

Meeting report on the ASM Conference on Mechanisms of Interbacterial Cooperation and Competition

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The ASM Conference on Mechanisms of Interbacterial Cooperation and Competition was held in Washington DC, from 1 to 4 March 2017. The conference provided an international forum for sociomicrobiologists from different disciplines to present and discuss new findings. The meeting covered a wide range of topics, spanning molecular mechanisms, ecology, evolution, computation and manipulation of interbacterial interactions, and encompassed social communities in medicine, the natural environment, and industry. This report summarizes the presentations and emerging themes.

The American Society for Microbiology Conference on Mechanisms of Interbacterial Cooperation and Competition was held in Washington DC, from 1 to 4 March 2017. The meeting was chaired by K. Foster (University of Oxford, Oxford, UK) and co-chaired by S. Brown (Georgia Institute of Technology, Atlanta, GA) and covered an exciting range of topics across the scope of sociomicrobiology research. It comprised 1 keynote lecture and 40 talks in 5 thematically organized sessions. The meeting also included two extensive poster sessions that featured 58 posters. In this review, we attempt to convey the depth and breadth of the topics that were presented during this meeting and to provide a synopsis of recent developments and emerging trends in the field.

Microbes use a plethora of mechanisms to cooperate and compete with each other. The first thematic session was mainly dedicated to contact-dependent toxins that can be injected into (type VI secretion systems (T6SS)) or placed onto (contact-dependent inhibition (CDI)) neighboring cells. This session provided emerging insights into the effect of these contact-dependent toxins on competence, immune response, spatial population structuring and stabilization of cooperative traits. In addition, contact-dependent mechanisms of communication and motility were discussed. The second session dealt with contact-independent mechanisms of competition, such as novel antibiotics and bacteriocins. Pioneering insights were presented on the remarkable complexity of strategies bacteria use in bacterial warfare, including sensing of competitors, coordinated defense and attack tactics and division of labor. The third session focused on mechanisms of cooperation, and especially on complex regulation by quorum sensing, strategies involving division of labor and stabilization of cooperation from cheater exploitation. Whereas most insights into mechanisms of cooperation and competition so far have been obtained using strongly simplified microbial communities, the fourth session illustrated a trend towards more complex community models, in which *in silico* approaches and inclusion of more complex ecological factors, such as phages, protists, mucins, or the host are central. The conference was concluded with a final session on emerging insights into the effects of bacterial cooperation and competition within the host, and the implications for patient treatment. In the following sections we provide an overview of recent insights and emerging trends in the field.

Cooperation and competition are intrinsically intertwined.

A key insight that emerged throughout the conference is that microbial cooperation and competition are strongly and intrinsically intertwined. On the one hand, conflict paves the way for cooperation, by protecting cooperating cells from exploitation by cheaters. On the other hand, competition against non-self cells often involves an act of cooperation between self cells.

In her thought-provoking keynote talk, P. Cotter (Univ. of North Carolina-Chapel Hill, Chapel Hill, NC) presented data on a binary role of CDI systems in *Burkholderia thailandensis* in mediating competition with non-self cells and simultaneously regulating cooperation between self-cells. Non-self cells are killed by toxins delivered through CDI, whereas self-cells contain immunity proteins and use the toxins for intercellular communication to promote cooperative traits. Combining cooperative signaling and competitive attack in one single system provides a way to protect cooperation between self-cells from exploitation by non-self cheaters. Another platform that combines cooperation and competition, was presented by D. Wall (University of Wyoming, Laramie, WY), who discovered that *Myxococcus xanthus* cells cooperate by transient exchange of their outer membrane in order to repair damaged cells. Recognition in outer membrane exchange is mediated by cell surface receptors, however, it also involves exchange of polymorphic membrane toxins, which provides additional protection against exploitation. Recipient cells that happen to contain compatible receptors, but are not true self cells, will not contain cognate immunity proteins and as a result are killed.

In addition, competition can induce spatial segregation, which is a well-known solution for stabilizing cooperation. W. Ratcliff (Georgia Institute of Technology, Atlanta, GA) used mathematical modelling and experiments with *Vibrio cholerae* to show that T6SS-mediated killing of adjacent non-self cells results in spatial segregation between self and non-self cells (Figure 1), and presented empirical support that spatial segregation stabilizes cooperation from exploitation. A. Septer (University of North Carolina, Chapel Hill, NC) showed that T6SS-mediated killing also induces spatial structuring of *V. fischeri* polyclonal populations *in vivo*, in the light organ of *Euprymna scolopes* squids. Non-killer (T6SS-) and killer (T6SS+) strains always occupied different crypts within the light organ, whereas different non-killer strains could co-colonize the same crypt. I. Mandic Mulec (University of Ljubljana, Ljubljana, Slovenia) presented a T6SS-independent competitive mechanism of spatial segregation during swarming in *Bacillus subtilis*. Genomic comparison and mutant analysis of non-mixing strains indicated that multifactorial molecular signatures, involving cell surface modifications and antagonisms, are responsible.

The two previous paragraphs explain how competitive attacks by cooperators against potential cheaters stabilize public goods cooperation. R. Kümmerli (University of Zurich, Zurich, Switzerland) and Ö. Özkaya (IGC-Gulbenkian Institute of Science, Oeiras, Portugal) presented two additional mechanisms to protect cooperators from cheaters that involve competition with a third party. R. Kümmerli showed that cooperation can be stabilized by competition with a strain that makes use of a different public good. *Pseudomonas aeruginosa* and *Burkholderia cenocepacia* make use of different siderophores to scavenge iron. *P. aeruginosa* is outcompeted by a *P. aeruginosa* cheat, which is deficient for siderophore production, but proficient for uptake. *B. cenocepacia*, on the other hand, is resistant to cheating, because it makes use of a siderophore that is (although inferior) inaccessible to *P. aeruginosa*. The sum of these interactions, resembling a rock-paper-

scissors configuration, was found to lead to a stable community. Ö. Özkaya showed that cheating on cheaters can also stabilize public good cooperation in *P. aeruginosa*. He combined empirical and modelling work to study the dynamics of polymorphic populations in an environment where two social traits -production of siderophores and elastase - are necessary, and found that the presence of cheaters for iron scavenging decreases the relative fitness of elastase production cheaters, thereby preventing a tragedy of the commons.

Competition thus stabilizes cooperation. A second link between cooperation and competition is that mechanisms of competition are often cooperative on their own. A good example was provided in the previous paragraph, where *P. aeruginosa* cells cooperate in producing siderophores in order to withdraw iron from and compete with *B. cenocepacia* (R. Kümmerli). Also the production of antibiotics and toxins by self cells to compete with non-self cells can be seen as an act of cooperation between self cells. A. Barrero-Tobon (UNC Chapel Hill, Chapel Hill, NC) and Z. Zhang (Leiden University, Leiden, Netherlands) presented evidence suggesting this cooperative attack can involve division of labor. A. Barerro-Tobon presented that only about 0.1% of the cells in a *B. thailandensis* population highly express the CDI system-encoding genes, and are thus prepared to eliminate invading non-self cells via contact-dependent inhibition. Similarly, Z. Zhang found that about 1% of the spores from wild-type colonies of *Streptomyces coelicolor* produce aberrant phenotypes that are phenotypically and genomically hypervariable (through massive genome deletions up to 1Mb). These cells show a strongly reduced growth, but hyperproduce variable types of antibiotics. Since antibiotic production is highly costly, it was hypothesized that this division of labor within *Streptomyces* colonies reduces the metabolic burden of secreted products while maximizing the colony-wide yield and diversity of costly metabolites.

Emerging themes in the study of competitive behaviour.

The conference was an ode to diversity in competitive behaviors. In addition to further insights in type VI secretion, several novel mechanisms and strategies of competition were presented, including novel plant-like bacterial alkaloids mediating competition between rizosphere bacteria (G. Lozano, Yale University, New Haven, CT), colicin-based coordinated attack behaviors in *Escherichia coli* (D. Mavridou, Imperial College London, London, UK), exchange of outer membrane toxins by Myxobacteria (D. Wall) and linarmycin antibiotics in *Streptomyces* that are transported by extracellular vesicles produced in concert with the antibiotics (P. Straight, Texas A&M University, College Station, TX). Competition not only occurs between bacteria or fungi, but also with viruses. K. Seed (University of California, Berkeley, CA) presented data showing that competition with predatory phages made epidemic *V. cholerae* evolve to use mobile genetic elements to defend against the phages. As opposed to mutations in cell surface molecules, which are often required for virulence, these mobile genetic elements do not compromise the integrity of core functions during infections and are therefore observed with increasing frequency in clinical *V. cholerae* isolates. Below, three emerging themes in the study of competitive behavior are discussed: (i) alternative functions of type VI secretion, (ii) 'competition sensing' and coordinated defense and attack strategies, and (iii) exchange of weaponry through horizontal gene transfer (HGT).

An important focus was on alternative functions of type VI secretion, in addition to its role in cell-cell killing. M. Blokesch (Swiss Federal Institute of Technology, Lausanne, Lausanne, Switzerland) presented data demonstrating that T6SS is part of the competence regulon of diverse pandemic *V.*

cholerae strains, and that T6SS mediated predation of neighboring bacteria fosters uptake of long stretches of intact DNA from (almost) alive competitors. W. Zhao (Harvard Medical School, Boston, MA) used an infant mouse model to show that T6SS killing activity of *V. cholerae* against commensal bacteria occurs *in vivo* during infection and that T6SS-mediated interaction with the commensals, in addition, elicits host immune responses and induces *V. cholerae* virulence gene expression. Finally, as discussed in the previous section, type VI secretion plays a role in stabilizing cooperation by inducing spatial segregation (W. Ratcliff and A. Septer).

Whereas animal aggression can involve sophisticated decision making, microbes are usually assumed to employ simplistic strategies for defense and attack. Throughout the conference, pioneering insights were presented revealing a remarkable complexity of strategies bacteria use to detect competitors and coordinate defense- and attack tactics. H. Steenackers (KU Leuven, Leuven, Belgium) presented data indicating that a focal *Salmonella* Typhimurium uses its stress response systems to detect competitors in a mixed species biofilm community ('competition sensing') and to launch a defensive response by inducing biofilm matrix production, epithelial invasion and antibiotic resistance. D. Mavridou used small colicin plasmids in a variety of ecologically-relevant settings to show that colicinogenic *Escherichia coli* strains can engage in a diverse array of coordinated attack tactics, despite the straightforward genetic control of colicin production. Colicinogenic strains perform pre-emptive attacks which are strong enough to inhibit competitors via a subpopulation that sacrifices itself to produce toxins, but also responsive attacks by upregulating toxin production when they are under treat. Finally, R. Kümmerli found that *P. aeruginosa* can sense the presence of *B. cenocepacia* in mixed culture and up-regulates siderophore production, as a measure to deprive its competitor from iron.

Increasing evidence is collected that bacteria can horizontally transfer genes encoding their weaponry to neighboring strains. P. Cotter and A. Barrero-Tobon showed that the genes encoding the *B. thailandensis* CDI system are located on a mobile genomic island flanked by IS2 transposases. A small subpopulation of cells (0.1%) produces many copies of this genomic island, present as dsDNA megacircles, and is thus prepared to transfer its CDI system-encoding genes to invading cells. This transfer can be explained from the perspective of the 'selfish gene', since transfer to invading bacteria that are capable of outcompeting the resident population would promote persistence of the CDI genes. In addition, W. Ratcliff presented computational data supporting that mutual exchange of weapons through HGT might on the long term also be advantageous for the competing cells. The cost of not exchanging weapons with a superior competitor (i.e. being killed) outweighs the cost of exchanging weapons with an inferior competitor (i.e. being slowed down). In that sense, HGT may serve as a hedge against unpredictable future competitors.

Novel insights in cooperative behaviour.

Cooperation is considered key to the functioning of microbial communities and a large variety of cooperative phenotypes were presented, including biofilm formation (M. Parsek, University of Washington, Seattle, WA and A. Dragos, Friedrich Schiller University Jena, Jena, Germany), metabolic cross-feeding (R. Rakoff-Nahoum, Harvard University, Boston, MA and A. Zomorodi, Boston University, Boston, MA), shared resistance mechanisms (D. McDougald, University of Technology Sydney, Sydney, Australia), siderophore production (R. Kümmerli ; Ö. Özkaya, M. Ghoul, University of Oxford, Oxford, UK and M. Schuster, Oregon State University, Corvallis, OR) and a form of contact-

dependent social motility by which *Pseudomonas fluorescens* and *Pedobacter* move together across hard agar surfaces, an environment where neither species is capable of moving alone (M. Silby, University of Massachusetts Dartmouth, North Dartmouth, MA). Below the following major themes are discussed: (i) novel strategies to stabilize cooperation, (ii) (evolution) of division of labor and (iii) the remarkable complexity of quorum sensing.

Although cooperation is inherently susceptible to cheater exploitation, several mechanisms and/or conditions allow stabilization of public good production. One interesting possibility is that public good cooperation lacks a fitness cost under specific conditions. M. Ghoul presented data showing that cheaters are not able to outcompete siderophore producers in *P. aeruginosa* in the late exponential and stationary phase of growth since siderophore production has stopped at this stage and the producer strain no longer pays the cost for cooperating. Similarly, M. Schuster made use of an unconventional continuous-culture approach to show that the cost of siderophore cooperation in *P. aeruginosa* is depending on the most limiting nutrient. If the building blocks of the public good are present in relative excess, there is no fitness cost for producing the public good and cheaters can no longer outcompete isogenic producers, confirming that the environmental-dependent cost of public good production is a key determinant for the evolutionary stability of cooperation. In addition, as described above, conflict paves the way for cooperation and several competition-associated mechanisms for stabilization of cooperation were presented (P. Cotter, W. Ratcliff, I. Mandic Mulec, R. Kümmerli and Ö. Özkaya).

Next to producing one common public good, cooperating bacteria can specialize in specific tasks increasing the fitness of the whole community. M. Parsek presented data illustrating such division of labor during early biofilm development by *P. aeruginosa*. Only a sub-population of cells that come into contact with the surface engage in c-di-GMP signalling to initiate attachment and found new biofilms, while other bacteria explore the surface to search for new attachment sites. But how evolutionarily stable is division of labor? A. Dragos explored the long term evolutionary dynamics of pellicle biofilms of *B. subtilis* formed through genetic division of labor between two mutants that each produce a different essential component of the matrix. Despite short term success, asymmetry in dependency and availability of the public goods exchanged by the cooperating partners eventually led to one strain outcompeting the other and collapse of the biofilm. These results indicate that the cost and availability of the public goods exchanged need to be similar in order for division of labor to be stable.

Under which conditions then does division of labor emerge? The Black Queen Hypothesis suggests that in microbial communities where microorganisms partially share (leak) essential costly functions with other members, the selective advantage of losing these functions could spark the emergence of division of labor. A. Zomorodi used genome-scale models of metabolism and game theory to investigate under which conditions these dependencies may thrive as evolutionarily stable and how the rise of these interactions varies across organisms and environments. While unidirectional metabolic dependencies can readily evolve across many conditions, cross-feeding only emerges at high levels of leakiness if essential leaky functions are lost in multiple stages, and is evolutionarily stable once established. S. Rakoff-Nahoum (Harvard University, Boston, MA) on the other hand used mouse models to study cooperation within the Bacteroidales *in vivo* and discovered a dedicated cross-feeding enzyme system in the prominent gut symbiont *Bacteroides ovatus*, which digests polysaccharide at a cost to itself but at a benefit to another species that provides benefits in

return. This research provides a rare example of naturally-evolved cooperation between microbial species within the mammalian intestinal microbiota.

A wide variety of cooperative traits are regulated by quorum sensing (QS), often involving multiple QS systems to regulate the same cooperative behavior. A. Eldar (Tel-Aviv University, Tel-Aviv, Israel) combined genomic exploration, modeling and experimental analyses to study the expansion of the number of QS systems in *Bacillus*, showing that accumulation of multiple quorum-sensing systems may be driven by a facultative cheating mechanism. A strain that has acquired an additional QS system can exploit its ancestor that possesses one fewer system, but resume full cooperation with its kin when it is fixed in the population. There is a complementary role for both horizontal gene transfer and gene duplication in acquiring these systems, each acting at a different level of genomic organization. S. Brown (Georgia Institute of Technology, Atlanta, GA) presented data illustrating that the combination of multiple QS systems also allows bacteria to differentiate between high bacterial density/high flow and low bacterial density/low flow conditions. Moreover, the complex QS regulatory architecture allows bacteria to match their investment in cooperation to the composition of the group, therefore allowing the maintenance of cooperation at lower levels of cooperators. One part of the QS regulatory architecture that is generally assumed to be essential, is the positive autoregulatory loop. However, R. Scholz (University of Washington, Seattle, WA) rebutted this idea by showing that positive autoregulatory loops are not required for the QS response, but serve to tightly synchronize the response. Autoinduction thus makes the response more effective at the expense of the ability to bet-hedge. Next to QS, bacteria can also make use of other communication systems. T. Gray (Wadsworth Center, Albany, NY) provided proof for a novel conjugal-based communication system in *Mycobacterium smegmatis*.

Towards more complex community models.

Most previous research on social interactions made use of relatively simple community models often composed of only two different strains or species. In order to increase relevance, information on interactions is increasingly derived from metagenome wide analyses of *in situ* communities such as the gut microbiota of humans. B. Ross (University of Washington, Seattle, WA) for example studied the landscape of T6SS across human gut microbiomes to unravel its role in community composition. However, for in depth mechanistic studies community models are required. There is a clear trend towards more complex and realistic community models and these were the topic of several talks. These improved community models contain higher numbers of strains and incorporate more complex environmental factors. Also novel, often computational, methods to study interactions in such complex communities were presented.

M. Traxler (University of California, Berkeley, Berkeley, CA) constructed a complex model to study the social behavior of Actinomycetes from soil, taking four criteria into account: the model should (i) approximate the natural system, (ii) contain detectable metabolites, (iii) consist of a simple microbial community and (iv) contain genetically traceable microbes. Similarly, R. Dutton (University of California, San Diego, La Jolla, CA) developed microbial community models for cheese rinds by deconstructing *in situ* communities and reconstructing them *in vitro* (Figure 2). The model communities, consisting of all dominant culturable species, are characterized by widespread interactions ranging from environmental modification to horizontal transfer of genes. Both types of

models are further being optimized, together with methods to study microbial interactions at the molecular level.

The inclusion of complex environmental factors in model systems can change how species interact with each other. Mucus forms a major ecological niche for microbiota in various locations of the human body. K. Ribbeck (Massachusetts Institute of Technology, Cambridge, MA) studied the effect of mucin, the main component of mucus, on interactions between two oral species. Mucin was found to promote the coexistence between two otherwise competing species, by pushing the microbes to the less competitive planktonic phase. These data thus clearly illustrate that the presence of complex environmental factors can lead to a decreased competition and stable coexistence. To further take complex environmental factors into account, animals are also increasingly used to study interactions between inoculated microbes in a relevant host environment (e.g. W. Zhao, S. Rakoff-Nahoum, A. Septer and A. MacPherson (University of Berne, Berne, Switzerland)).

When the complexity of a community increases, studying interactions becomes more challenging. Interaction networks can be useful to understand the behavior of such complex communities. H. Mendes-Soares (Mayo Clinic, Rochester, MN) developed a computational approach, called MMinte that uses microbial models of metabolism to predict community metabolic networks, which describe the metabolic relationships between the microbes. A potential application is to predict how changes in diet influence the microbial community composition and interactions in the gut. G. Lozano, on the other hand, established an inhibitory interaction network for microbes in the rhizosphere. Analyzing the interactions in the inhibitory network led to the discovery of strong inhibitors, but also species that offer protection against these inhibitors. A better understanding of competitive interactions in the rhizosphere can be applied to improve agriculture. An important challenge when constructing interaction networks is the prediction of combined effects of multiple concurrent interactions. Whereas many current models assume additivity of effects conferred by concurrent interactions, B. Momeni (Boston College, Chestnut Hill, MA) stressed that this assumption is not generally valid and that combined effects can also be antagonistic or synergistic in nature.

Microbial social interactions, disease and implications for patient treatment.

It is becoming increasingly clear that social interactions in microbial communities are central to human health and disease. Here we discuss emerging insights in how social interactions affect pathogen persistence during infection. We end with implications for patient treatment.

A subset of social interactions enhances pathogen persistence. J. Scott (Geisel School of Medicine at Dartmouth, Hanover, NH) made use of an *in vitro* co-culture model of *P. aeruginosa* and *Streptococcus ssp.* grown on cystic fibrosis derived bronchial epithelial (CFBE) cell monolayers to investigate how social interactions between these pathogens may affect the outcome of cystic fibrosis biofilm infections. *P. aeruginosa* was found to promote *Streptococcus constellatus* biofilm viability by 1000-fold, an effect that could be attributed at least partly to protection against peroxide-mediated killing offered by *P. aeruginosa*. Using a similar co-culture model on CFBE cells, G. Orazi (Dartmouth, Hanover, NH) showed that *P. aeruginosa* in addition increases the tolerance of *Staphylococcus aureus*, another major pathogen involved in CF, to multiple classes of antibiotics. Mechanistic studies suggested a model in which *P. aeruginosa* causes *S. aureus* to shift to slower,

fermentative growth, leading to reduced antibiotic susceptibility. These studies underscore the impact of interspecies interactions among pathogens on the responsiveness to treatment.

On the other hand, social interaction between symbionts and pathogens can protect the host. J. Maurer (The Univ. of Georgia, Athens, GA), for example, presented transcriptome-based data showing that the microbiota of a mature chicken, in contrast to the microbiota of a juvenile chicken, can exclude *Salmonella* from the gut environment by starving it of essential nutrients. Also in humans the gut microbiota offer protection against pathogens. J. Xavier (Memorial Sloan-Kettering Cancer Ctr., New York, NY) presented a mathematical model based on metagenome data of more than 1 000 patients at the Memorial Sloan-Kettering Centre to understand how gut microbes interact with each other to make a protective microbiota and how antibiotics perturb these interactions to open the way to colonization by antibiotic-resistant pathogens (Figure 3).

The protective effect of symbiotic microbes against pathogens inspires treatment strategies based on competitive pathogen exclusion. S. Hong (Illinois Institute of Technology, Chicago, IL) presented data illustrating that competition with the probiotic strain *E. coli* Nissle 1917 reduces biofilm formation of several pathogens including EHEC, *Enterococcus faecalis*, *P. aeruginosa* and *Serratia marcescens*. Spent media experiments indicated an excreted factor to be responsible. A. Horswill (University of Iowa, Iowa City, IA) discovered a number of *Staphylococcus* species living as commensals on the skin that can modulate QS of *S. aureus* and MRSA. In case of the commensal *Staphylococcus caprae* this cross-talk with MRSA was found to be mediated by the native autoinducing peptide (AIP) of *S. caprae*, which was identified as an 8-residue peptide. This AIP was shown to inhibit QS, lesion formation and bacterial load in a murine model of MRSA skin infection, again demonstrating the potential of commensals and commensal-derived competitive factors in antimicrobial therapy. In addition, according to J. Xavier, increased understanding of ecology in the gut microbiota is expected to lead to improved transplantation of whole microbiota communities to prevent or even treat antibiotic-resistant infections. However, care should be taken when applying strategies based on competitive pathogen exclusion. As described above, H. Steenackers presented data suggesting that pathogens can respond to competitors by enhancing epithelial invasion and antibiotic resistance. If so, an interesting alternative would be to specifically inhibit traits that allow pathogens to compete, such as antibiotic or bacteriocin production. This approach has the potential to both reduce the frequency of a focal pathogen and competition-associated traits in the remaining community.

Since public good cooperation is crucial for the persistence of bacterial pathogens, also antimicrobial treatment strategies that exploit the invasive abilities of cheaters are an option. M. Ghoul and M. Schuster, however, presented data indicating that whether a non-producing cheater can invade will depend upon when the non-producer arises, as well as the population structure and nutrient conditions. These factors should thus be taken into account when designing cheater-strategies for biotechnological and pharmaceutical applications.

Conclusions.

The sociomicrobiology field is rapidly growing, and the ASM Conference on Mechanisms of Interbacterial Cooperation and Competition provided a platform for researchers from different scientific disciplines to discuss and exchange ideas in all aspects of sociomicrobiology research, including (i) fundamental questions on molecular mechanisms and evolution (emergence and

stability) of interbacterial interactions and (ii) strategies for their control, and encompassing social communities in medicine, in the natural environment, and in industry. In search of answers a wide variety of interdisciplinary approaches are being used, including dedicated molecular analyses, complex community models, animal models, metagenome sequencing and a broad range of computational techniques. A key insight that emerged throughout the conference is that microbial cooperation and competition are strongly and intrinsically intertwined. Conflict paves the way for cooperation, while competition against non-self involves cooperation between self. Emerging themes within the study of competitive behavior are: (i) alternative functions of type VI secretion, (ii) 'competition sensing' and coordinated defense and attack strategies and (iii) exchange of weaponry through horizontal gene transfer. Major topics on cooperation include: (i) novel strategies to stabilize cooperation, (ii) evolution of division of labor and (iii) the remarkable complexity of quorum sensing. There is a clear trend going on towards *in situ* analysis of social interactions and more complex community model systems, and strong efforts are being made to translate knowledge on social interactions into optimized and novel antimicrobial strategies.

The next and 2nd edition of the ASM biofilm conference is planned in 2020 and will be chaired by S. Brown (Georgia Institute of Technology, Atlanta, GA) and co-chaired by I. Mandic Mulec (University of Ljubljana, Ljubljana, Slovenia).

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Figures

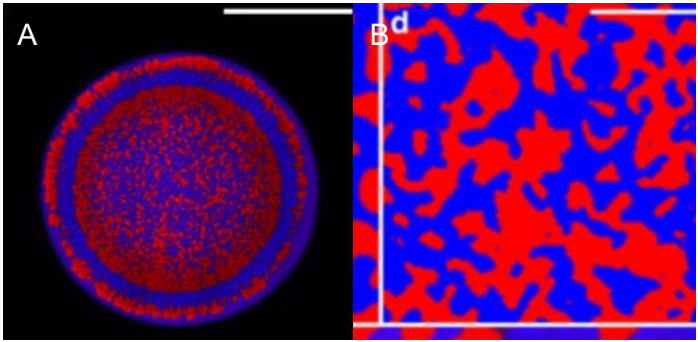


Figure 1. Colony (A) and phase separation model (B) of red and blue *V. cholerae* capable of mutual killing by T6SS. Scale bars denote 1 mm (A) and 100 μ M (B) (1).



Figure 2. Cross-sections through naturally aged cheeses show rind biofilm communities growing on the surface of the cheese curd. (A) A bloomy rind biofilm, (B) a natural rind biofilm, and (C) a washed rind biofilm (2).

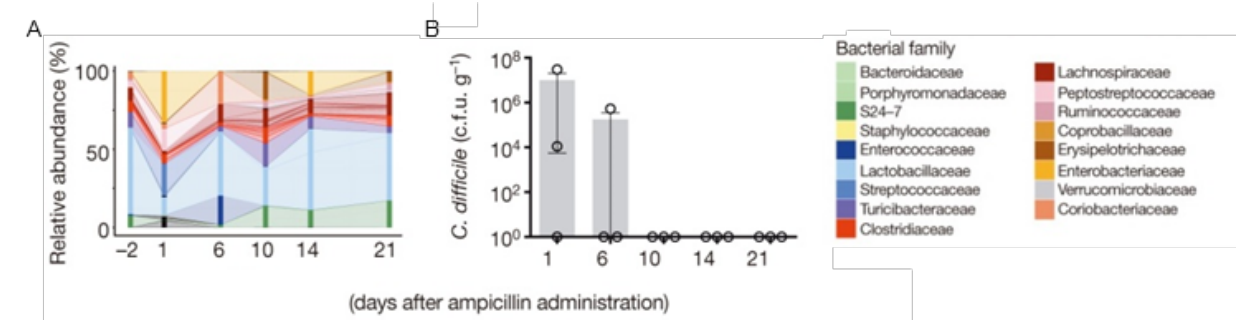


Figure 3. Antibiotic induced changes to microbiota composition (A) affect resistance to *Clostridium difficile* infections (B) (3).

References.

1. McNally L, Bernardy E, Thomas J, Kalziqi A, Pentz J, Brown SP, Hammer BK, Yunker PJ, Ratcliff WC. 2017. Killing by Type VI secretion drives genetic phase separation and correlates with increased cooperation. *Nat Commun* 8:14371.
2. Wolfe BE, Button JE, Santarelli M, Dutton JR. 2014. Cheese rind communities provide tractable systems for *in situ* and *in vitro* studies of microbial diversity. *Cell* 158(2):422–433.
3. Buffie CG, Bucci V, Stein RR, McKenney PT, Ling L, Gobourne A, No D, Liu H, Kinnebrew M, Viale A, Littmann E, van den Brink MR, Jenq RR, Taur Y, Sander C, Cross JR, Toussaint NC, Xavier JB, Pamer EG. 2015. Precision microbiome restoration of bile acid-mediated resistance to *Clostridium difficile*. *Nature* 517(7533): 205–208.