Bioelectronic control of a microbial community using surface-assembled electrogenetic cells to route signals

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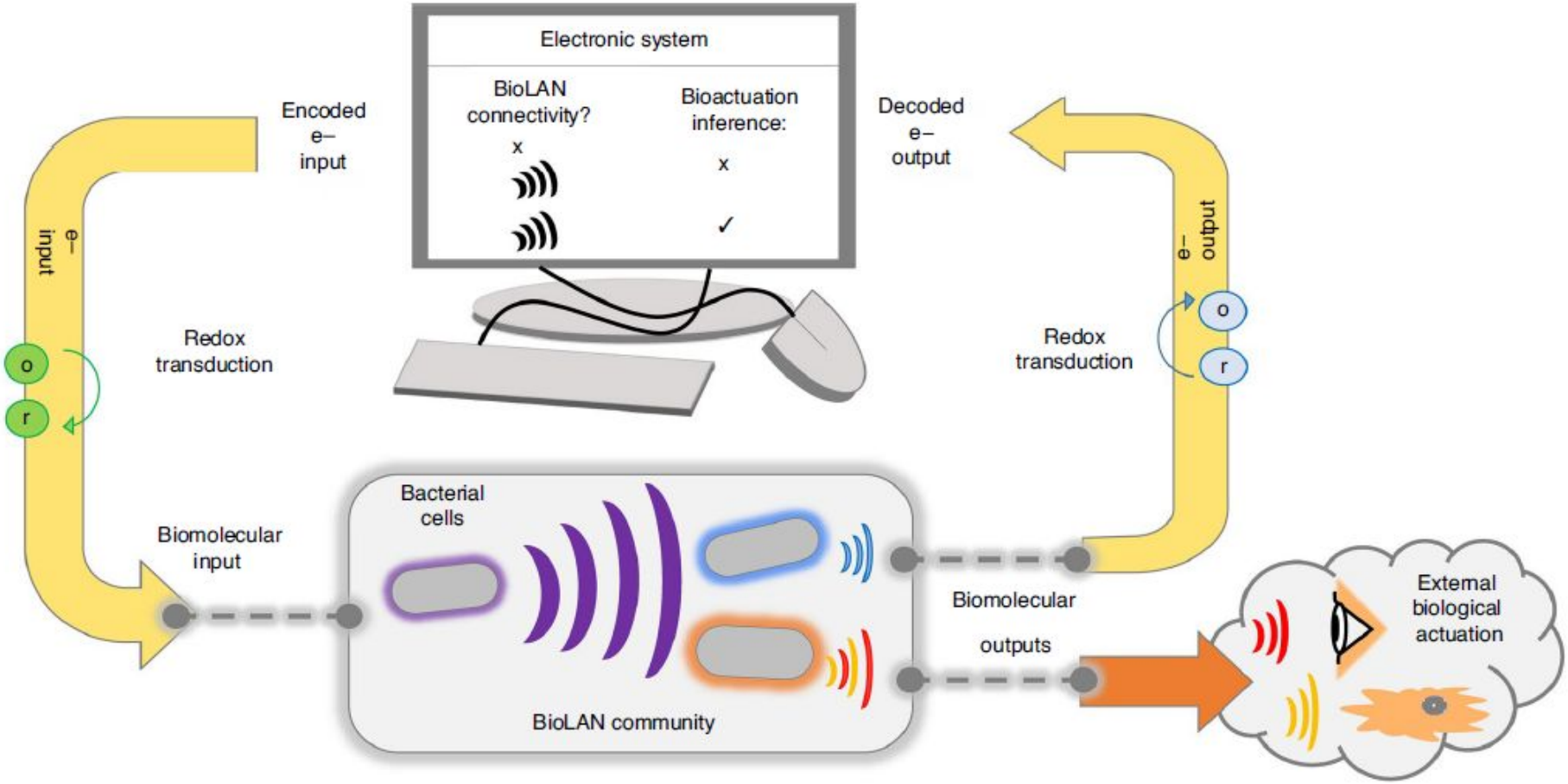
Zoom link : https://us04web.zoom.us/j/73359047312?pwd=UbjCybbZAFbCjXbpDUGpmeg0nx0XZF.1

Introduction

- Two different systems: A biological system and an electronic system
    1. Biological system : uses the ion gradient
    2. Electronic system : uses the flow of electrons

Objective:

Create a system linking both systems => use of redox modality


Electronic system
BioLAN connectivity?
x
Bioactuation inference:
x
✓
Encoded e– input
Decoded e– output
e– input
e– output
Redox transduction
Redox transduction
o
r
o
r
Bacterial cells
Biomolecular input
Biomolecular outputs
BioLAN community
External biological actuation

The main objectives

1 - Link electronic input and biological behaviour

2 - Find optimal conditions for a uniform electrogenetic induction

3 - Find a way to engineer cells directly onto the electrode

4 - Transmit the signal emitted by the first cell population

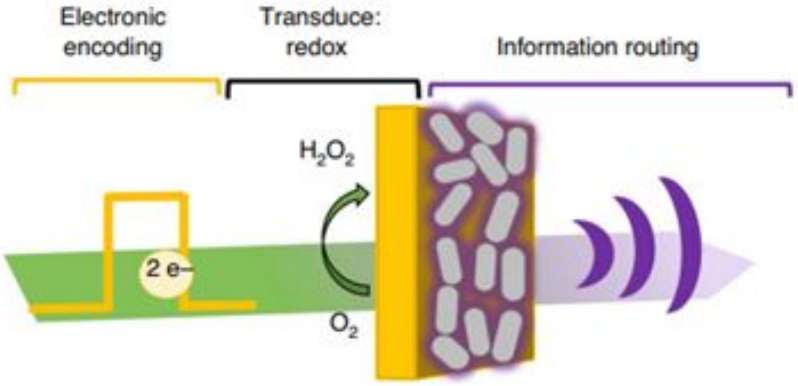
5 - Get a verification of the signal transmission on the computer

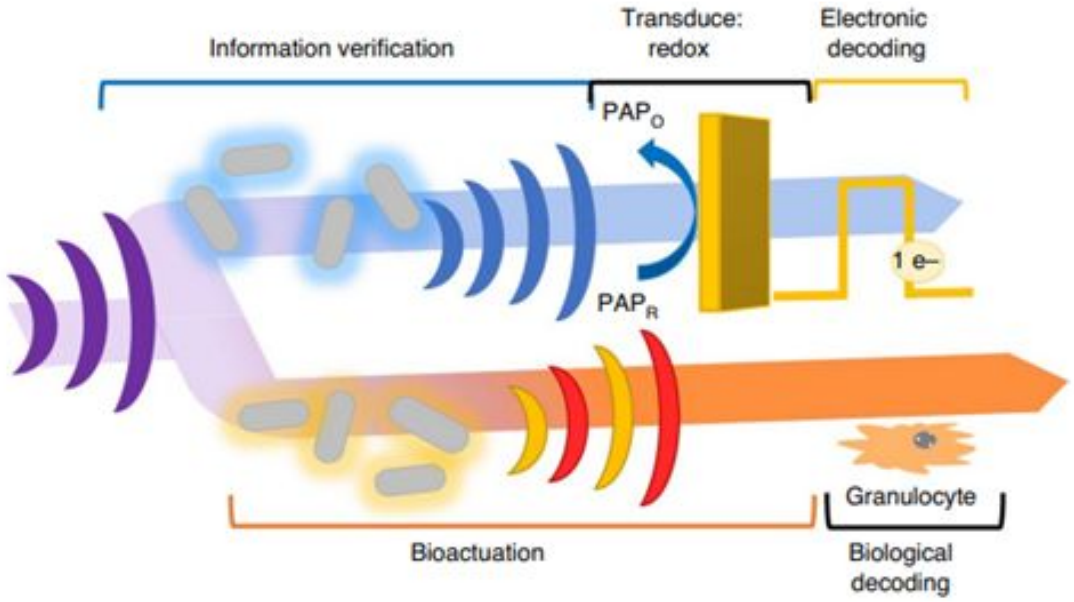
6 - Couple the bioactuator cells to the circuit

The Approach

Routing cells relay the electronic signal as biological information to

- **Verifier cells** which verify the received signal
- **Actuator cells** which convert the signal into a desired molecular product

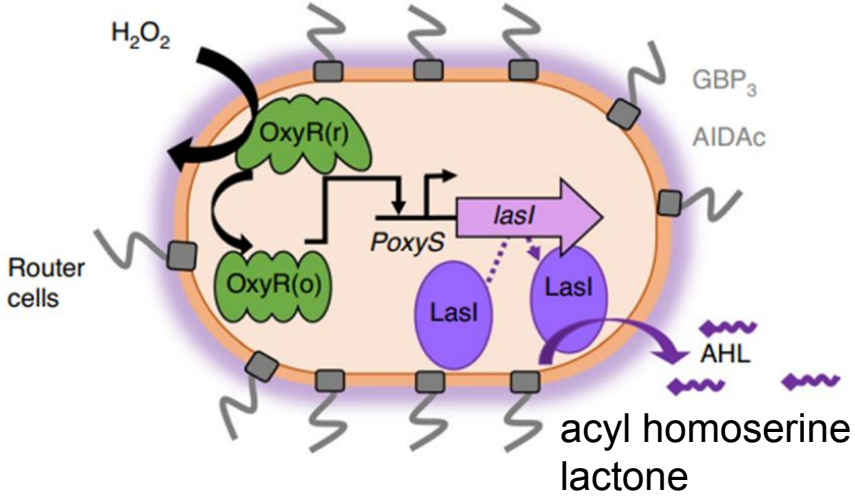




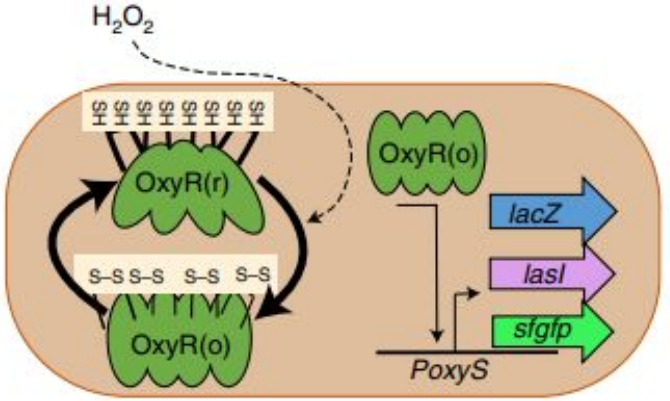
Routing cells

Respond to H_2O_2

➔ oxidizes OxyR
➔ induces *PoxyS* to express LasI
➔ synthesis of AHL
➔ relays information



0-100 μM H_2O_2 provided a benign induction range

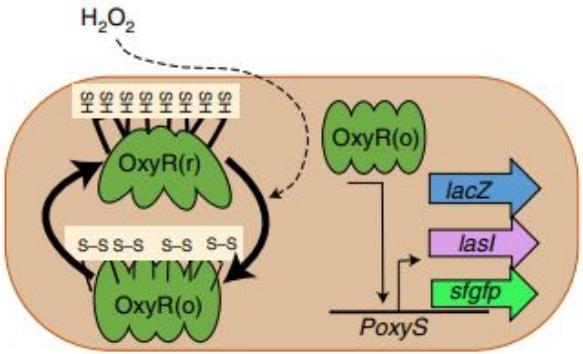


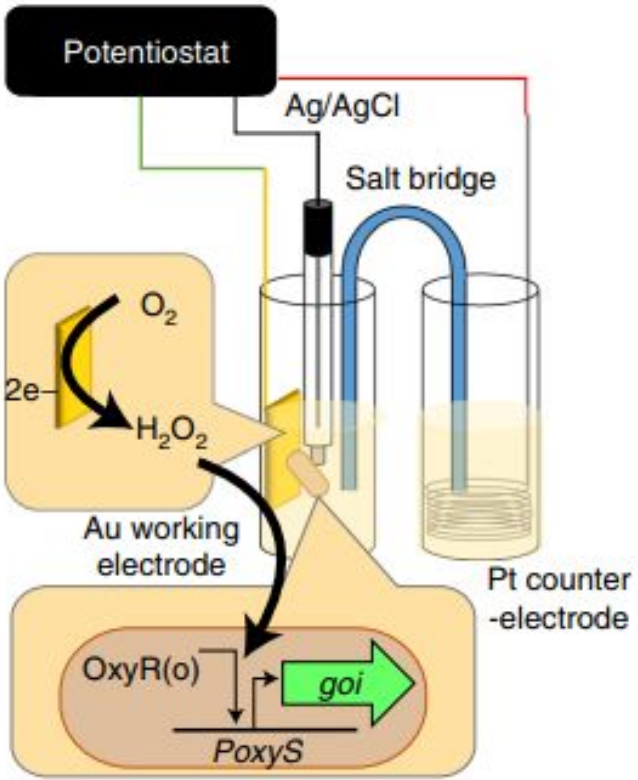
Electrical to biological signal

H_2O_2 can be generated electrochemically at benign voltages at physiological conditions

Maximum charge dose produced expression-saturating OxyR(o) levels

- corresponds to 25 μM exogenously induced control

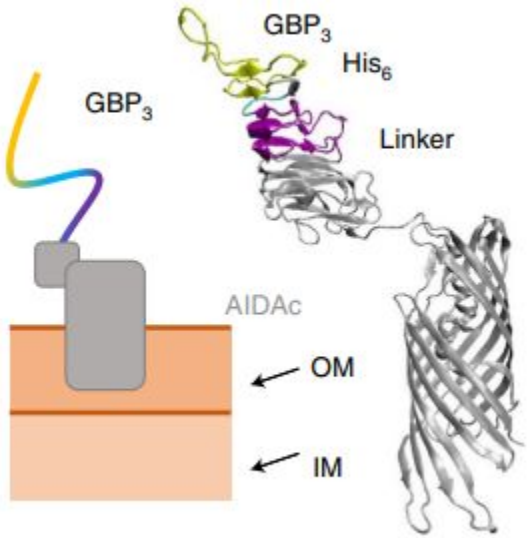




Electrode

Routing cells immobilized onto the Au working-electrode to ensure sufficient signal transfer

Assembly via peptide-mediated affinity interactions



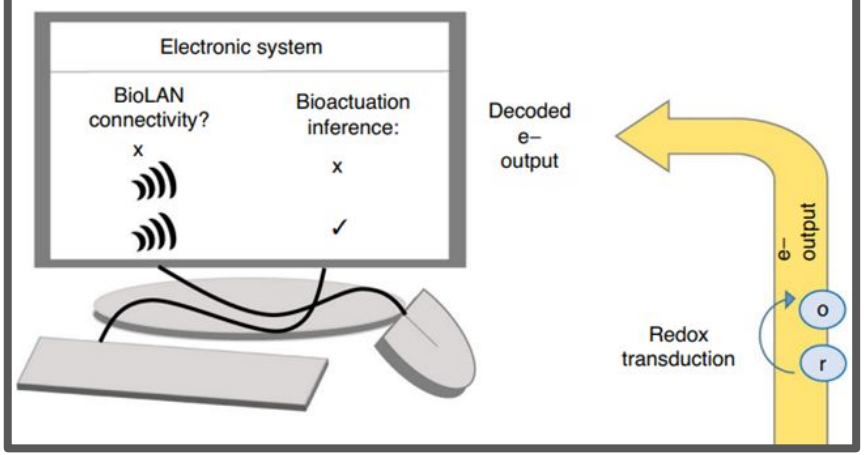
Verifier cells

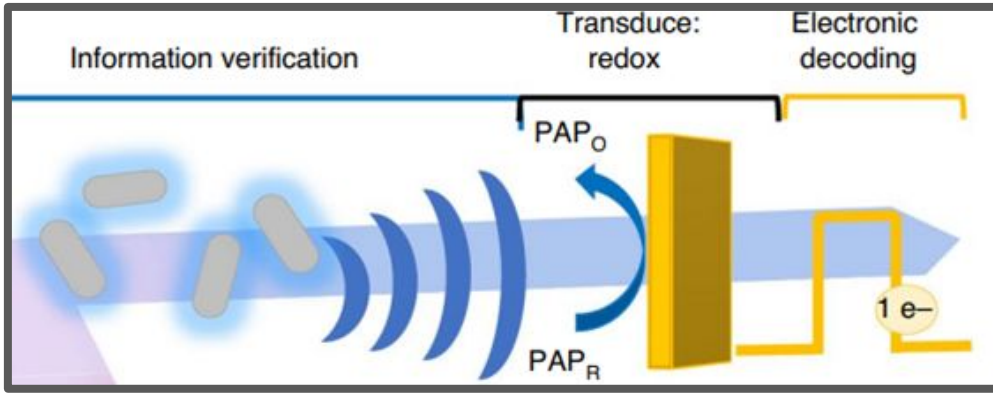
Detect the AHL signal via LasR

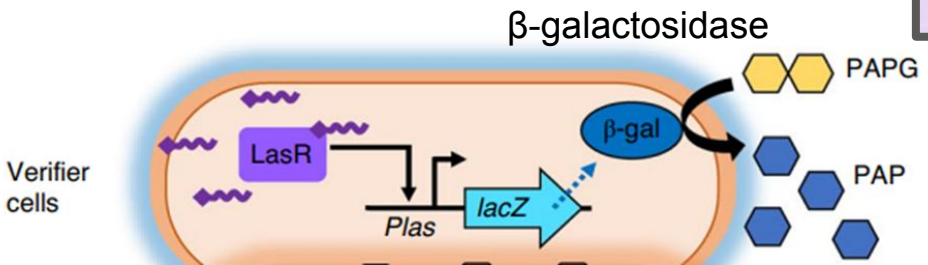
Produce β-gal

➔ cleaves PAPG to PAP

The signal is converted back to electrical through oxidation of PAP







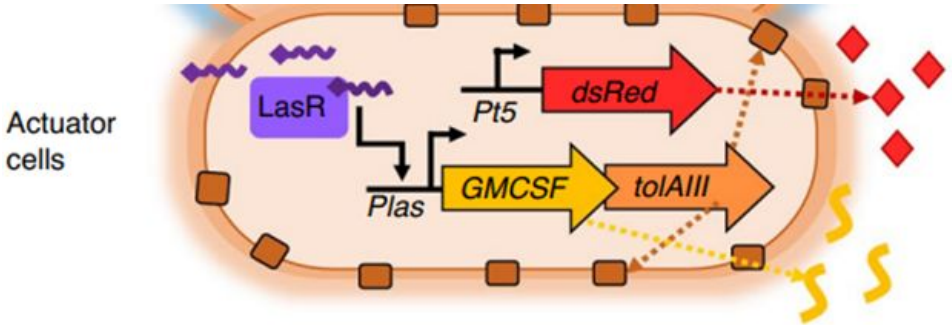
Actuator cells

Detect the AHL signal via LasR

Produce GMCSF

Up-regulate TolAIII-mediated membrane porosity

Overexpression of DsRed

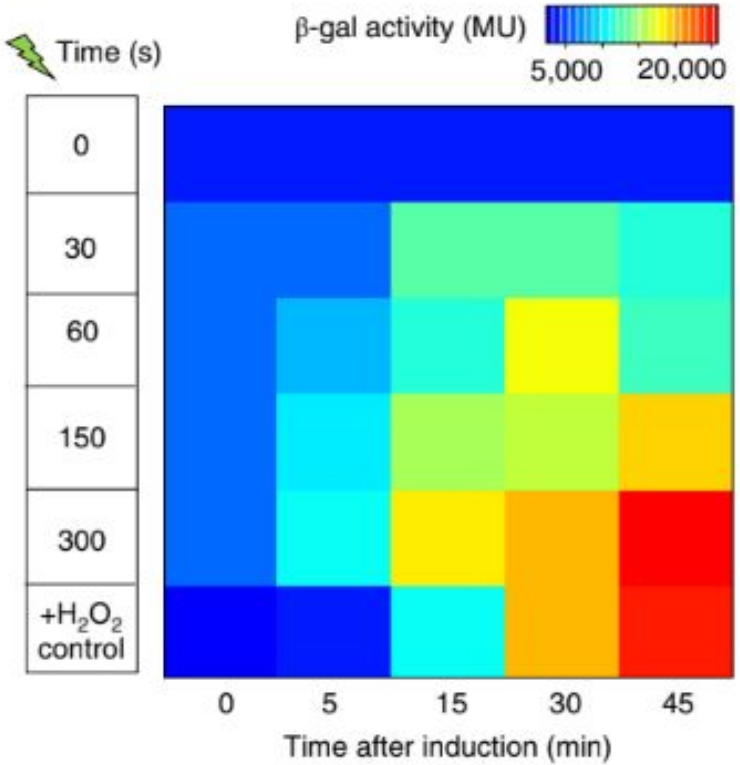


granulocyte macrophage colony-stimulating factor

Results

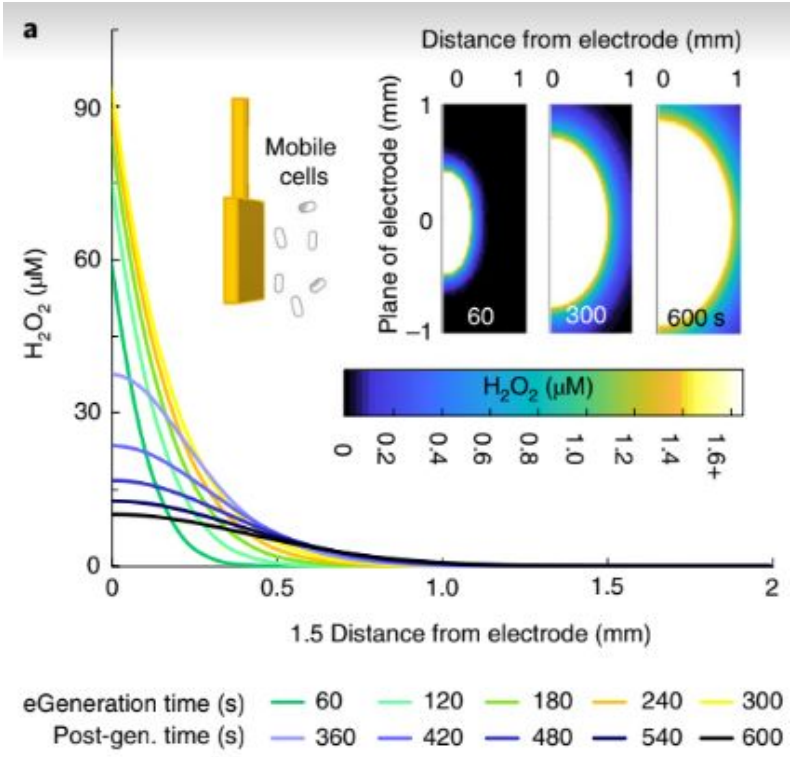
1 - Link electronic input and biological behaviour

- Tested by monitoring β-gal activity
- Cells exhibited same growth behaviour in both electrochemically produced and exogenously supplied peroxide conditions.
- Direct link between electronic input and biological behaviour



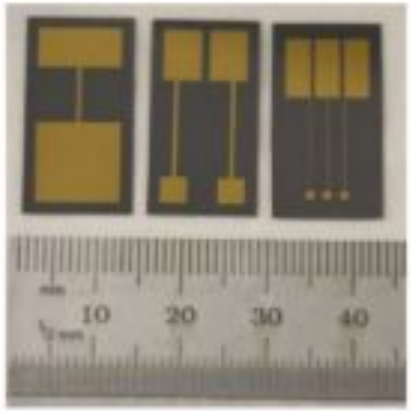
2 - Find optimal conditions for a uniform electrogenetic induction

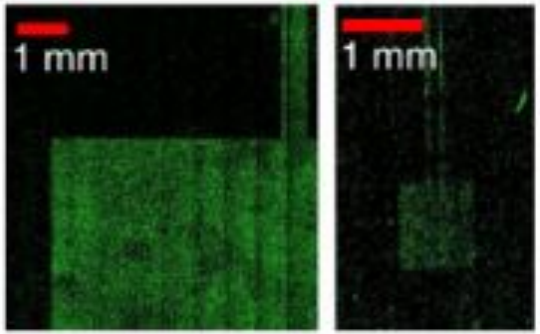
- Conditions optimized with simulation
- Peroxide gradient at the electrode in the presence of cells was tested
- Cell position was another parameter for testing
- Optimal conditions were found!



3 - Find a way to engineer cells directly onto the electrode

- The mobility of the cells needed limits for the cells so stay close to the electrode
- Cell surface was modified to have high affinity for gold
- Further testing showed a high degree of immobilized cells bound to the gold electrodes





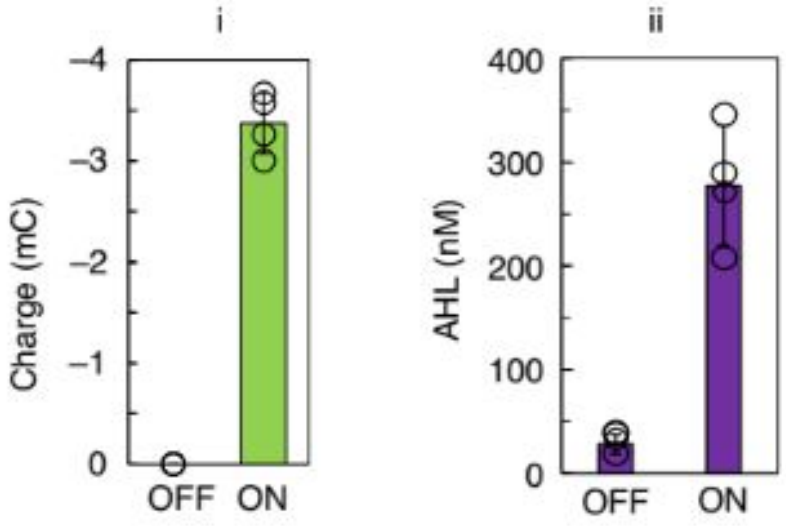
4 - Transmit the signal emitted by the first cell population

5 - Get a verification of the signal transmission on the computer

- Tested by having one culture route the signal to another culture for verification

- Verification confirmed through the electrochemical output done by the verification culture

- Demonstrates electronic-to-bio-to-electronic information exchange was a success

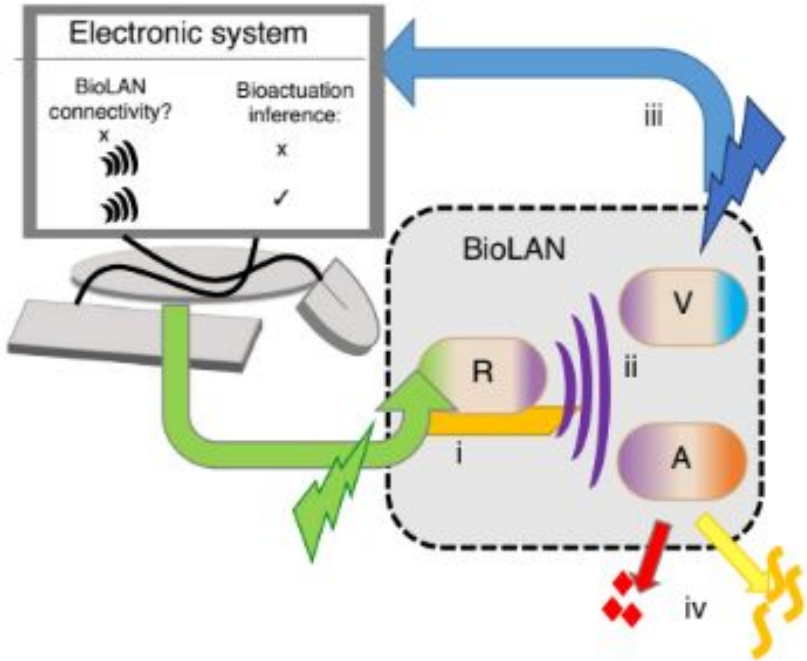


6 - Couple the bioactuator cells to the circuit

- Consortia of various composition of router, verifier and actuator cells were probed for various outputs to test actuation

- When a successful electrochemically triggered and read molecular information relay was found, parameters were further optimized

- The found BioLAN is modular and further expands the communication repertoire, thus resulting in a great success for electronic-biological interfacing



Conclusion

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- Connection of an electronic and a biological system
- Interconversion of the signal by redox molecules
- BioLAN : engineered cells with distinct roles.
- Potential applications : connect biological systeme to any electronic devices
    - ingestibles capsules, environmental sensors, electronic tattoos
    - therapy and diagnostic


Thank
you

References

Terrell et al. *Bioelectronic control of a microbial community using surface-assembled electrogenetic cells to route signals.* Nature Nanotechnol. (2021). https://doi.org/10.1038/s41565-021-00878-4