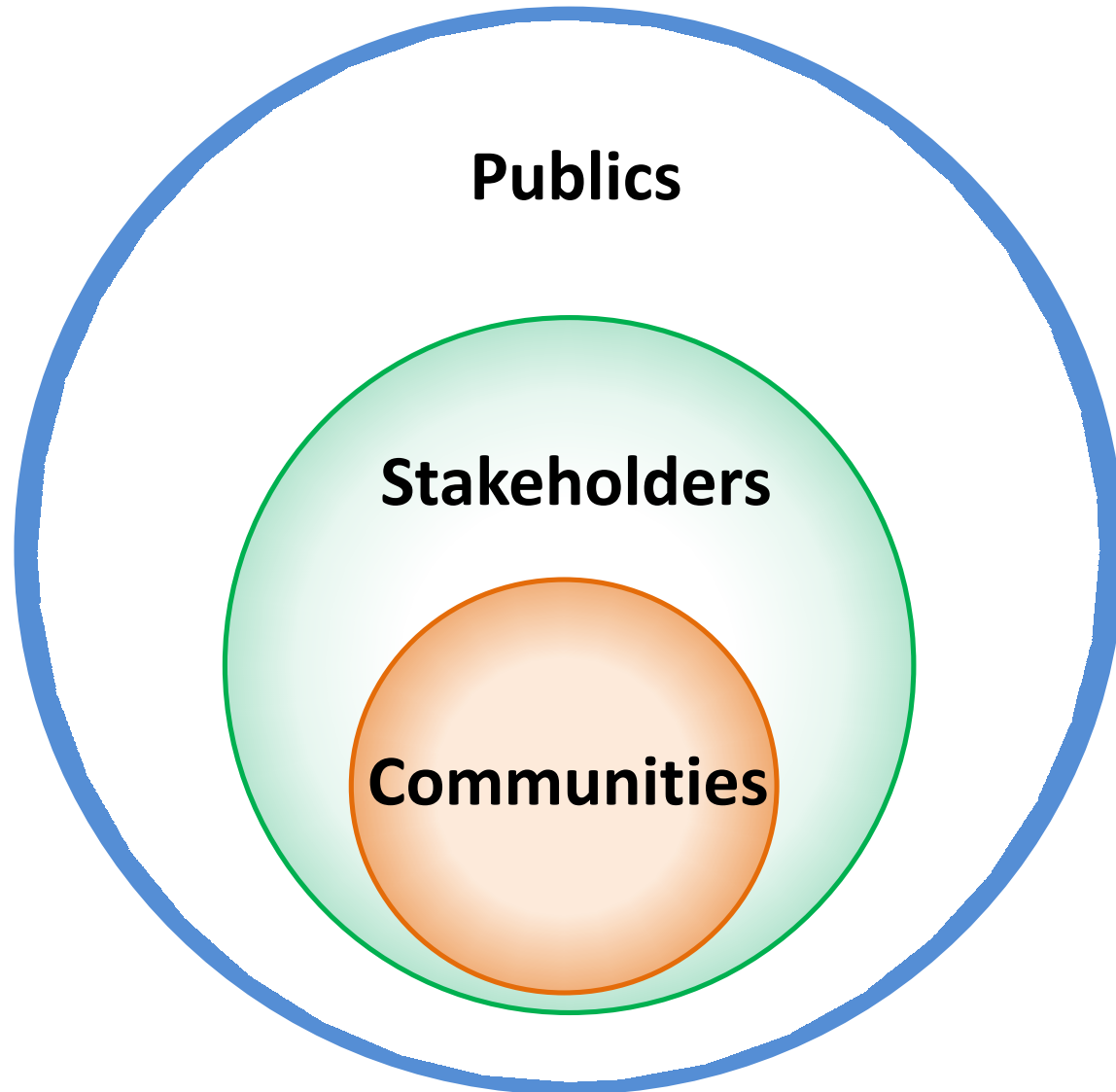


Remove engineered genes from environments to return to baseline

Values

Deeply held, complicated, sometimes evolving beliefs about what kinds of things – in humans' lives and the world at large – should be fostered, protected, or avoided.

Public engagement



Governance

INSIGHTS | PERSPECTIVES



BIOTECHNOLOGY

Regulating gene drives

Regulatory gaps must be filled before gene drives could be used in the wild

“...[gene] drives may present environmental and security challenges as well as benefits.”

Risk/Precaution



TECHNOLOGY GOVERNANCE

Precaution and governance of emerging technologies

Precaution can be consistent with support of science

Science

(2016) AAAS

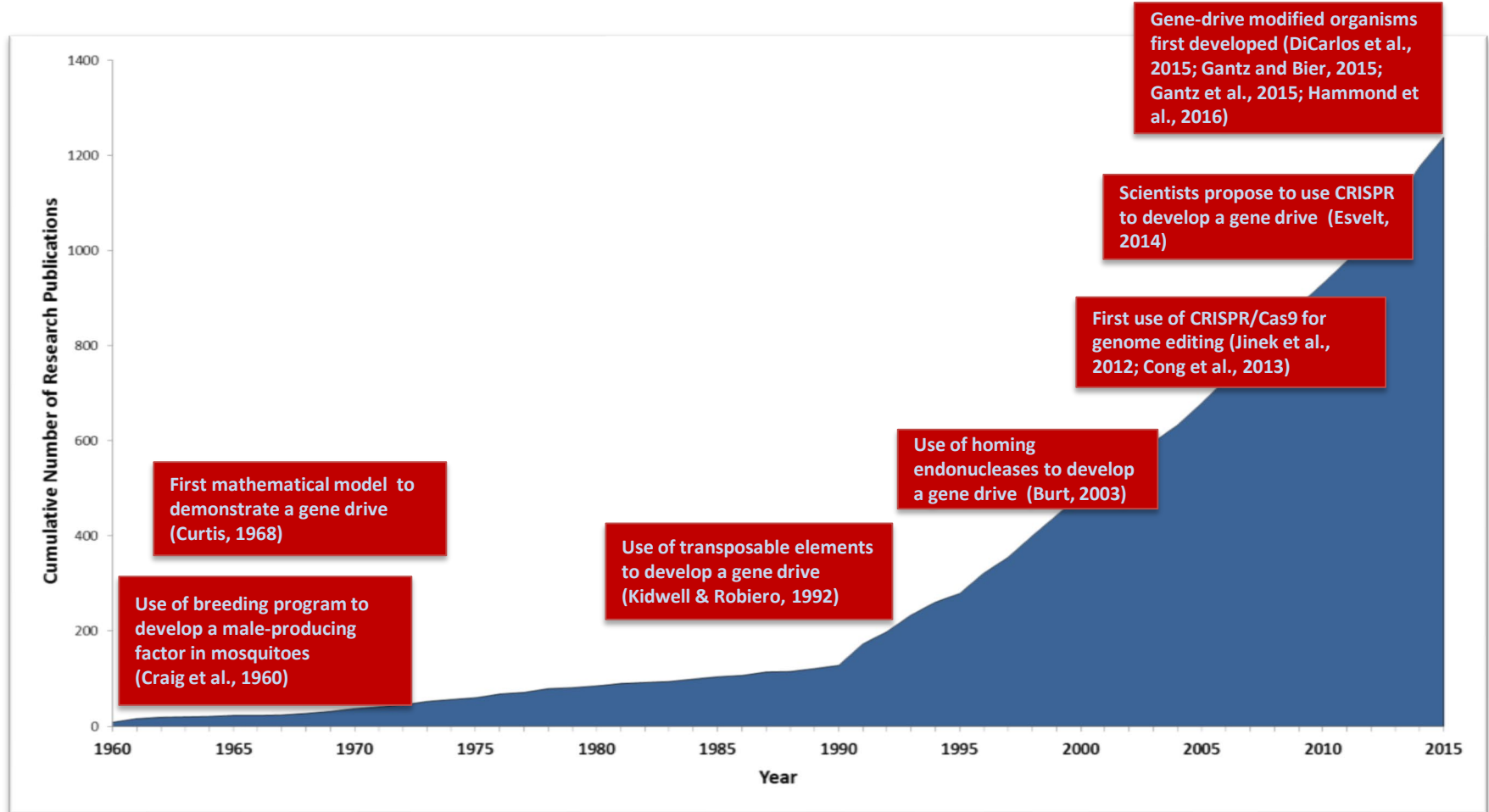
Question/Topic 4

What are potential strategies for identifying a new biotechnology on the horizon and how can we anticipate these new developments? When has a technology “emerged”? Is there a baseline of scientific understanding that must be reached?

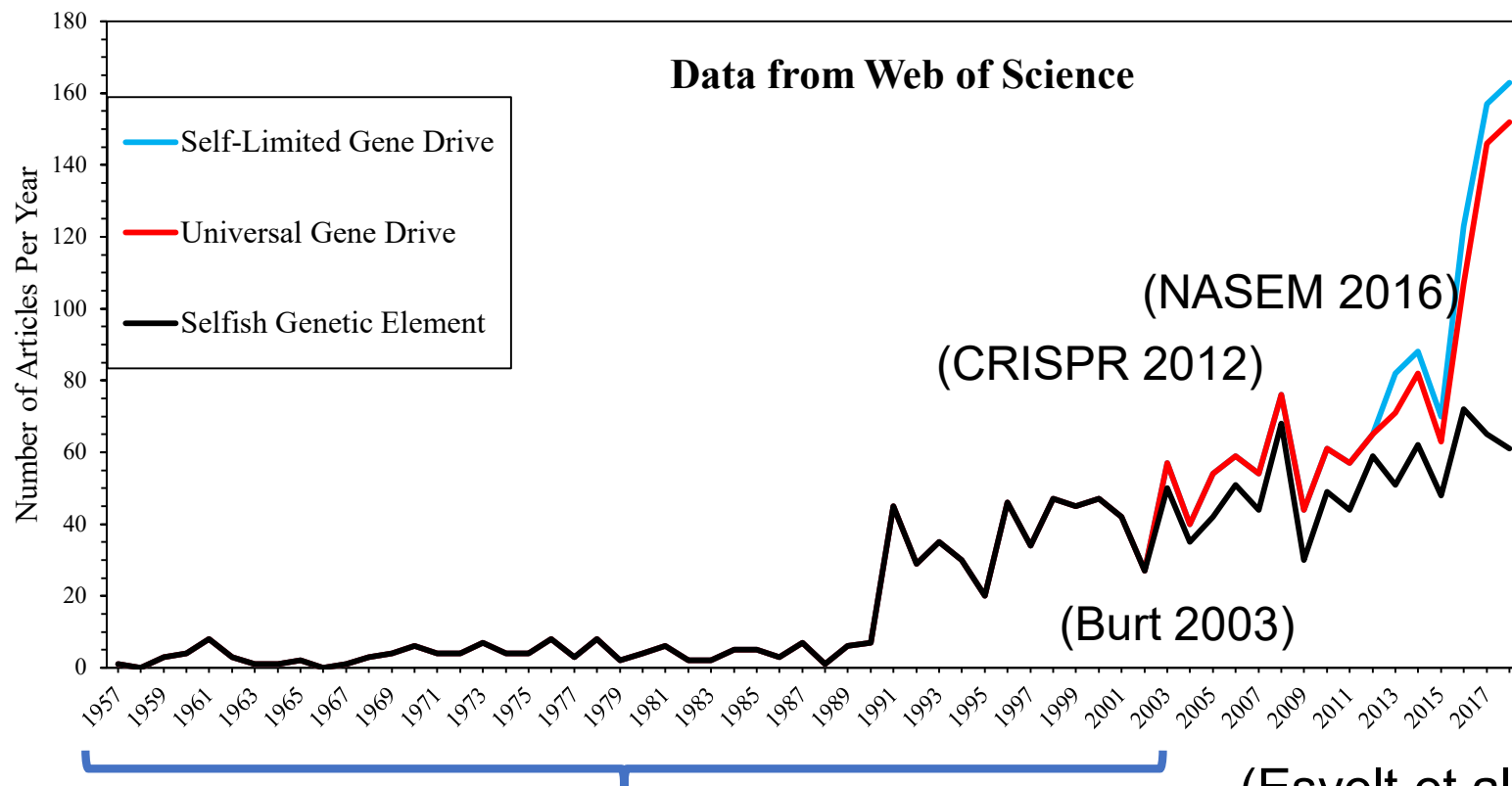
Motivations for the Study

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Conceptual and epistemological changes in the field of selfish genetic elements and gene drive (O'Toole and Collins)



meiotic drive (Novitski and Sandler 1957), selfish genetic element, preferential transmission, parasitic gene, ultra-selfish gene, outlaw gene, selfish gene (Dawkins 1976)

(Esvelt et al. 2014)
(2015, 2016: successful gene drives in yeast and mosquitoes)

What is a gene drive?

A gene drive is a process of inheritance by which a gene is guaranteed to pass from one generation to the next, and ultimately throughout a population.

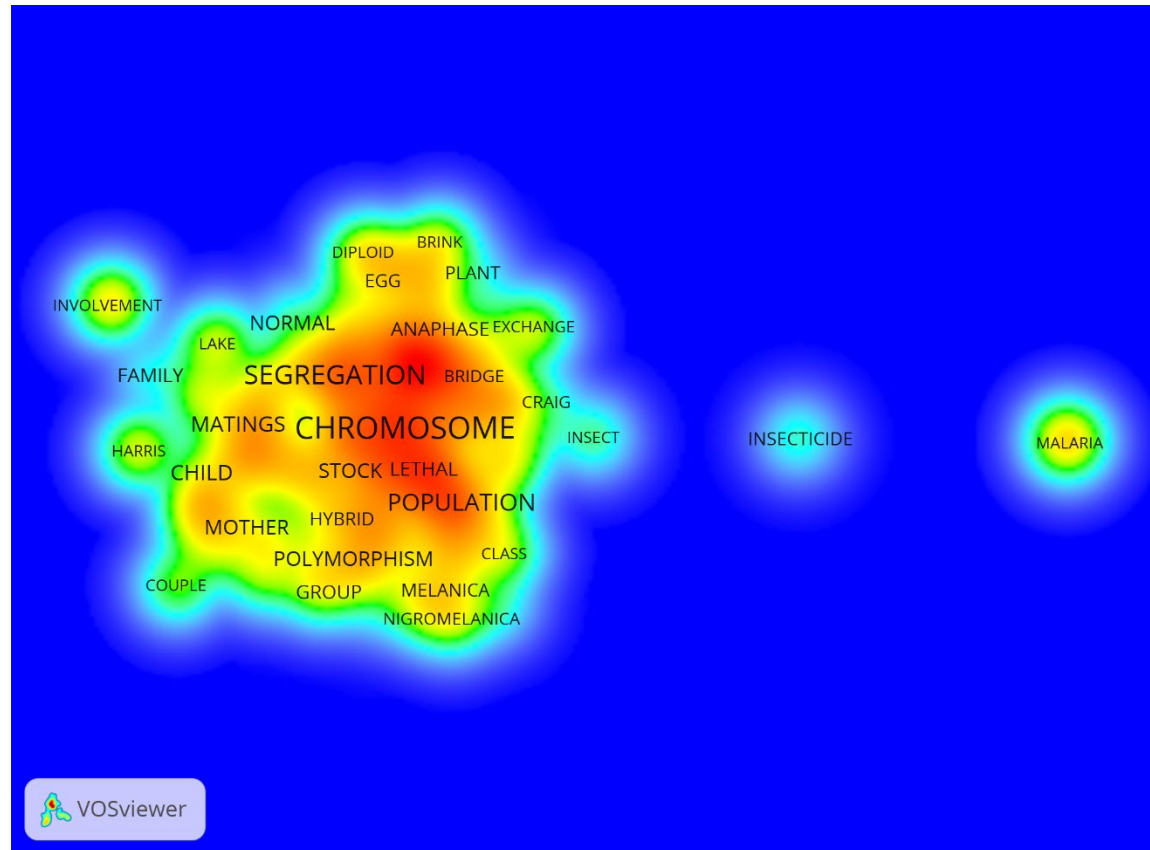
Operational Definition

Gene(s) *engineered* to be inherited in a *biased manner*, not conforming to expected Mendelian ratios, such that a trait can spread through a population, even if it does nothing good for the individual organism.

(Burt and Trivers. *Genes in conflict*. 2006; NASEM 2016)

Keyword Analysis: Selfish Genetic Element Corpus

Heat maps illustrate patterning of the discourse
1957-1966



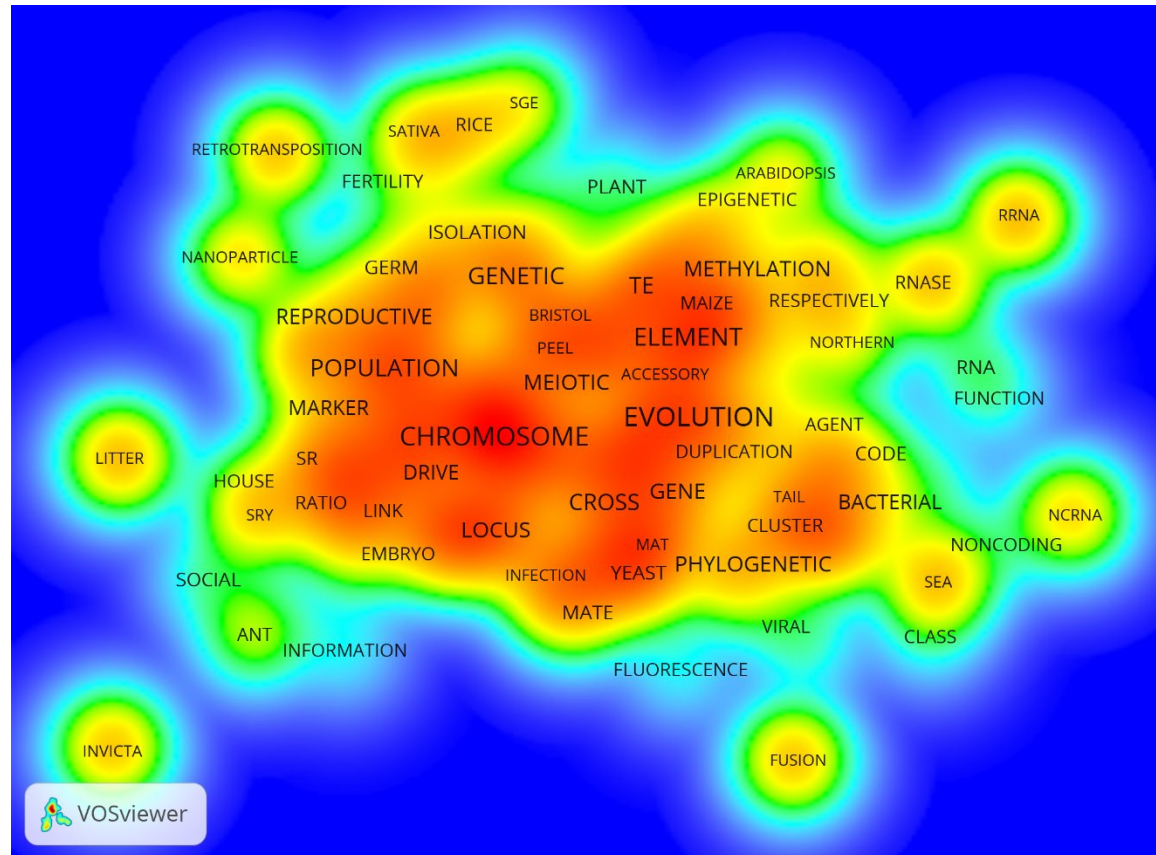
1957 Sandler and Novitski coin meiotic drive

1959 Sandler et al use segregation distortion for the first time

1960 Craig breeding program suggests threshold dependent population control

Keyword Analysis: Selfish Genetic Element Corpus

Heat maps illustrate patterning of the discourse
2016-2018



Close knit community, the clusters get larger rather than developing more clusters, clusters on the outside suggest possible sources of new innovation in the field, main words used in the discourse have not changed

Conclusion

Revolutionary breakthroughs in gene editing and its application in a technology such as gene drives offer a powerful tool for improving human health and sustaining biodiversity.

Conclusion

These advances also raise complex questions:

- ❖ What counts as natural?
- ❖ What are acceptable ways for applying new technologies to alter populations and communities?

Gene drives: A case of post-normal science

Post-normal science:

facts are uncertain, values are in dispute, stakes are high, and decisions are urgent.

Before release of gene edited organisms, the complexity of natural systems and the relevance of human commitments and values must be taken into account.

(Brossard et al. 2019)