2. Chan, C.S., Guzman, J.N., Ilijic, E., Mercer, J.N., Rick, C., Tkatch, T., Meredith, G.E., and Surmeier, D.J. (2007). "Rejuvenation" protects neurons in mouse models of Parkinson's disease. Nature *447*, 1081–1086.

3. Pissadaki, E.K., and Bolam, J.P. (2013). The energy cost of action potential propagation in dopamine neurons: clues to susceptibility in Parkinson's disease. Front. Comput. Neurosci. *7*, 13.

4. Matsuda, W., Furuta, T., Nakamura, K.C., Hioki, H., Fujiyama, F., Arai, R., and Kaneko, T. (2009). Single nigrostriatal dopaminergic neurons form widely spread and highly dense axonal arborizations in the neostriatum. J. Neurosci. *29*, 444–453.

5. Pacelli, C., Giguère, N., Bourque, M.-J., Lévesque, M., Slack, R.S., and Trudeau, L.-É. (2015). Elevated mitochondrial bioenergetics and axonal arborization size are key contributors to the vulnerability of dopamine neurons. Curr. Biol. *25*, 2349–2360.

6. Nair-Roberts, R.G., Chatelain-Badie, S.D., Benson, E., White-Cooper, H., Bolam, J.P., and Ungless, M.A. (2008). Stereological estimates of dopaminergic, GABAergic and glutamatergic neurons in the ventral tegmental area, substantia nigra and retrorubral field in the rat. Neuroscience *152*, 1024–1031.

7. Bolam, J.P., and Pissadaki, E.K. (2012). Living on the edge with too many mouths to feed: Why dopamine neurons die. Mov. Disord. *27*, 1478–1483.

8. Harris, J.J., Jolivet, R., and Attwell, D. (2012). Synaptic energy use and supply. Neuron *75*, 762–777.

9. Zhou, C., Huang, Y., and Przedborski, S. (2008). Oxidative stress in Parkinson's disease: a mechanism of pathogenic and therapeutic significance. Ann. N. Y. Acad. Sci. *1147*, 93–104.

10. Sian, J., Dexter, D.T., Lees, A.J., Daniel, S., Agid, Y., Javoy-Agid, F., Jenner, P., and Marsden, C.D. (1994). Alterations in glutathione levels in Parkinson's disease and other neurodegenerative disorders affecting basal ganglia. Ann. Neurol. *36*, 348–355.

11. Kim-Han, J.S., Antenor-Dorsey, J.A., and O'Malley, K.L. (2011). The Parkinsonian mimetic, MPP^+, specifically impairs mitochondrial transport in dopamine axons. J. Neurosci. *31*, 7212–7221.

12. Liang, C.L., Wang, T.T., Luby-Phelps, K., and German, D.C. (2007). Mitochondria mass is low in mouse substantia nigra dopamine neurons: Implications for Parkinson's disease. Exp. Neurol. *203*, 370–380.

13. Cheng, H.-C., Ulane, C.M., and Burke, R.E. (2010). Clinical progression in Parkinson disease and the neurobiology of axons. Ann. Neurol. *67*, 715–725.

Biofilms: How Structure Emerges from Conflict

Nicole Vega and Jeff Gore
Physics of Living Systems, Department of Physics, Massachusetts Institute of Technology, Cambridge, MA 02139, USA
Correspondence: nvega@mit.edu (N.V.), gore@mit.edu (J.G.)
http://dx.doi.org/10.1016/j.cub.2015.07.007

Natural bacterial populations often live on surfaces in complex communities called biofilms. These stress-resistant groups are often thought to result from cooperative interactions between disparate species, but recent experiments argue that biofilms are primarily a protective response to competition.

Historically, microorganisms have generally been studied in isogenic, planktonic cultures, with the microorganisms floating free from attachment in simple, well-mixed environments. In modern microbiology, however, there is a great deal of interest in what happens when microbes abandon their free-living lifestyle to form self-adhered communities known as biofilms. This interest is not merely academic — biofilms are extremely common in nature, and they frequently run afoul of human interests [1]. Clinical biofilms on implanted and indwelling devices (such as catheters and stents) and elsewhere in the body (for example, *Pseudomonas aeruginosa* biofilms in the lung) form infections that are extremely difficult to eradicate (Figure 1A). In the wider world, 'biofouling' by overgrowth of microbial biofilms is an expensive and ubiquitous problem in industries ranging from aquaculture to shipping to oil production (Figure 1B). Given that biofilms are an example of apparently successful group living, many researchers have thought of biofilms as examples of microbial cooperation. A recent paper by Oliveira *et al.* [2], however, provides evidence that biofilm formation is often induced as a result of competition.

The idea of biofilms as cooperative endeavors has a substantial recent history. This idea comes partly from the surprising structural and functional complexity within these communities [3]. Consistent with the idea that biofilms are cooperative, cell–cell communication has been shown to direct aspects of biofilm establishment and maturation, such as microcolony aggregation and cell differentiation [4,5]. It has even been suggested that these events are part of a multicellular developmental program that has evolved in the spatially localized niche provided by surface-associated biofilms, which can integrate multiple microbial species into a physically adhered and physiologically coordinated community [3].

Other recent work suggests that this sort of coordinated, communication-mediated growth and differentiation is not always necessary to explain biofilm development. A variety of stresses have been shown to induce biofilm formation, including exposure to antibiotics [6] and other natural products that cause cell damage [7]. Biofilm formation can therefore represent a protective response for bacteria experiencing physiological stress [8].

Furthermore, much of our understanding comes from the study of isogenic biofilms in the laboratory, making it unclear how well the cooperative model describes the taxonomically diverse biofilms present in nature [9]. It has been suggested that competition, rather than cooperation, should dominate in

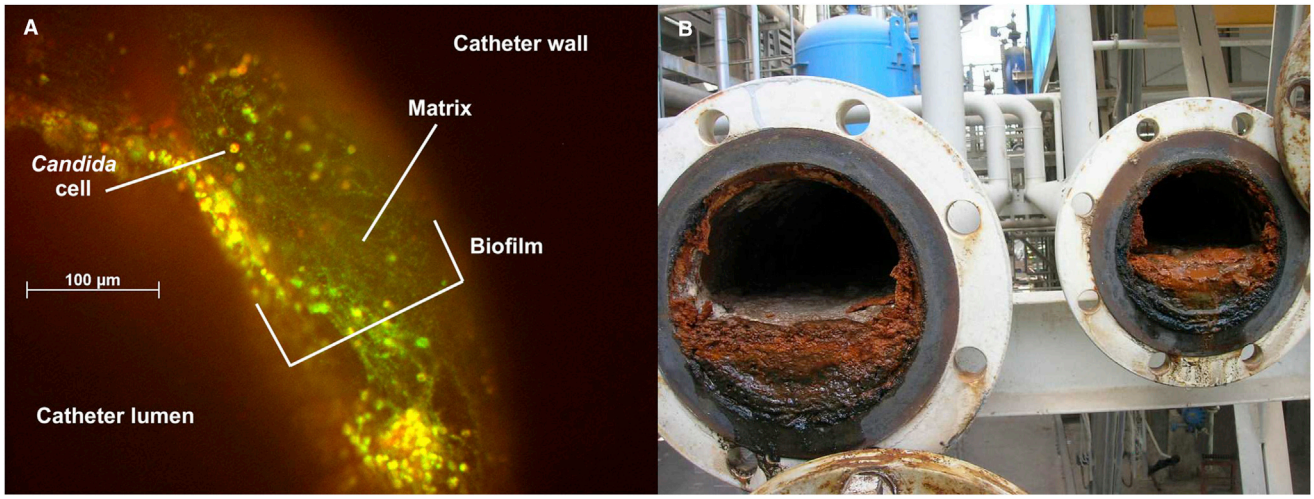

Figure 1. Commonly occurring biofilms in medical and industrial settings.
(A) Fluorescence image of *in vivo Candida* albicans biofilm inside a medical catheter [20]. (B) Biofouling in a seawater pipe. Photo: MERUS GmbH.

polymicrobial communities [10], raising the question of how common cooperative multicellular behavior is likely to be in diverse biofilms [11,12].

Oliveira *et al.* [2] tie these ideas together by demonstrating a case in which competition, rather than cooperation, between strains is the driving force behind biofilm formation. Specifically, they found that biofilm formation is induced as a protective response to antibiotic production by competing strains. The observed behavior is a form of 'competition sensing' [13], in which bacteria sense an environmental cue (in this case, a sub-lethal concentration of antibiotic) that signals the presence of another strain, and then interpret this signal as a cue of impending competition. Importantly, in the new study [2], though biofilm formation was triggered by sub-lethal concentrations of antibiotic (cell death was not required), cellular damage did seem to be required, implying that the observed increase in biofilm formation was a response to antimicrobial warfare rather than to reception of the antibiotic as an innocuous extracellular signal.

This study provides evidence against an increasingly common view of low-dose antibiotics as non-toxic signaling molecules. It has previously been suggested that, at the low concentrations likely found in those natural environments shared by disassociated microbes, antibiotics could have evolved as signals rather than as agents of warfare [14,15]. The work by Oliveira *et al.* [2] presents an interesting counterpoint, providing evidence that secreted antibiotics can both act as agents of bacterial warfare and provide information at low concentrations, and that this information can be used to inform the behavior of competing bacteria.

This new study builds on a body of work indicating that competitive interactions might be more important than previously suspected in directing biofilm formation and structure. Indeed, previous work from the same lab demonstrated how competition between strains in a biofilm could promote secretion of the extracellular polymeric substance (EPS) that forms the structure of biofilms, as secretion of this EPS matrix allows producing strains to push their growing colonies into more favorable nutrient/oxygen conditions [16]. Further, this group has shown how quorum-sensing-directed cooperative behavior within strains can be used to direct competitive EPS production, allowing strains to compete more effectively in mixed biofilms [17]. The authors suggest that competition-sensing-dependent biofilm formation could work in conjunction with these mechanisms: by increasing attachment and/or biomass production early, a bacterial strain could achieve dominance in a 'young' biofilm, putting itself in a better position to make use of density-dependent competitive tools.

Intriguingly, though the end result (increased biofilm) is consistent throughout the data reported by Oliveira *et al.* [2], the nature of the physiological response to competition seems to differ between bacterial strains. Increased biofilm formation is not always accompanied by increased attachment, as observed in flow cell assays in the present study. It remains unclear whether there are distinct advantages to only increasing biofilm accumulation, versus increasing initial attachment, and if so, what determines those advantages for a particular strain and/or environmental scenario.

Furthermore, it will be interesting to see how this result applies to other combinations of bacterial strain and antibiotic. The dose–response relationship of antibiotic to biofilm formation is anything but simple; although there is a characteristic biphasic response, with low doses resulting in biofilm stimulation and high doses resulting in biofilm inhibition, U-shaped and multiphasic responses are common [6]. In a few cases, as with azithromycin treatment of *P. aeruginosa*, the opposite effect has been observed, in which subinhibitory concentrations of antibiotic decreased biofilm formation [18]. It remains to be determined whether these observations are relevant for natural biofilms containing antibiotic-secreting strains and their competitors.

The generality of the new findings will doubtless be of considerable interest, particularly at increasing taxonomic distances. The present study intentionally focused on competition sensing between closely related strains of the same

bacterial species, as these are expected to have high levels of ecological overlap and therefore strong ecological competition. As the authors state, this scenario may be directly relevant for clinical biofilms of *P. aeruginosa*, as different strains can and do encounter one another in the lung [19]. It will be interesting to see how the strength of the competition-sensing effect is altered by taxonomic distance on larger scales, and whether there is a role for co-evolution of strains that frequently encounter one another in natural environments. Furthermore, although contests between strains in this study produced clear victors, with one strain dominating in the biofilm while the loser was all but wiped out, the role of competition in stable, taxonomically diverse biofilms remains to be clarified.

REFERENCES

1. Costerton, J.W., Cheng, K.J., Geesey, G.G., Ladd, T.I., Nickel, J.C., Dasgupta, M., and Marrie, T.J. (1987). Bacterial biofilms in nature and disease. Annu. Rev. Microbiol. *41*, 435–464.

2. Oliveira, N.M., Martinez-Garcia, E., Xavier, J., Durham, W.M., Kolter, R., Kim, W., and Foster, K.R. (2015). Biofilm formation as a response to ecological competition. PLoS Biol. *13*, e1002191.

3. Stoodley, P., Sauer, K., Davies, D.G., and Costerton, J.W. (2002). Biofilms as complex differentiated communities. Annu. Rev. Microbiol. *56*, 187–209.

4. Webb, J.S., Givskov, M., and Kjelleberg, S. (2003). Bacterial biofilms: prokaryotic adventures in multicellularity. Curr. Opin. Microbiol. *6*, 578–585.

5. Davies, D.G., Parsek, M.R., Pearson, J.P., Iglewski, B.H., Costerton, J.W., and Greenberg, E.P. (1998). The involvement of cell-to-cell signals in the development of a bacterial biofilm. Science *280*, 295–298.

6. Kaplan, J.B. (2011). Antibiotic-induced biofilm formation. Int. J. Artif. Organs. *34*, 737–751.

7. López, D., Fischbach, M.A., Chu, F., Losick, R., and Kolter, R. (2009). Structurally diverse natural products that cause potassium leakage trigger multicellularity in *Bacillus subtilis*. Proc. Natl. Acad. Sci. USA *106*, 280–285.

8. Hoffman, L.R., D'Argenio, D.A., MacCoss, M.J., Zhang, Z., Jones, R.A., and Miller, S.I. (2005). Aminoglycoside antibiotics induce bacterial biofilm formation. Nature *436*, 1171–1175.

9. Zengler, K., and Palsson, B.O. (2012). A road map for the development of community systems (CoSy) biology. Nat. Rev. Microbiol. *10*, 366–372.

10. Foster, K.R., and Bell, T. (2012). Competition, not cooperation, dominates interactions among culturable microbial species. Curr. Biol. *22*, 1845–1850.

11. Mitri, S., Xavier, J.B., and Foster, K.R. (2011). Social evolution in multispecies biofilms. Proc. Natl. Acad. Sci. USA *108*, 10839–10846.

12. Nadell, C.D., Xavier, J.B., and Foster, K.R. (2009). The sociobiology of biofilms. FEMS Microbiol. Rev. *33*, 206–224.

13. Cornforth, D.M., and Foster, K.R. (2013). Competition sensing: the social side of bacterial stress responses. Nat. Rev. Microbiol. *11*, 285–293.

14. Fajardo, A., and Martínez, J.L. (2008). Antibiotics as signals that trigger specific bacterial responses. Curr. Opin. Microbiol. *11*, 161–167.

15. Romero, D., Traxler, M.F., López, D., and Kolter, R. (2011). Antibiotics as signal molecules. Chem. Rev. *111*, 5492–5505.

16. Xavier, J.B., and Foster, K.R. (2007). Cooperation and conflict in microbial biofilms. Proc. Natl. Acad. Sci. USA *104*, 876–881.

17. Nadell, C.D., Xavier, J.B., Levin, S.A., and Foster, K.R. (2008). The evolution of quorum sensing in bacterial biofilms. PLoS Biol. *6*, e14.

18. Ichimiya, T., Takeoka, K., Hiramatsu, K., Hirai, K., Yamasaki, T., and Nasu, M. (1996). The influence of azithromycin on the biofilm formation of *Pseudomonas aeruginosa* in vitro. Chemotherapy *42*, 186–191.

19. Renders, N., Verbrugh, H., and Van Belkum, A. (2001). Dynamics of bacterial colonisation in the respiratory tract of patients with cystic fibrosis. Infect. Genet. Evol. *1*, 29–39.

20. Andes, D., Nett, J., Oschel, P., Albrecht, R., Marchillo, K., and Pitula, A. (2004). Development and characterization of an *in vivo* central venous catheter *Candida albicans* biofilm model. Infect. Immun. *72*, 6023–6031.

Social Learning: Parents May Not Always Know Best

Simon C. Griffith* **and Culum Brown**
Department of Biological Sciences, Macquarie University, Sydney, NSW 2109, Australia
*Correspondence: simon.griffith@mq.edu.au
http://dx.doi.org/10.1016/j.cub.2015.07.022

The efficiency with which animals learn new skills depends on their ability to choose good tutors. A new study shows that early-life stress causes young zebra finches to switch tutor preference from parents to unrelated adults.

For over half a century, we have been fascinated by the way in which animal populations acquire novel behavioural skills that spread from individual to individual. The copying of behaviour, and the regional differences that often develop, can shine a light on the evolution of human culture [1]. One of the earliest examples of the spread of innovative behaviour in animals was made by Fisher and Hinde [2], who described the diffusion of the stealing of cream from foil-capped milk bottles by various British tit species — a behaviour that spread across the country from the 1920s to 1940s. While this original study was observational, and could potentially have been caused by individual learning, a recent experimental study [3] revisited this classic example and demonstrated that blue tits (*Cyanistes caeruleus)* can efficiently acquire the necessary skills to exploit this very unnatural — but rich — resource by observing others.

