iGEM 2024 GRAND JAMBOREE

Responsibility CONFERENCE 2024

Synthesis Screening: The Future of Writing and Hacking DNA

October 24, 2024

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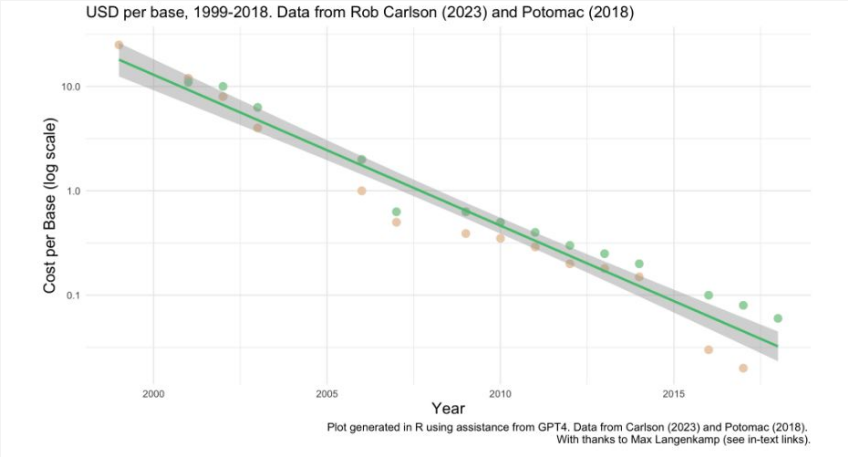
Synthesis Screening: Introduction

Tessa Alexanian

Tech Lead, International Biosecurity and Biosafety Initiative for Science

It’s easier than ever to read, write and edit DNA & RNA

Decreasing cost and increasing length



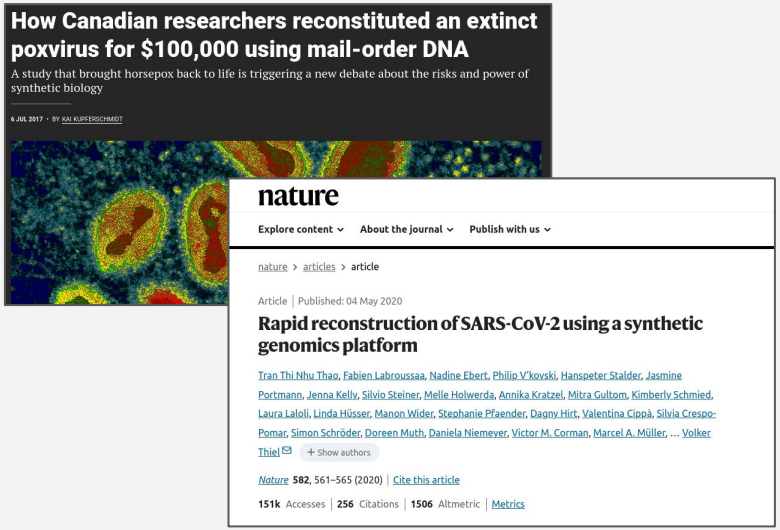
Custom Mail-Order

Benchtop Printers

Images: Founder’s Pledge, Aric Crabb/Bay Area News Group, DNAScript

Synthetic DNA could be accidentally or deliberately misused

Acquisition: from a digital sequence to functional pathogen



How Canadian researchers reconstituted an extinct poxvirus for $100,000 using mail-order DNA

A study that brought horsepox back to life is triggering a new debate about the risks and power of synthetic biology

6 JUL 2017 · BY KAI KUPFERSCHMIDT

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Article | Published: 04 May 2020

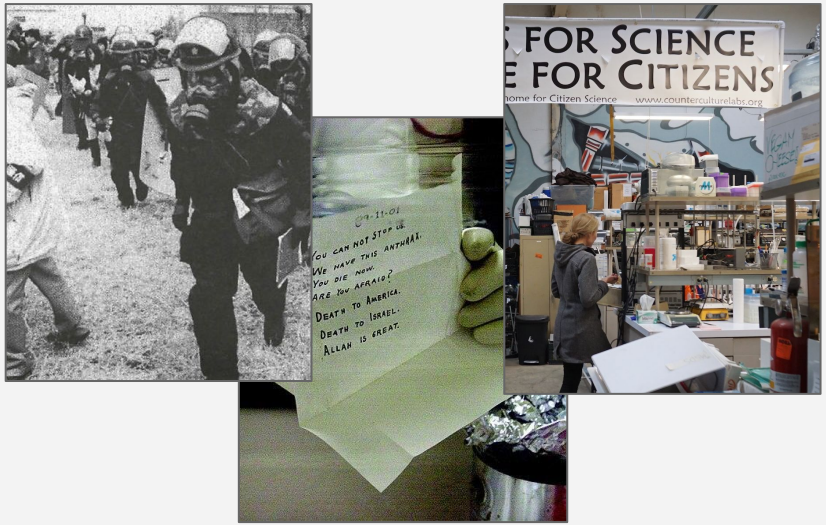
Rapid reconstruction of SARS-CoV-2 using a synthetic genomics platform

Tran Thi Nhu Thao, Fabien Labroussaa, Nadine Ebert, Philip V'kovski, Hanspeter Stalder, Jasmine Portmann, Jenna Kelly, Silvio Steiner, Melle Holwerda, Annika Kratzel, Mitra Gultom, Kimberly Schmied, Laura Laloli, Linda Hüsser, Manon Wider, Stephanie Pfaender, Dagny Hirt, Valentina Cippà, Silvia Crespo-Pomar, Simon Schröder, Doreen Muth, Daniela Niemeyer, Victor M. Corman, Marcel A. Müller, … Volker Thiel + Show authors

Nature **582**, 561–565 (2020) | Cite this article

151k Accesses | **256** Citations | **1506** Altmetric | Metrics

Engineering: more people able to engineer pathogens and toxins



Images: Counter Culture Labs

How do we balance access and security?

1. Recognize potentially risky sequences
toxins, pathogen genomes, virulence factors

2. Decide whether to trust user or customer
with risky sequences by screening legitimacy

Images: Waterloo iGEM 2015, Counter Culture Labs

How do we balance access and security?

Sequence Screening

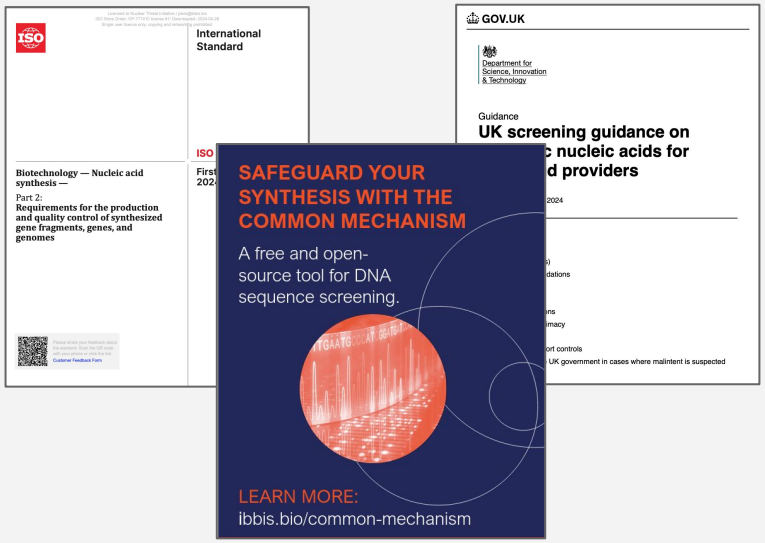
Customer Screening

Images: Waterloo iGEM 2015, Counter Culture Labs

Why are we talking about screening right now?

Changing risk landscape: AI tools, long synthesis, biofoundries, benchtop printers

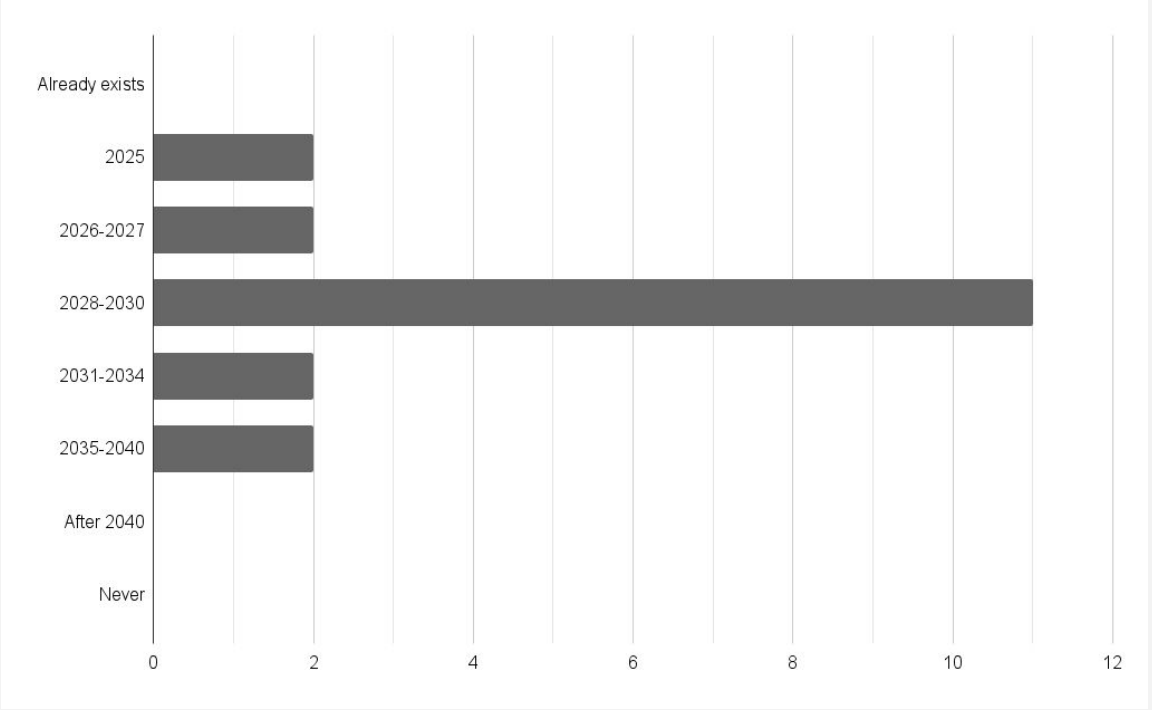
New standards, tools and regulations changing incentives around screening



Images: Kilobaser, Counter Culture Labs

Predictions | **Accessibility** | By what year do you think this will exist?

Synthesis of 10kb of custom DNA available for <1 cent/base



Slido poll; range of 2025-2040

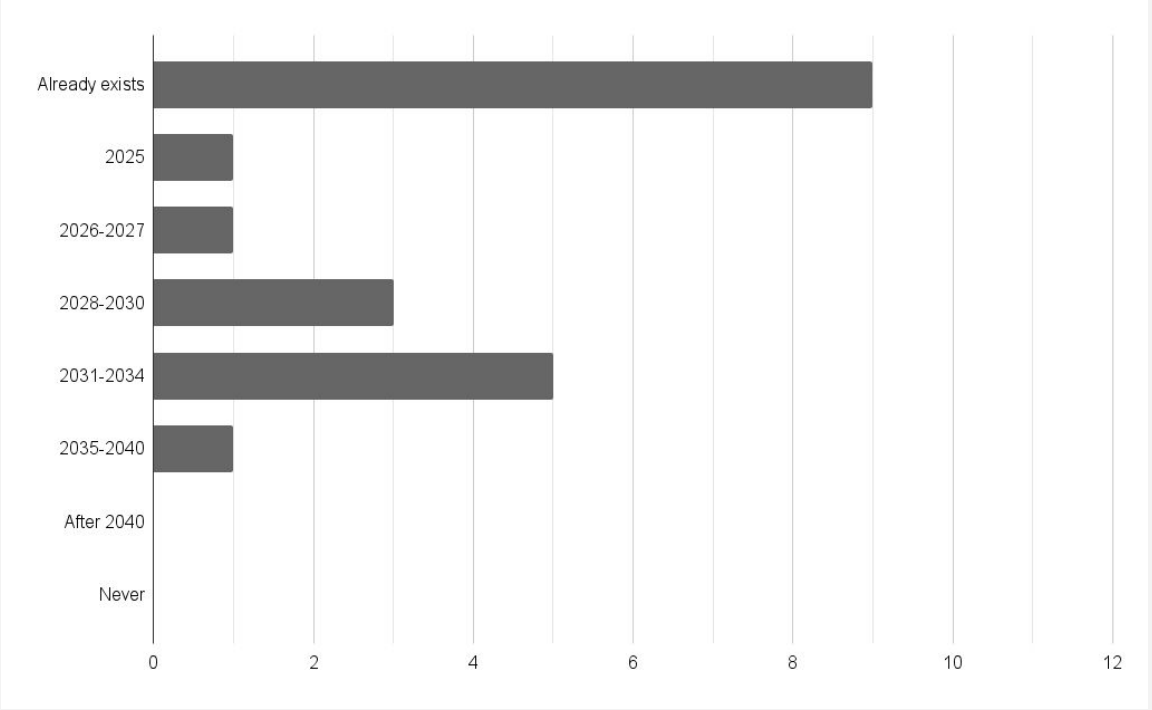
58% of respondents predict 2028 - 2030

Predictions | **Accessibility** | By what year do you think this will exist?

A benchtop synthesizer that can make fragments >50bp without needing proprietary reagents or highly skilled operators

Slido poll; range of already exists - 2040

45% of respondents say this already exists

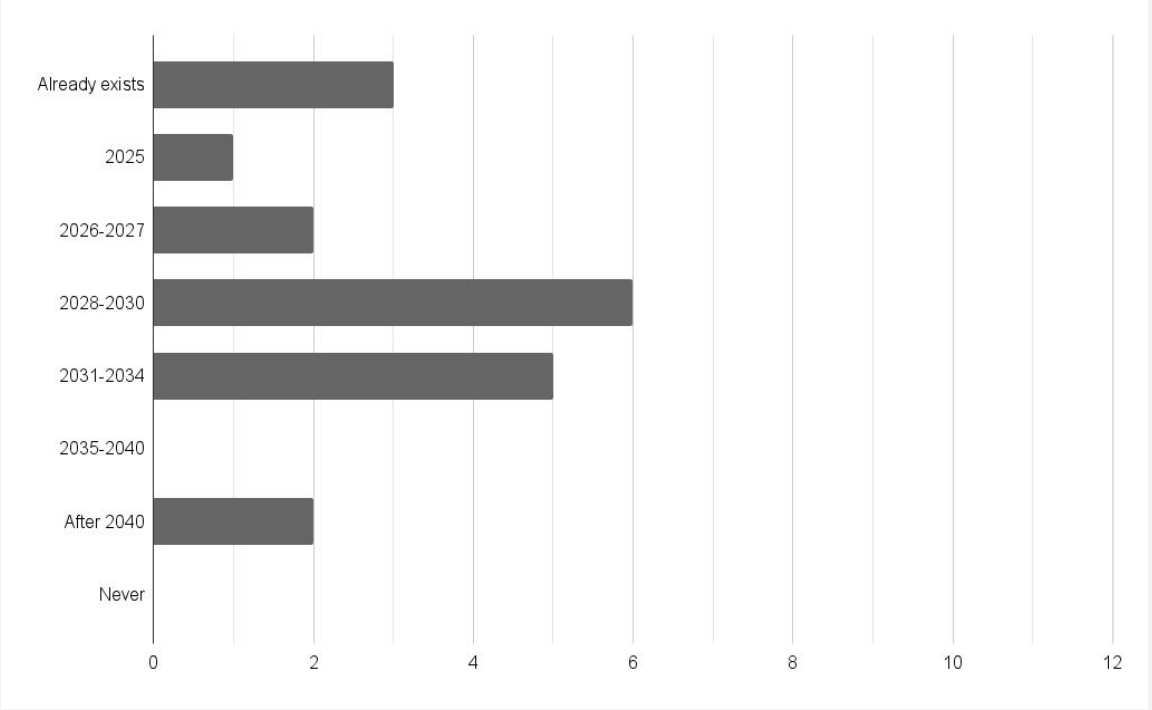


Predictions | **AI-Bio** | By what year do you think this will exist?

Generative AI design of enzyme variants where >80% preserve catalytic activity while having <10% sequence identity to any natural protein

Slido poll; range of already exists - after 2040

Little consensus among participants

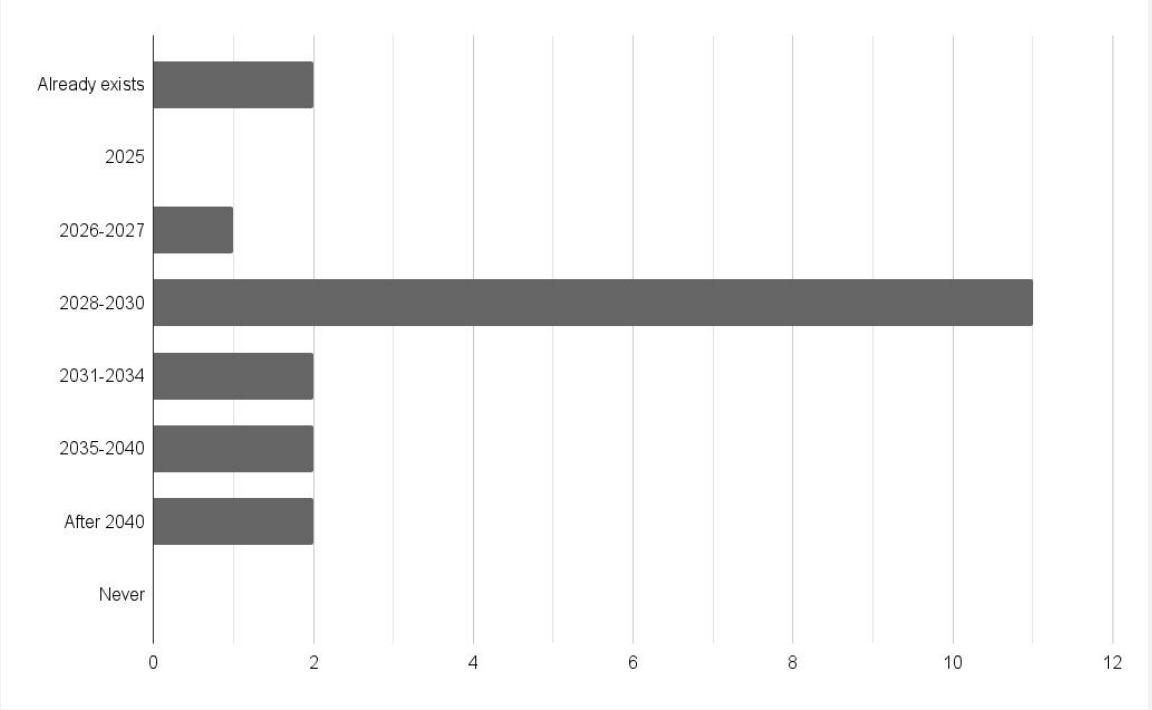


Predictions | **AI-Bio** | By what year do you think this will exist?

A replication-competent virus designed entirely in silico with <50% sequence identity to any natural virus

Slido poll; range of already exists - after 2040

55% of respondents predict 2028-2030

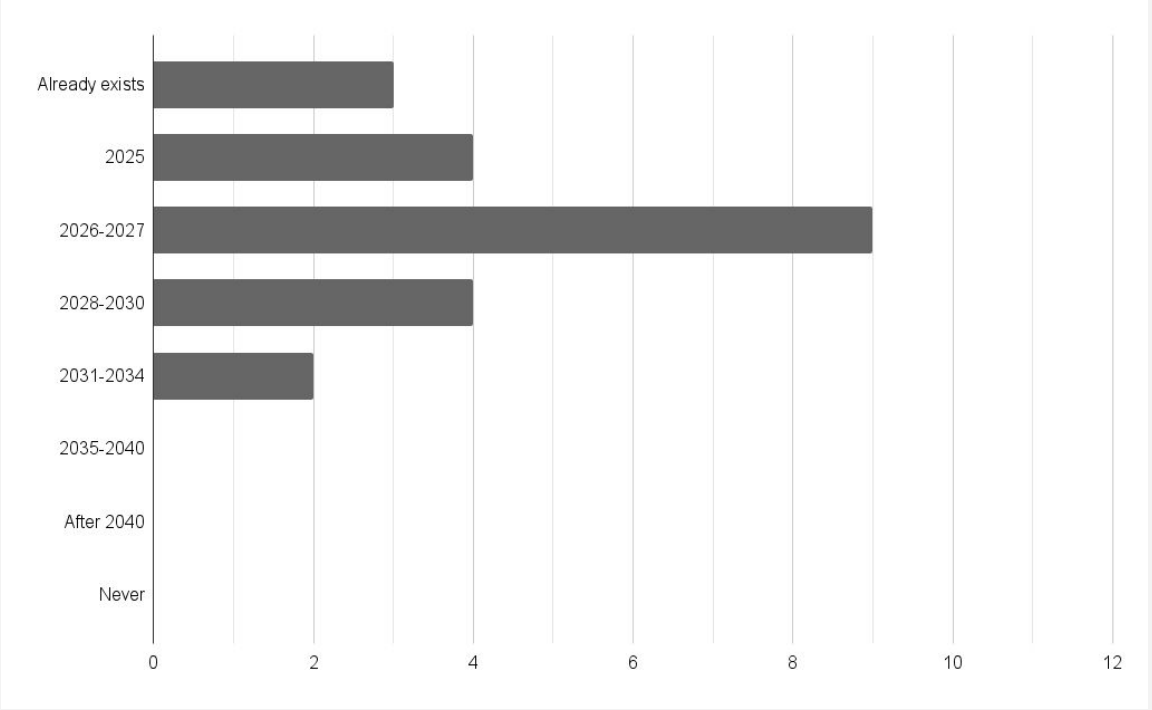


Predictions | **Accessibility** | By what year do you think this will exist?

Regulations requiring or strongly incentivising synthesis screening in at least 3 of the China, EU, India, UK, USA

Slido poll; range of already exists to 2034

Agreement that this will happen in the next decade



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Synthesis Screening: Panel Discussion

The Future of Writing and Hacking DNA

Jake Beal, Adam Clore, Shrestha Rath, Nikki Teran

Moderator: Sophie Peresson

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Jake Beal

Engineering Fellow (RTX BBN)

Nikki Teran

Founder (Scientific Legitimacy Verification)

Adam Clore

Technical Director of Synthetic Biology (IDT)

Shrestha Rath

PhD Fellow (Johns Hopkins Public Health)

Sophie Peresson

Biosecurity Expert (Sciences Po)

> **AI is less of a threat than we fear**, because it can't change biochemistry.

Jake Beal
Engineering Fellow (RTX BBN)

> Scientists must proactively implement biosecurity tools. If **government acts first it will likely be too much and too late**, a restrictive overreaction after something bad has already happened.

Nikki Teran

Founder (Scientific Legitimacy Verification)

> Accurate and transparent reporting by **the media is a stronger incentive for synthesis screening** than any fines or penalties imposed by law.

Adam Clore

Technical Director of Synthetic Biology (IDT)

> We must shift from democratizing biotech to **democratizing biosecurity**. Shared responsibility means local responsibility. Different bioeconomies need to own synthesis screening.

Shrestha Rath

PhD Fellow (Johns Hopkins Public Health)

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Jake Beal

Engineering Fellow (RTX BBN)

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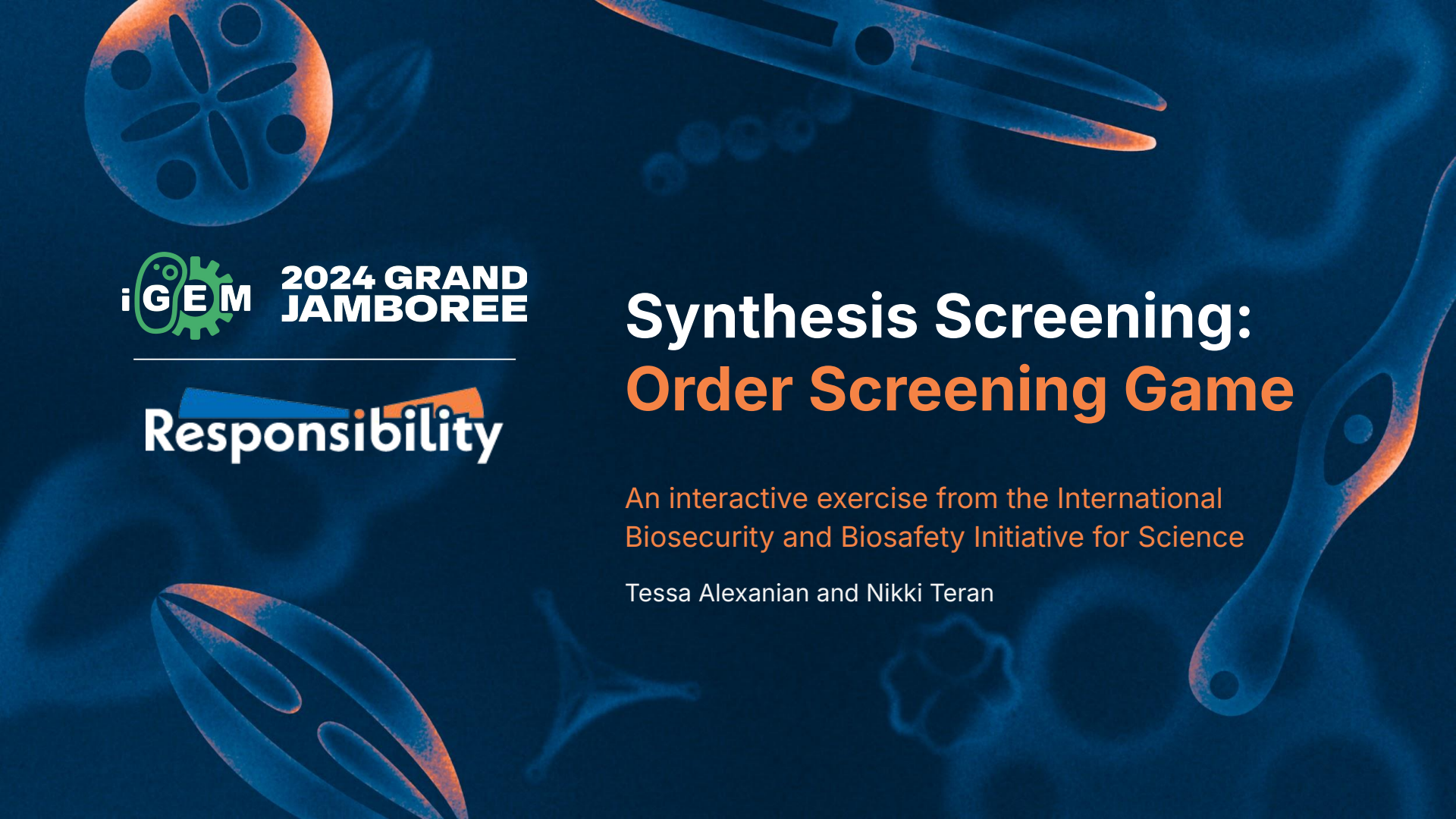


Synthesis Screening: Order Screening Game

An interactive exercise from the International Biosecurity and Biosafety Initiative for Science

Tessa Alexanian and Nikki Teran

Each of you will play a synthesis screener and a customer.

Customer profiles based on real examples of legitimate scientists and attempted bioterror

Flagged orders (including iGEM parts!) screened using the Common Mechanism

Images: Miguel Andrade/Wikimedia Commons

Step one: who are you?

1. Read your customer profile.
2. Find a partner. **Do not show them your profile!**
3. Decide who will play the customer first. The other person will be the screener.
4. The customer should **hand their order** to the screener.

Screening Game Round 1: will you send the order to the customer?

As the customer, you want the screener to send the sequence.

As the screener, you decide to:

1. **Fulfill** the order
2. **Deny** the order
3. **Deny** and *report to law enforcement*

Images: WoCInTechChat/Flickr

switch!

change screener and customer roles

Screening Game Round 2: will you send the order to the customer?

As the customer, you want the screener to send the sequence.

As the screener, you decide to:

1. **Fulfill** the order
2. **Deny** the order
3. **Deny** and *report to law enforcement*

Images: WoCInTechChat/Flickr

reveal!

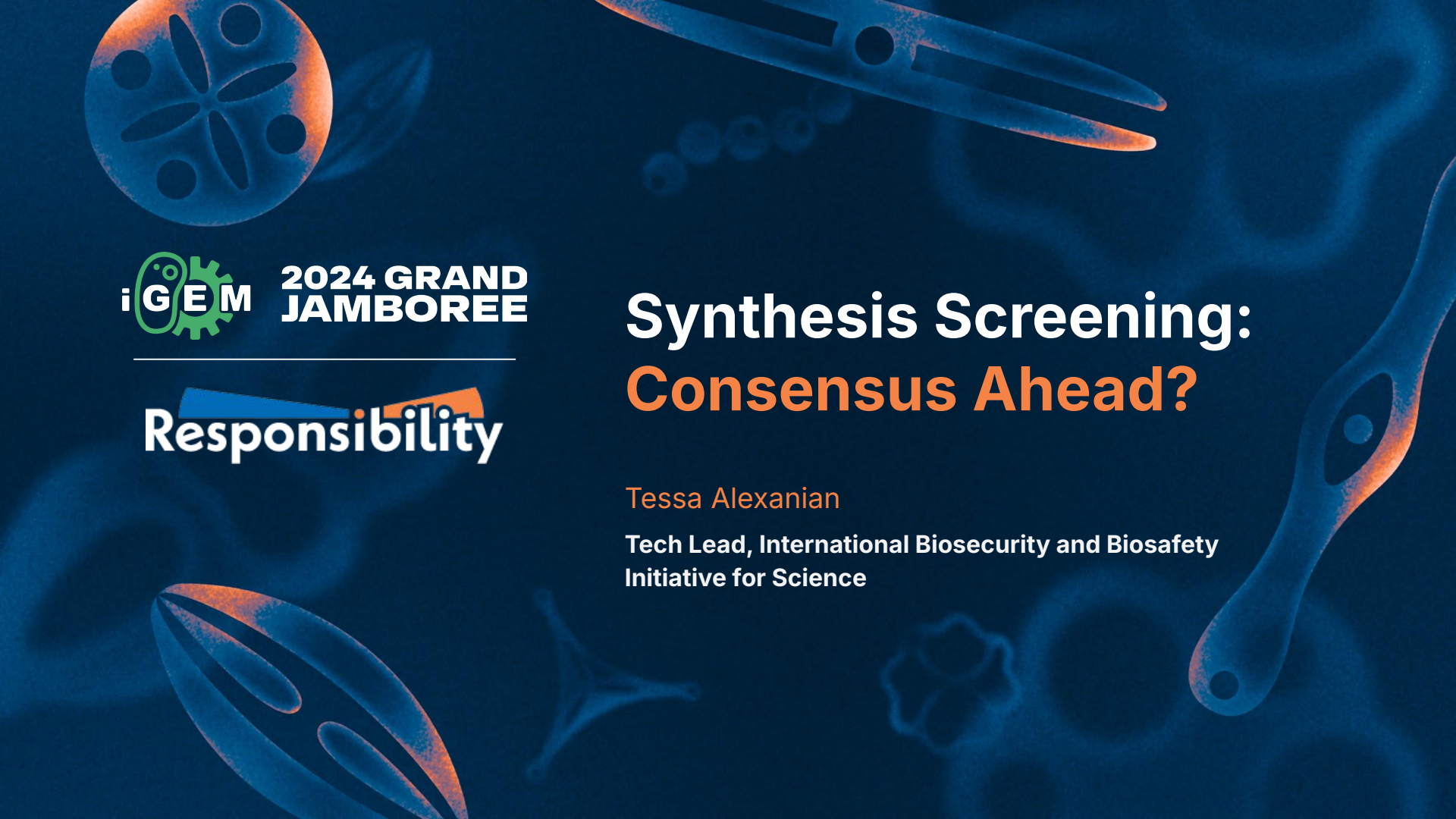
show your partner your card

Debrief: what do you think about synthesis screening?

Join 1-2 other pairs.

Discuss:

- What did you notice?
- What information did you wish you had?
- What systems would help with synthesis screening?

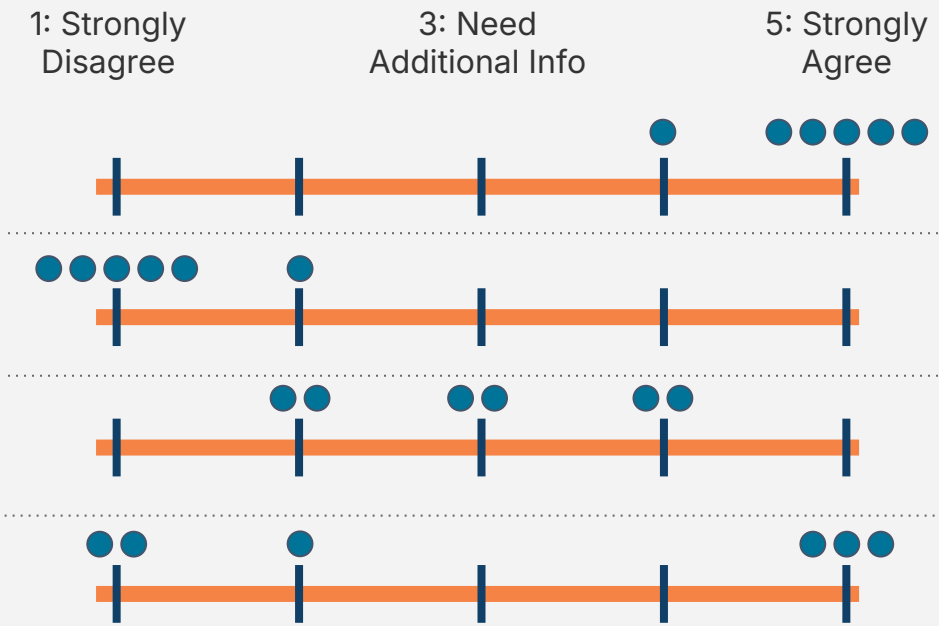


Synthesis Screening: Consensus Ahead?

Tessa Alexanian

Tech Lead, International Biosecurity and Biosafety Initiative for Science

Finding Gradients of Agreement



Questions to ask

Why do we all agree?

What alternative statement might we all agree with?

What changes or information would strengthen opinions in either direction?

Where are the differences in our perspectives coming from?

Images: visualizations designed by the Engineering Biology Research Consortium

Read each statement, and **circle your level of agreement** with it.

Statement	Level of Agreement				
1. All customers for synthetic nucleic acids should be required to verify their identity (i.e. orders should not be sent to anonymous customers).	1 Strongly disagree	2 Disagree	3 Need more info	4 Agree	5 Strongly agree
2. It should be the synthesis provider's responsibility to determine whether a customer is legitimate once a sequence of concern (SOC) is flagged in an order.	1 Strongly disagree	2 Disagree	3 Need more info	4 Agree	5 Strongly agree
3. Not every sequence that poses a significant biological hazard is from an agent or toxin regulated by a government.	1 Strongly disagree	2 Disagree	3 Need more info	4 Agree	5 Strongly agree
4. Different SOCs have different risk profiles; it is appropriate to treat them differently.	1 Strongly disagree	2 Disagree	3 Need more info	4 Agree	5 Strongly agree

Read each statement, and **circle your level of agreement** with it.

Statement	Level of Agreement				
5. In the next 1-2 years, a shared understanding is needed of the tiers of SOC risk and how customer screening processes adapted the risk profile of each SOC.	1 Strongly disagree	2 Disagree	3 Need more info	4 Agree	5 Strongly agree
6. Sequence screening tools are or can be made sufficiently robust to AI-designed and/or obfuscated sequences.	1 Strongly disagree	2 Disagree	3 Need more info	4 Agree	5 Strongly agree
7. Red-teaming of screening providers should be conducted regularly to see if SOCs can be acquired by customers who have not proven their legitimacy.	1 Strongly disagree	2 Disagree	3 Need more info	4 Agree	5 Strongly agree

Read each statement, and **circle your level of agreement** with it.

Statement	Level of Agreement				
8. Providers should be required through a legal mandate or strong regulatory incentives to screen every order they receive.	1 Strongly disagree	2 Disagree	3 Need more info	4 Agree	5 Strongly agree
9. Benchtop devices should be required through a legal mandate or strong regulatory incentives to screen every sequence they produce for possible SOCs.	1 Strongly disagree	2 Disagree	3 Need more info	4 Agree	5 Strongly agree
10. Sequence and customer screening practices can and should be harmonized internationally so that screening is similar around the world.	1 Strongly disagree	2 Disagree	3 Need more info	4 Agree	5 Strongly agree

Finding Gradients of Agreement

1. Find a group of 4-6 people.
2. On your own, circle your level of agreement with each of the 10 statements.
3. Once you have all finished, compare your answers. **What is surprising?**

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Synthesis Screening: get in touch!

screening@ibbis.bio