Cell

SnapShot: Electrochemical Communication in Biofilms

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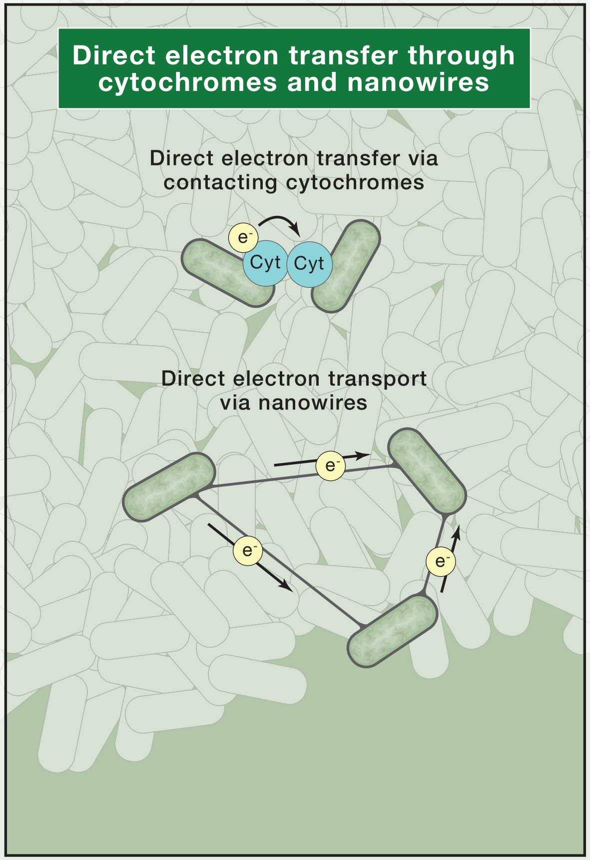
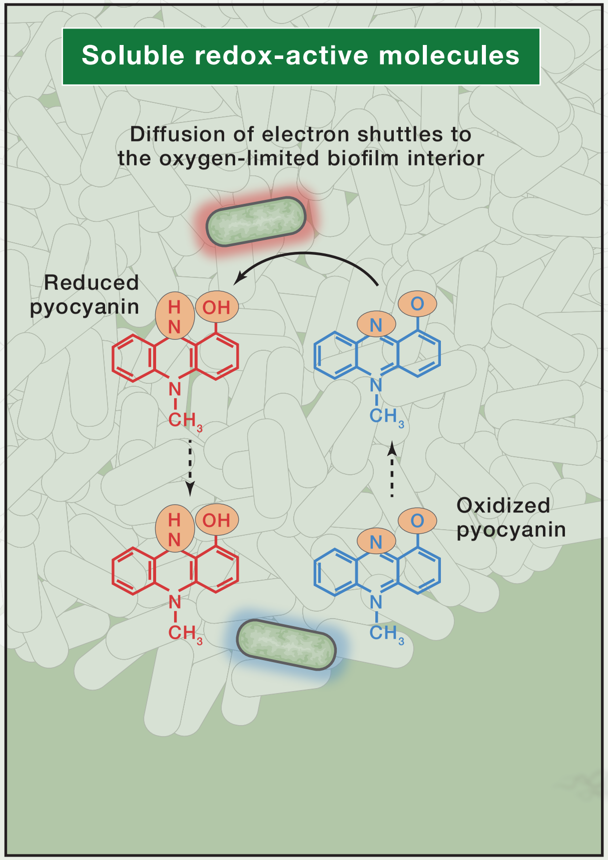
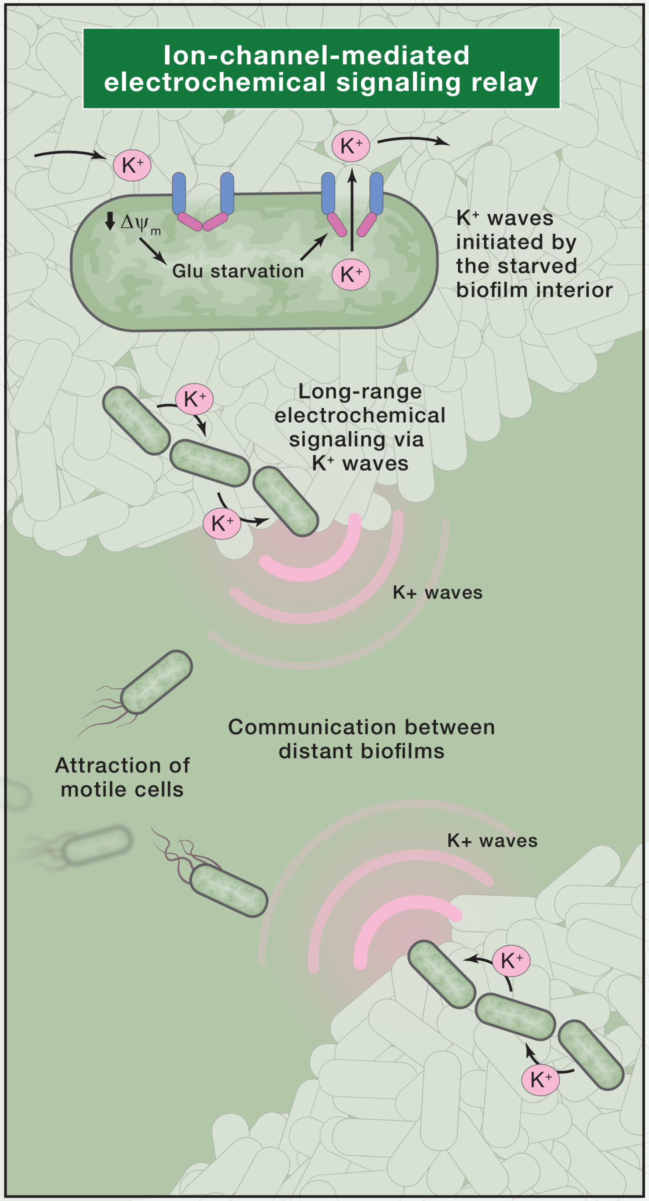


Direct electron transfer through cytochromes and nanowires



Soluble redox-active molecules



Ion-channel-mediated electrochemical signaling relay

Category	Mechanism of action	Organisms
Cytochromes and nanowires	Electron transfer through direct cell-cell contact	*Geobacter sulfurreducens*, *Shewanella oneidensis*
Soluble redox-active molecules	Electron transport via passive diffusion of shuttle molecules	*Shewanella oneidensis*, *Pseudomonas aeruginosa*
Ion-channel-mediated electrical signaling	Potassium waves propagated by active cell-cell relay	*Bacillus subtilis*

See online version for legends and references

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The role of electricity in biological systems was first appreciated through electrical stimulation experiments performed by Luigi Galvani in the 18th century. These pioneering experiments demonstrated that the behavior of living tissues is governed by the flow of electrochemical species—an insight that gave rise to the modern field of electrophysiology. Since then, electrophysiology and electrical signaling among cells has largely remained a bastion of neuroscience. However, exciting recent developments have demonstrated that even simple bacteria use electrochemical communication to coordinate population-level behaviors. These recent works are defining the emerging field of bacterial biofilm electrophysiology.

Bacteria within communities utilize electrochemical communication in three general ways: (1) direct contact via membrane-bound cytochromes and bacterial nanowires, (2) diffusive electron transfer via soluble redox-active molecules, and (3) active long-range electrochemical signaling mediated by ion channels. The identification of mechanisms that coordinate metabolic activity in biofilms is fundamental to understanding biofilm development and may enable new strategies for biofilm control. In addition, understanding how bacteria communicate using electrochemical signals may reveal new avenues for biotechnologies that harness these living systems by transmitting signals to and from cells at hybrid living-synthetic interfaces.

Electrochemical Communication by Direct Contact: Cytochromes and Bacterial Nanowires

Multiple bacterial species can undergo electrochemical communication by direct contact, either through membrane-associated cytochromes (McGlynn et al., 2015) or along bacterial nanowires (Gorby et al., 2006; Reguera et al., 2005; Malvankar et al., 2011; Pfeffer et al., 2012). Electrochemical communication through direct contact thus involves short-range interactions between bacteria in biofilm communities. While the range of interaction is generally limited, direct electron transfer may provide increased stability of interaction relative to the exchange of a diffusible signal, where environmental fluctuations have more influence over the communication process.

Cells within *Geobacter sulfurreducens* biofilms are known to make direct electrical contacts via outer-surface c-type cytochromes. In recent work, metabolic interactions among consortia of uncultured methane-oxidizing archaea and sulfate-reducing bacteria provided the first evidence for syntrophic coupling through direct electron transfer via cytochromes in these important paired organisms (McGlynn et al., 2015). *Shewanella oneidensis* (Gorby et al., 2006) and *G. sulfurreducens* (Reguera et al., 2005; Malvankar et al., 2011) are known to produce electrically conductive pilus-like appendages called bacterial nanowires in direct response to electron-acceptor limitation. Further, recent work has shown that electrically conductive appendages are not exclusive to dissimilatory metal-reducing bacteria (Pfeffer et al., 2012).

Electrochemical Communication through Passive Diffusion: Soluble Redox-Active Molecules

A number of both Gram-negative and Gram-positive bacteria have the ability to produce redox-active electron shuttles to promote electron transfer between cells at a distance. This approach is advantageous since electrons would normally require a discrete pathway to traverse long distances.

The concept of self-produced electron shuttles originated from studies that demonstrated that *S. oneidensis* can perform electron transfer to reduce iron when not in direct contact, which was attributed to the release of flavin in *S. oneidensis* cultures (Marsili et al., 2008). *S. oneidensis* can reduce flavins at the outer cell surface with the c-type cytochrome MtrC, which is part of a multiprotein complex that transports electrons from the periplasm to the outer surface of the cell and serves as flavin reductase. Further, since some redox-active molecules have profound effects on the structural organization of biofilms formed by divergent bacteria, it shows that such secondary metabolites play important conserved roles in gene expression and development (Dietrich et al., 2008).

Electrochemical Communication through Active Signaling: Ion-Channel-Mediated Electrical Signaling

It was recently shown that ion channels conduct long-range electrical signals within *Bacillus subtilis* biofilms through spatially propagating waves of potassium (Prindle et al., 2015). Importantly, the process of active signaling (cell-cell relay of the extracellular signal) enables the electrochemical coordination of metabolism over greater distances than would be possible through passive diffusion alone.

The concept of a prokaryotic paradigm for active, long-range electrical signaling mediated by ion channels originated from studies that demonstrated that metabolic oscillations in *B. subtilis* biofilms were synchronized by waves of extracellular potassium (Prindle et al., 2015). Using this model system, it was recently shown that extracellular potassium emitted from the biofilm alters the membrane potential of distant cells, thereby directing their motility to attract them to the biofilm (Humphries et al., 2017). In a related study, it was shown that two *B. subtilis* biofilm communities undergoing metabolic oscillations could engage in a time-sharing behavior in which each community takes turns consuming nutrients, thus enabling biofilms to counterintuitively increase growth under reduced nutrient supply (Liu et al., 2017).

Conclusions

While electrophysiology has generally been associated with neuroscience, multiple recent developments have demonstrated that bacteria within communities also utilize electrochemical communication. It may thus be that collective behaviors in the brain share some mechanistic links with phylogenetically ancient metabolic stress response strategies dating back to biofilm communities. It will be exciting to see what further discoveries will be made in the coming years within this emerging field of biofilm electrophysiology.

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