been used in computer-assisted simulations that resulted in realistically migrating cells [11]. Despite their innate beauty, validation of these models depends on the identification of the molecular components that represent the parameters of the model; in particular, the so-called local inhibitor that facilitates the negative feedback has remained elusive. Arpin is now a prime candidate for this local inhibitor, given that it is a competitive inhibitor of actin filament nucleation and has been shown experimentally to contribute to the collapse of lamellipodia.

The current research opens up various new avenues of research. One of immediate interest is whether loss of Arpin function is associated with increased cell motility in epithelial–mesenchymal transition during the progression of cancer. The inhibitory effect of Arpin on cell migration could potentially be used to control metastasis. Another open question is whether the steering of the cells is coupled to the gradient-sensing machinery. Bacterial cells chemotax by inducing turns in decreasing concentrations of chemoattractant and by persisting in their current direction when the concentration of chemoattractant increases. Arpin-mediated control of migratory persistence might be utilized to direct eukaryotic cells in a similar manner.

With the ever-growing number of genomic sequences, database searches are an increasingly successful way to identify new protein interactions that have thus far remained undetected using biochemical or immunological assays and it remains to be seen how many new proteins that are involved in cell migration can be identified. Speed is of the essence though, as by my count, the number of mammalian proteins with undescribed acidic carboxy-terminal motifs has now decreased to one.

References
1. Dang, I., Gorelik, R., Sousa-Blin, C., Derivery, E., Guerin, C., Linkner, J., Nemethova, M., Dumortier, J.G., Giger, F.A., Chipysheva, T.A., et al. (2013). Inhibitory signalling to the Arp2/3 complex steers cell migration. Nature 503, 281–284.
2. Boczkowska, M., Rebowski, G., Petoukhov, M.V., Hayes, D.B., Svergun, D.I., and Dominguez, R. (2008). X-ray scattering study of activated Arp2/3 complex with bound actin-WCA. Structure 16, 695–704.
3. Ti, S.C., Jurgenson, C.T., Nolen, B.J., and Pollard, T.D. (2011). Structural and biochemical characterization of two binding sites for nucleation-promoting factor WASp-VCA on Arp2/3 complex. Proc. Natl. Acad. Sci. USA 108, E463–E471.
4. Wagner, A.R., Luan, Q., Liu, S.L., and Nolen, B.J. (2013). Dip1 defines a class of Arp2/3 complex activators that function without preformed actin filaments. Curr. Biol. 23, 1990–1998.
5. Chan, K.T., Creed, S.J., and Bear, J.E. (2011). Unraveling the enigma: progress towards understanding the coronin family of actin regulators. Trends Cell Biol. 21, 481–488.
6. Shina, M.C., Unal, C., Eichinger, L., Muller-Taubenberger, A., Schleicher, M., Steinert, M., and Noegel, A.A. (2010). A Coronin7 homolog with functions in actin-driven processes. J. Biol. Chem. 285, 9249–9261.
7. Pan, Y.F., Viklund, I.M., Tsai, H.H., Pettersson, S., and Maruyama, I.N. (2010). The ulcerative colitis marker protein WAFL interacts with accessory proteins in endocytosis. Int. J. Biol. Sci. 6, 163–171.
8. Viklund, I.M., Kuznetsov, N.V., Lofberg, R., Daperno, M., Sostegni, R., Astegiano, M., Rizzetto, M., von Stein, O., D'Amato, R., von Stein, P., et al. (2008). Identification of a new WASP and FKBP-like (WAFL) protein in inflammatory bowel disease: a potential marker gene for ulcerative colitis. Int. J. Colorect. Dis. 23, 921–930.
9. Veltman, D.M., King, J.S., Machesky, L.M., and Insall, R.H. (2012). SCAR knockouts in Dictyostelium: WASP assumes SCAR's position and upstream regulators in pseudopods. J. Cell Biol. 198, 501–508.
10. Meinhardt, H. (1999). Orientation of chemotactic cells and growth cones: models and mechanisms. J. Cell Sci. 112, 2867–2874.
11. Neilson, M.P., Veltman, D.M., van Haastert, P.J., Webb, S.D., Mackenzie, J.A., and Insall, R.H. (2011). Chemotaxis: a feedback-based computational model robustly predicts multiple aspects of real cell behaviour. PLoS Biol. 9, e1000618.
12. Robinson, R.C., Turbedsky, K., Kaiser, D.A., Marchand, J.B., Higgs, H.N., Choe, S., and Pollard, T.D. (2001). Crystal structure of Arp2/3 complex. Science 294, 1679–1684.
13. Oda, T., Iwasa, M., Aihara, T., Maeda, Y., and Narita, A. (2009). The nature of the globular- to fibrous-actin transition. Nature 457, 441–445.

MRC Laboratory of Molecular Biology, Francis Crick Avenue, Cambridge Biomedical Campus, Cambridge CB2 0QH, UK.
E-mail: dveltman@mrc-lmb.cam.ac.uk

Evolution: 'Snowed' In with the Enemy

Explaining the origins and maintenance of cooperation in nature is a key challenge in evolutionary biology. A recent study demonstrates two novel mechanisms through which the natural ecology of sinking ocean aggregates — colloquially called 'marine snow' — promotes cooperation.

Manoshi Sen Datta[1] and Jeff Gore[2,*]

It was 1930 when William Beebe, peering out from the porthole of his deep-sea bathysphere (Figure 1), first witnessed the ever-present shower of flocculent, rapidly sinking aggregates that we now know as 'marine snow' [1]. Composed of dead phytoplankton, zooplankton fecal pellets, and other nutrient-rich detritus, marine snow particles are hotspots of microbial activity in an otherwise barren ocean landscape (Figure 2) [2]. Indeed, as they descend through the water column,

particles of marine snow are rapidly colonized by bacteria, which form dense biofilm communities on the particle surface [2,3]. In some cases, only a portion of bacterial colonizers can degrade the complex polysaccharides that comprise marine snow, but they often produce smaller, freely diffusing nutrients that can be consumed by the entire community [3,4]. However, producers of these shared nutrients can be taken advantage of by free-riding non-producers that consume the nutrients without paying the metabolic cost of

contributing to the pool themselves [4]. How do 'cooperating' producers survive in the face of these 'cheating' non-producers in the marine snow environment? A new study in this issue of Current Biology by Drescher et al. [5] demonstrates that non-producers can indeed exploit producers in particle-associated bacterial communities, but also suggests novel mechanisms through which the natural ecology of marine snow may allow producers to subvert their free-riding neighbors.

To be sure, the question of how cooperating individuals can avoid exploitation by cheaters — often framed as the so-called 'public goods dilemma' — has interested evolutionary biologists for decades. Despite the costs of cooperation (for instance, the metabolic cost of producing carbohydrate-degrading

Figure 1. The famed marine biologist, William Beebe, regarding the world from his bathysphere.
From 1930 to 1934, Beebe, along with engineer Otis Barton, used the bathysphere to dive thousands of feet below the ocean's surface, setting several consecutive world records for the deepest dive ever performed by a human. (© Wildlife Conservation Society.)

enzymes) and the benefits afforded to cheating free-riders, cooperative behaviors are common in nature, ranging from siderophore production in marine bacteria to the formation of communities in human populations [6,7]. In an effort to reconcile this disparity, the field has largely focused on identifying general mechanisms through which cooperators can persist in the environment. Such mechanisms are numerous, varying from kin selection to reciprocity, and have been studied in a wide range of contexts both theoretically and experimentally [6,8–10]. Recently, several studies have suggested that natural ecological factors, including interspecies competition, range expansion, and biofilm formation, can favor cooperation [11–15]. Although these studies provide a long list of possible explanations for the maintenance of cooperative behaviors, tests of these mechanisms in natural contexts are few and far between. Notable exceptions include studies of *Dictyostelium discoidium* and *Myxococcus xanthus*, which suggest that kin discrimination and active cheater control play an important role in the maintenance of cooperation and the evolution of multicellularity [16–18].

In the new study, Drescher *et al.* [5] have taken an important step towards understanding the public goods dilemma in the natural world. In lieu of studying naturally occurring aggregates, whose compositional variability would significantly complicate analyses, the authors developed a simple model system to explore the dynamics of the public goods dilemma. To model marine snow, they considered particles made of chitin, a complex polysaccharide that constitutes one of the most abundant organic substances in nature and a major component of marine snow aggregates. A highly insoluble polymer, chitin cannot be consumed directly, but instead must be broken down into smaller degradation products (including N-acetylglucosamine mono- and di-saccharides, collectively referred to here as 'GlcNAc') before it can be consumed [4,19].

In this chitinous environment, producers (wild-type *Vibrio cholerae*), which can convert chitin into consumable GlcNAc, were grown together with non-producers (*ΔchiA-1*, *ΔchiA-2*) that can consume the GlcNAc public good, but cannot produce it themselves. Non-producers outcompeted producers in this environment, where chitin was the sole source of

carbon and nitrogen, suggesting that the degradation of chitin by producers is indeed a cooperative behavior that can be exploited by non-producers. Given the prevalence of chitin and other complex polysaccharides in the natural environment, it is quite possible that these public goods interactions are a generic feature of microbial communities far beyond those associated with marine snow.

In light of this public goods dilemma, how do GlcNAc producers survive on marine snow? To answer this question, Drescher *et al.* [5] explored two aspects of the natural ecology of marine snow that enable cooperating producers to subvert exploitative non-producers. They first considered the thickness of the surface-associated bacterial biofilm, hypothesizing that a thicker biofilm may limit the diffusion of GlcNAc to non-producers, thereby shifting selection in favor of the producers. In line with these predictions, a producer mutant that creates biofilms nearly four times thicker than the wild type is now able to outcompete non-producers in the chitinous environment in which the non-producers had originally flourished. A simple mathematical model corroborates this idea, predicting that the concentration of GlcNAc within the biofilm decays precipitously with increasing

Figure 2. Marine snow falling on the sea floor.
Image from ROV Holland I during a deep-water expedition by National University of Ireland Galway, funded by the Marine Research Sub-programme of the National Development Plan 2007–2013. (Copyright Marine Institute.)

distance from the aggregate surface. This effectively eliminates GlcNAc access for non-producers away from the surface. Since dense bacterial communities often form on marine snow aggregates, these experiments provide a plausible mechanism through which producers may subvert free-riding non-producers in nature. Interestingly, the authors note that matrix hyper-producing mutants of *Pseudomonas aeruginosa* have been isolated from the lungs of cystic fibrosis patients, an environment that also contains an array of exploitable complex nutrients. Thus, it is possible that the formation of thick biofilms allows producers and non-producers to coexist in many natural environments.

Drescher *et al.* [5] next considered the effect of flow over the particle surface on the public goods interactions between producers and non-producers. As marine snow descends through the water column, seawater flows over the aggregate surface, often at speeds of tens of microns per second or more. Hypothesizing that such flows could quickly disperse any released GlcNAc (thereby selectively favoring the producers), the authors designed a microfluidic device that allowed them to control the unidirectional velocity of liquid flow over chitin particles as they were colonized. Under these conditions, the producers strongly outcompeted non-producers even at the lowest imposed flow velocity, which corresponds to the sinking speed of a particle that is significantly smaller than the average marine snow aggregate. A mathematical model of flow over a biofilm surface predicts that the concentration of GlcNAc is lower at the biofilm surface than in the absence of flow and rapidly declines with distance away from the surface. In these limiting GlcNAc conditions, producers, which retain some preferential access to the GlcNAc that they produce, are able to outcompete non-producers on the surface. Since marine snow aggregates are estimated to spend weeks sinking to the ocean floor [1], flows over aggregate surfaces are likely to have a profound effect on the dynamics of the bacterial communities that inhabit them.

In many ways, this study is just the tip of the iceberg — there are many things that we still don't understand about how the public goods dilemma plays out in nature. How prevalent are cheating behaviors in the natural environment? To what extent do such public goods interactions dictate the composition, structure, and dynamics of microbial communities? A separate study by Rakoff-Nahoum *et al.* [20], also published in this issue, begins to address these questions, suggesting that the public goods dilemma may play a significant role in shaping the human microbiome. As the authors note, many bacteria within the human gut survive by digesting the complex polysaccharides that comprise our diet and consuming the breakdown products. However, by screening several gut bacterial isolates for growth on a range of complex polysaccharides, Rakoff-Nahoum *et al.* demonstrate that not all bacteria possess the ability to degrade these nutrients. Indeed, while some cooperating bacteria produce the enzymes necessary for breaking down complex polysaccharides, cheaters also exist (even within the same human host) that consume the breakdown products without contributing to the nutrient pool. In many cases, the enzymes required for degradation were secreted extracellularly over a long range, allowing even spatially distant cheaters to benefit from cooperative degradation activity. The authors speculate that such public goods interactions provide a possible mechanism through which diverse bacterial species can stably coexist at high densities within the human gut. Together, these studies by Drescher *et al.* [5] and Rakoff-Nahoum *et al.* [20] add to a growing body of knowledge suggesting that cooperative interactions between cells play an important role in shaping natural microbial communities.

References
1. Miller, C.B., and Wheeler, P.A. (2012). Biological Oceanography (John Wiley & Sons).
2. Stocker, R., and Seymour, J.R. (2012). Ecology and physics of bacterial chemotaxis in the ocean. Microbiol. Mol. Biol. Rev. *76*, 792–812.
3. Azam, F., and Malfatti, F. (2007). Microbial structuring of marine ecosystems. Nat. Rev. Microbiol. *5*, 782–791.
4. Beier, S., and Bertilsson, S. (2011). Uncoupling of chitinase activity and uptake of hydrolysis products in freshwater bacterioplankton. Limnol. Ocean *56*, 1179–1188.
5. Drescher, K., Nadell, C.D., Stone, H.A., Wingreen, N.S., and Bassler, B.L. (2014). Solutions to the public goods dilemma in bacterial biofilms. Curr. Biol. *24*, 50–55.
6. Nowak, M.A. (2006). Five rules for the evolution of cooperation. Science *314*, 1560–1563.
7. Cordero, O.X., Ventouras, L.-A., DeLong, E.F., and Polz, M.F. (2012). Public good dynamics drive evolution in iron acquisition strategies in natural bacterioplankton populations. Proc. Natl. Acad. Sci. USA *109*, 20059–20064.
8. Damore, J.A., and Gore, J. (2012). Understanding microbial cooperation. J. Theor. Biol. *299*, 31–41.
9. Julou, T., Mora, T., Guillon, L., Croquette, V., Schalk, I.J., Bensimon, D., and Desprat, N. (2013). Cell–cell contacts confine public goods diffusion inside Pseudomonas aeruginosa clonal microcolonies. Proc. Natl. Acad. Sci. USA *110*, 12577–12582.
10. Momeni, B., Brileya, K.A., Fields, M.W., and Shou, W. (2013). Strong inter-population cooperation leads to partner intermixing in microbial communities. ELife *2*, e00230.
11. Celiker, H., and Gore, J. (2012). Competition between species can stabilize public-goods cooperation within a species. Mol. Syst. Biol. *8*, 621.
12. Datta, M.S., Korolev, K.S., Cvijovic, I., Dudley, C., and Gore, J. (2013). Range expansion promotes cooperation in an experimental microbial metapopulation. Proc. Natl. Acad. Sci. USA *110*, 7354–7359.
13. Van Dyken, J.D., Müller, M.J.I., Mack, K.M.L., and Desai, M.M. (2013). Spatial population expansion promotes the evolution of cooperation in an experimental prisoner's dilemma. Curr. Biol. *23*, 919–923.
14. Smukalla, S., Caldara, M., Pochet, N., Beauvais, A., Guadagnini, S., Yan, C., Vinces, M.D., Jansen, A., Prevost, M.C., Latgé, J.-P., *et al*. (2008). FLO1 is a variable green beard gene that drives biofilm-like cooperation in budding yeast. Cell *135*, 726–737.
15. Xavier, J.B., and Foster, K.R. (2007). Cooperation and conflict in microbial biofilms. Proc. Natl. Acad. Sci. USA *104*, 876–881.
16. Strassmann, J.E., Zhu, Y., and Queller, D.C. (2000). Altruism and social cheating in the social amoeba Dictyostelium discoideum. Nature *408*, 965–967.
17. Travisano, M., and Velicer, G.J. (2004). Strategies of microbial cheater control. Trends Microbiol. *12*, 72–78.
18. Celiker, H., and Gore, J. (2013). Cellular cooperation: insights from microbes. Trends Cell Biol. *23*, 9–15.
19. Li, X., and Roseman, S. (2004). The chitinolytic cascade in Vibrios is regulated by chitin oligosaccharides and a two-component chitin catabolic sensor/kinase. Proc. Natl. Acad. Sci. USA *101*, 627–631.
20. Rakoff-Nahoum, S., Coyne, M.J., and Comstock, L.E. (2014). A social network of polysaccharide utilization among human intestinal symbionts. Curr. Biol. *24*, 40–49.

[1]Computational and Systems Biology Graduate Program, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Bldg. 13-2008, Cambridge, MA 02139, USA. [2]Department of Physics, MIT Center for Physics of Living Systems, Computational and Systems Biology Graduate Program, Microbiology Graduate Program, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Bldg. 13-2008, Cambridge, MA 02139, USA.
*E-mail: gore@mit.edu