

This distinctive structure produces a highly interconnected and interpenetrating pathway for both electrons and ions, which is desirable for achieving a high rate capability even in thick electrodes with practical levels of mass loading. Both a high capacity and a high rate capability at a high mass loading can be realized. Specifically, even at a rate of 10 C (requiring about 6 min for charge or discharge), there is little difference in specific capacity at mass loadings ranging from 1 to 11 mg cm⁻², the latter being near that required for practical cells (3).

This work should inspire further efforts in the rational design of electrode material structure for the development of practical electrodes with high mass loadings. For example, the integration of this 3D HGF scaffold with silicon nanostructures or sulfur may improve the cell-level capacity and rate capability of these electrode materials. Continued efforts in designing novel electrode structures that could further promote the charge delivery rate will lead to an even higher rate capability, thus accelerating the development of superior active materials in practical cells. These innovative electrode structures and processing technologies may also allow the design of electrochemical cells with many new features, such as flexibility, intelligence, integration, and miniaturization.

In an ideal future world, we might realize the dream of being able to freely use electrical energy at any time and in any place. To help make this dream come true, the performance of energy-storage cells will need to be improved through innovations from nanotechnology. New electrode-material configurations will also need advances in fabrication technologies, such as freeze-casting, 3D printing, and holographic patterning. Meanwhile, we should not only construct novel configurations of active materials but also innovate electrolytes and separators because it is important to develop smart technologies to fabricate all of the components of energy-storage cells in an economically viable and time-efficient manner. ■

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BIOFILMS

Coupling and sharing when life is hard

Bacterial colonies coordinate growth dynamics when nutrients are limited

By Vernita Gordon

Biological systems interact in a multitude of complex ways. For example, constituent cells in a multicellular organism communicate with each other, often using diffusible chemical signals. Another example is competition among organisms for resources, a phenomenon observed even in the simplest ecologies. Such interactions typically are not character-

Oscillations occur as a result of a negative feedback loop; for example, springs or gravity can provide restoring forces and thus negative feedback in mechanical oscillators. This generality allows concepts that are developed for mechanical systems that undergo periodic displacement in space to be applied to many other systems in which interactions are not mechanical and the oscillating quantity is not spatial. Oscillations in predator-prey systems arise because the prey serves as a resource supporting growth of the predator population, creating two linked negative feedback loops. Liu *et al.* use experimental measurements and physical modeling to examine two bacterial colonies that are grown in contact with the same reservoir of fluid growth medium. These colonies do not touch each other, but their growth rates oscillate in phase when intercolony signaling dominates and out of phase when intercolony competition dominates.

Alone, each colony's growth rate can oscillate as a result of rapid growth that depletes a key resource—this provides the requisite negative feedback loop. These oscillations are controlled by diffusible signals, which can be transported outside their originating colony to the other colony, and thereby synchronize

the two colonies' oscillations in growth rate. Liu *et al.* developed a mathematical model to describe the resulting "communication" between colonies. Coupling by communication promotes in-phase oscillations. However, these two colonies are also coupled in another way—by competition for the growth resource glutamate. Thus, if the two colonies synchronize their oscillations in growth rate, as communication would have them do, they will each experience high competition from the other colony at times of rapid growth. This is a disadvantage of synchronized oscillations, which would tend to reduce overall growth rates. A naïve analogy with mechanical oscillators might suggest



Biofilm communities of *Bacillus subtilis* that compete for the same resources can synchronize their growth dynamics (*B. subtilis* on a semisolid medium is shown).

ized by oscillations—that is, there is no regular, cyclic variation in the value of a relevant parameter. Tellingly, the most striking exception to this generalization is found in some predator-prey dynamics in which the size of the prey population oscillates out of phase with the size of the predator population (1). On page 638 of this issue, Liu *et al.* (2) report that the oscillatory growth rates of two discrete bacterial colonies become coupled, a behavior that is linked to their competition for a common and limited resource.

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that competition acts like a damping factor, similar to when friction reduces the amplitude of oscillation. Instead, something entirely different happens. Under conditions of high competition (corresponding to low nutrient availability and low communication), the two colonies adjust their oscillations such that they are out of phase with each other. This allows each colony to maximize its overall growth, because each colony is in the rapid-growth time of its cycle when its competitor is in the slow-growth time of its cycle. This has some similarity to the out-of-phase oscillations of predator and prey populations, except there is also a “hidden” mediating resource in the form of glutamate availability.

Resource competition occurs widely in biological, economic, and social sciences. For resource competition to occur, the system must be correctly characterized by multiple competitors, whether single-celled microbes or multicellular organisms. That resource competition is a meaningful characteristic of the two-colony biofilm studied by Liu *et al.* highlights the ambiguity inherent in the nature of biofilms. In one sense, each bacterial colony may be thought of as a population of individuals, each of which competes for, and can deplete, growth resources. Such a view has been adopted by prior biofilm studies (3, 4). However, on longer length scales, discrete colonies interact with each other as if each colony were a single multicellular organism. This ties in to an emerging area of study on how the spatial structure of biofilms affects their biology. Here, “spatial structure” encompasses the arrangement of distinct cell types within a single colony or aggregate, and the sizes, spacing, and cell types of multiple colonies and aggregates (5). This is important because many real-world biofilms, such as those found in human infections, are composed of multiple species and multiple small, discrete aggregates (6). Bacteria can interact, both within and across species, in ways that could alter disease course (7). However, how spatial arrangement governs these interactions is not well understood. About a century ago, Albert Einstein objected to “spooky action at a distance.” Studies such as that of Liu *et al.* show an approach to understanding biological action at a distance in a way that is not at all spooky. ■

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CELL BIOLOGY

Keeping in touch with the ER network

Growth factor receptor internalization occurs at sites of transient membrane contacts

By Xiaojun Tan¹ and Richard A. Anderson²

The epidermal growth factor receptor (EGFR) has fundamental roles in physiology and cancer. It is rapidly internalized (endocytosed) from the cell surface upon ligand binding and activation and can either sustain its signaling by being recycled back to the plasma membrane or get delivered to the lysosome where it is degraded (1). After much debate, it is currently thought that EGFR endocytosis involves clathrin-mediated (CME) and

“These membrane contacts, transient or constant, dynamically control local cellular events...”

nonclathrin (NCE) mechanisms depending on the ligand concentration and cellular context, with the molecular details of the latter route poorly defined (1, 2). On page 617 of this issue, Caldieri *et al.* (3) report that the NCE pathway involves transient endoplasmic reticulum (ER)–plasma membrane contacts formed close to the sites of EGFR internalization.

Using a proteomic approach, Caldieri *et al.* found more than 100 proteins enriched in purified EGFR-containing NCE vesicles. Further RNA-silencing experiments identified nine of these proteins as EGFR-NCE regulators, including, surprisingly, four ER proteins. Among them, the ER tubulation factor reticulon 3 (RTN3) was found to be an essential regulator. Although RTN3 localized specifically to the ER in all conditions tested, it was found in close proximity to activated EGFR. This suggests the involvement of potential ER–plasma membrane contacts because the ER has frequent contacts with various organelles (4). The

authors further demonstrated that RTN3 is required for transient ER–plasma membrane contacts at sites of membrane invagination where EGFR is endocytosed. These membrane contact sites showed increased Ca²⁺ release from the ER, an event that is required for membrane fission, which is the final step of EGFR internalization. Indeed, Ca²⁺ release has been observed at the site of ER contact with other organelles and plays fundamental roles in local trafficking events (5). The findings of Caldieri *et al.* advance our understanding of EGFR-NCE by defining ER–plasma membrane contacts as an essential signaling platform that regulates nonclathrin-mediated invagination, maturation, and fission of EGFR-containing membrane.

Intriguingly, the ER–plasma membrane contacts were selectively observed in EGFR-NCE but not for CME. The NCE pathway is correlated with the lysosomal degradation of activated EGFR, whereas a large percentage of receptor recycling occurs downstream of CME (6). Whether NCE activates specific downstream signaling molecules that are different from those in CME remains to be determined. However, EGFR-NCE, in response to various pathological and therapeutic stress stimuli, results in unusual EGFR functions in many cancer cells that provide a survival advantage and resistance to therapeutics (7). Given the increasing interest of cancer biology fields in ligand-independent, stress-induced EGFR trafficking and signaling pathways, many of which are based on EGFR-NCE (7), it would be interesting to investigate the roles of ER–plasma membrane contacts in EGFR endocytosis in these situations. Understanding the molecular mechanisms and physiological and pathological consequences of EGFR-NCE could be important for developing approaches to overcome cancer therapeutic resistance.

Is it so surprising to find a role for ER–plasma membrane contacts in EGFR-NCE? Although all cellular functions are ultimately carried out by proteins, whole-cell and compartmental structures are based on lipids and membranes. The physical and functional interactions between proteins

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Coupling and sharing when life is hard

Vernita Gordon (May 11, 2017)

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