Advanced Research + Invention Agency ARIA

Bioenergetic Engineering

Opportunity space

v1.0

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CONTEXT

This document describes an early opportunity space from which we believe one or more funding programmes can emerge. We've sketched out some of our early thinking to spark your interest, and invite you to imagine relevant potential programmes with us, or suggest new directions. We'll publish updated versions of this document as our thinking evolves.

Sign up **here** to receive those updates and learn about any funding opportunities that emerge from this opportunity space.

An ARIA opportunity space should be

+ important if true (i.e. could lead to a significant new capability for society),
+ under-explored relative to its potential impact, and
+ ripe for new talent, perspectives, or resources to change what's possible.

SUMMARY

In his seminal 1944 work *What is Life?* Schrödinger proposed that fundamentally, life accumulates order by harvesting *energy*, and preserves its capacity to do this via *information* (i.e. genetics). Genetic engineering now lets us control life's *information*, yet the engineering of life's *energy* remains underdeveloped. A powerful set of new tools could bridge the gap, enabling breakthroughs ranging from treatments for neurodegenerative disease to biohybrid solutions for environmental remediation and resilience.

BELIEFS

The core beliefs that underpin/bound this area of opportunity.

1. While *information* has been the major focus of modern biology, *energy* and *information* are both fundamental to life ⟶ **bioenergetic engineering has the potential to catalyse advances on the scale of the genetic revolution**.
2. Life uses powerful energy building blocks, like ATP, that are unlike any used in engineering ⟶ **leveraging these primitives will enable a range of bio-hybrid devices and other systems whose performance far exceeds today's best designs.**
3. The feedback loop between engineering disciplines and fresh insights is accelerating ⟶ **we're at an inflection point where scientists and engineers from many disciplines can begin treating life's energy machinery as a design space.**

OBSERVATIONS

Some signposts as to why we see this area as important, underserved, and ripe.

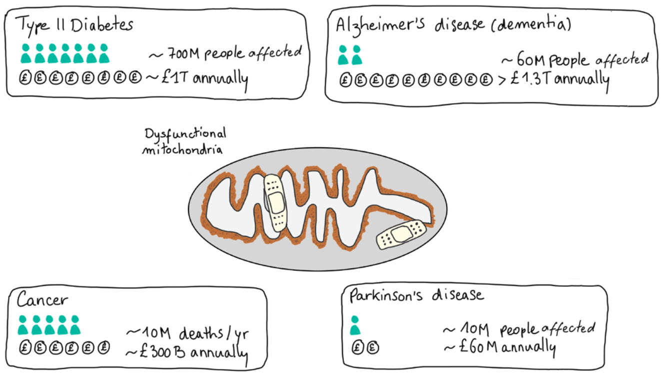
Bioenergetic engineering could unlock groundbreaking applications across a range of problems:

Environment: Engineered microbes could improve carbon capture,[1] nutrient cycling, and biosequestration, opening new strategies for environmental resilience.

Health: Conditions underpinned by energetic dysfunction, including neurodegenerative [2] and metabolic diseases, as well as unhealthy ageing, could be high-leverage targets for bioenergetic treatments. [3, 4]

Technology: Bioenergetic components could power soft robotics, adaptive biomaterials, and small scale bio-hybrid systems that move, sense, and compute, combining the strengths of biological and engineered systems. [5]

Fig 1 - Diseases that could be treated by targeting the energy flows in cells



Genetics-based inventions have seen over 1m patent filings, whereas bioenergetics have netted fewer than 20k.**

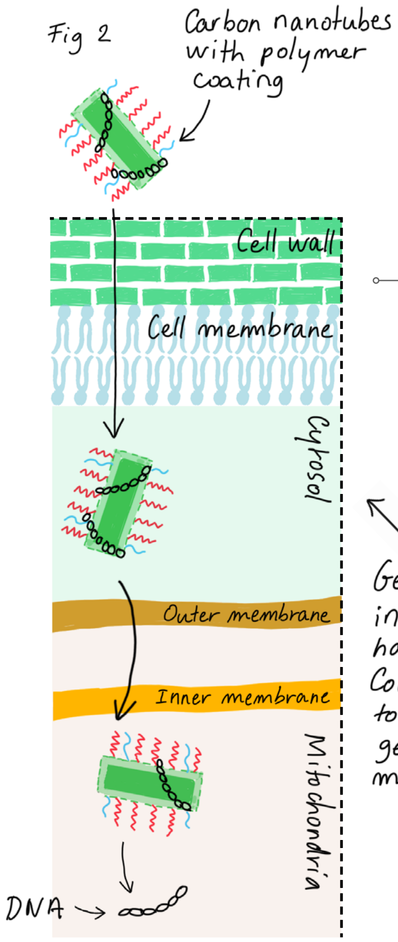
An emerging toolkit [6] is rapidly expanding what's possible, as illustrated by advances across multiple disciplines:

Materials science and nanotechnology: functionalised nanoparticles, [8] engineered extracellular vesicles, novel AAV capsids, and surfactant-based carriers could enable the targeted delivery of molecules and synthetic constructs — including nucleic acids or organelles — to specific intracellular compartments or tissues.

Synthetic biology and genomics: techniques for the design of organelles and synthetic regulatory circuits could permit construction of pathways for dynamic control over energy in living or bio-hybrid systems. [7]

Biophysics and bioengineering: optogenetic [9] and photothermal actuators [10] hold potential for dynamic, real-time modulation of membrane potential and energy flow.

Fig 2



Getting nucleic acids into mitochondria is hard, but it can be done. Could this open the door to getting synthetic genomes into mitochondria?

Increasing lifespan with light!

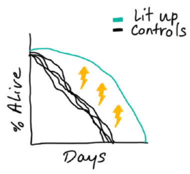
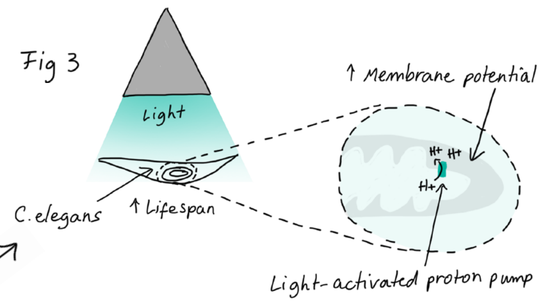
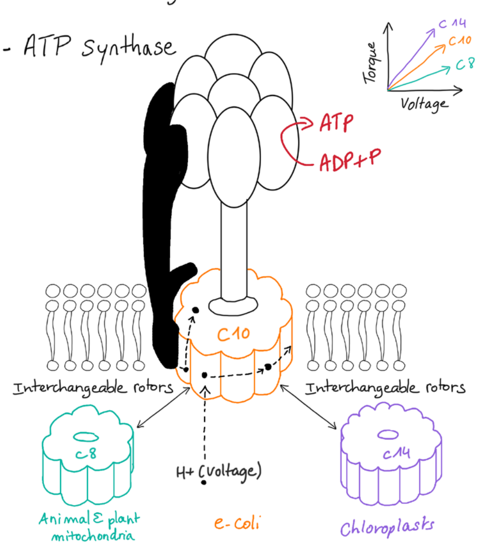


Fig 3



Emerging tools are powerful– what other, still-undiscovered, methods might enable bioenergetic engineering?

Fig 4 - ATP Synthase



Living systems excel in energy utilisation for complex tasks, especially at small scales, and rely on a versatile (often universal) set of energy primitives, including ion gradients, ATP synthase, and ATP [11, 12] — the universal energy currency that powers all known life. These mechanisms handle energy conversion, storage, and transduction with remarkable efficacy. [13, 14, 15]

Biology already powers molecular motors with ultra-dense fuels like sugar and fat. What if we used them to engineer tiny new machines – a bio-hybrid "butterfly" that could soar 100 miles on a single drop of honey?

**Patent Public Search 1.0.35: bioenergy+bioenergetic = 15,313; gene+genetic = 1,051,620

SOURCES

A compiled, but not exhaustive list of works helping to shape our view and frame the opportunity space (for those who want to dig deeper).

1. Engineered Microbes for Carbon Sequestration
2. Mitochondrial Dysfunction in Neurodegenerative Diseases
3. Mitochondria at the Crossroads of Health and Disease
4. The Role of Mitochondria in Aging
5. Bio-hybrid Systems for Soft Robotics
6. Engineering the Mitochondrial Genome
7. Mitochondrial DNA in cancer: small genome, big impact
8. Polymer-coated carbon nanotube hybrids with functional peptides for gene delivery into plant mitochondria
9. Optogenetic Control of Mitochondrial Metabolism
10. Modulation of Local Cellular Activities Using a Photothermal Dye-Based Subcellular-Sized Heat Spot
11. The Vital Question
12. Engineering rotor ring stoichiometries in the ATP synthase
13. Understanding the Efficiency of Autonomous Nano- and Microscale Motors
14. Energy consumption during insect flight and bioinspiration for MAV design
15. Nonequilibrium Energetics of a Single F1-ATPase Molecule
16. Toward Artificial Mitochondrion: Mimicking Oxidative Phosphorylation in Polymer and Hybrid Membranes
17. Rejuvenation by Heterochronic Parabiosis
18. Schrödinger's What is Life?

ENGAGE

You can provide feedback on this opportunity space **here.**

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