

How did we get here?

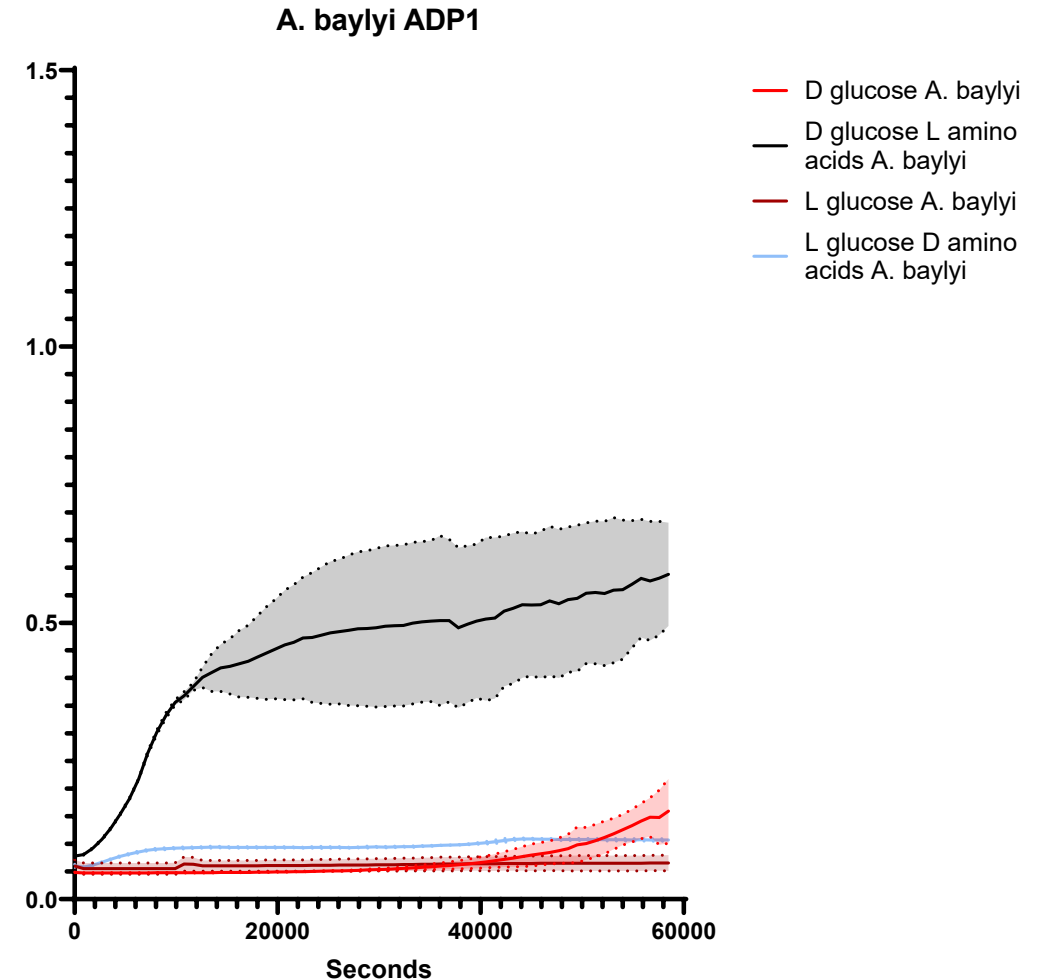
“We therefore recommend that research with the goal of creating mirror bacteria not be permitted, and that funders make clear that they will not support such work. Governance of a subset of enabling technologies should also be considered to ensure that anyone attempting to create mirror bacteria will continue to be hindered by multiple scientifically challenging, expensive, and time-consuming steps.”

- Adamala et al. *Science*

- A relatively small number of scientists have brought these issues to the attention of a larger community, but without that community’s widespread involvement
- The proposed hazards mostly hinge on two suppositions:
 - That mirror life will likely have few predators in the wild
 - That mirror pathogens will likely be unrecognizable by the immune system

Will mirror organisms have a growth advantage in the wild?

- Experiments can be carried out to assess these hazards
- Studies have shown that organisms can grow in a mirror environment, *but there are few comparisons of relative growth advantage.*
- We are in the process of determining the ‘Hamming distance’ to a fully functional mirror surrogate



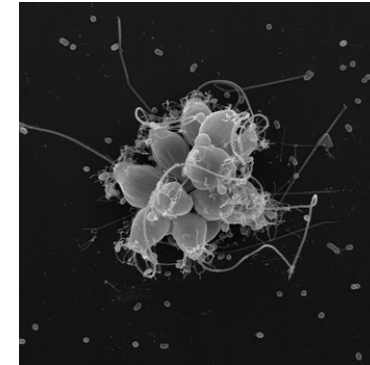
The example of *A. baylyi* is extreme, but in general there appears to be a huge growth defect in a mirror environment

Will mirror organisms avoid predation in the wild?

- The Technical Report suggests that protists may be significant predators, but that:

“Protists are highly diverse, and the molecular mechanisms involved in the tracking, recognition, engulfment, and killing of prey are not well-characterized in any organism.” (p. 159)

- While *Dictyostelium* rely on chiral signals to find prey, many protists are indiscriminate:
 - Choanoflagellates, which prey on diverse bacteria, likely do not depend on chirality
 - Ciliates do not rely on phagocytosis and filter feed by using a non-discriminating oral funnel
 - Protist enzymes targeting peptidoglycans in cell wall deal with L- and D-amino acids



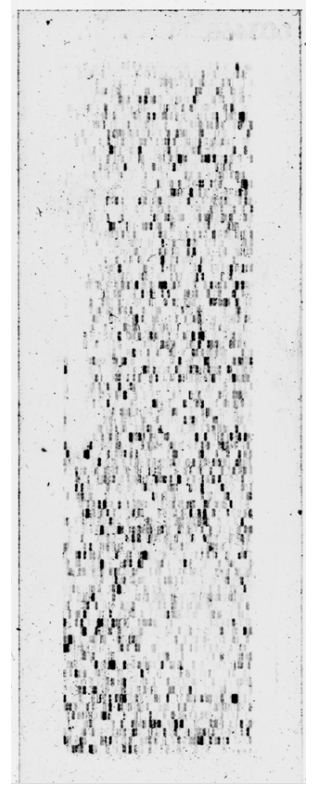
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Will mirror organisms avoid an immune response?

- There is good evidence that D-proteins are less immunogenic than L-, and it is reasonable to suspect they might not be recognized by Pattern Recognition Receptors
- However, immune responses are diverse and complex:
 - Broadly neutralizing antibodies across populations may provide nascent defense against a mirror organism
 - Example: Peptide arrays reveal a breadth of bound chemistry by broadly neutralizing antibodies
 - Antimicrobial peptides (AMPs) are available across the phylogenetic spectrum, and frequently rely on mechanisms that have little to do with chirality
 - Example: string together positive charges, and you often have an excellent AMP



Rituximab



Broadly
neutralizing
anti-flu Ab

Specific aspects of a threat scenario must be considered

- A 'mirror pathogen' would not likely be an effective pathogen, given that virulence factors and interactions with the human host would be non-functional
- The most probable scenario for a mirror pathogen may be an ESKAPE pathogen, whose pathogenic mechanism (biofilm formation) is largely achiral
- Even so, mirror ESKAPE pathogens would be subject to the same competition issues as any other mirror bacteria and gaining a foothold would not be straightforward
- **It is unclear whether the possibility of a subset of mirror nosocomial infections represents a catastrophic threat to human life**

Assessing the probability of a threat

- The probability of a catastrophic biothreat is difficult to evaluate with the evidence available, but is likely much lower than has been argued
- Much additional research is needed before a moratorium is considered, well beyond those studies suggested here
- This research must be approached incrementally and responsibly and with accountability to the public, following the pattern of other public dialogues and regulatory regimes (CRISPR, genAI, nuclear fusion, etc.)
- What has largely been lost in the conversation is the great good that will come from manipulation of the chemistry of living systems
- Stopping these chemistries now will also stop progress towards diagnostics, prophylactics, therapeutics, and agricultural, environmental, and process biotechnologies that will be of great benefit to all