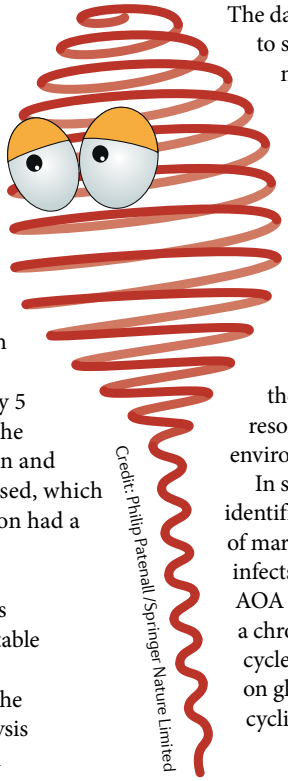
Next, the authors investigated the effect of NSV infection on the AOA hosts. During the first days post-infection, viral DNA replication increased, whereas AOA growth and ammonia oxidation were unaffected. However, host cell growth was halted after 2 days post-infection, and by day 5 the authors noticed that the rate of ammonia oxidation and nitrite production decreased, which suggests that viral infection had a negative impact on host metabolic activity.

In addition, the authors did not observe any detectable degradation of the host chromosome, damage to the cell envelope or host cell lysis following infection, which indicates that the budding process of NSVs might occur in a non-lytic manner, as reported for enveloped eukaryotic viruses.



Credit: Philip Patenall/Springer Nature Limited

The data led the authors to speculate that a non-lytic mode of replication, which enables continuous virion production and release, as well as the observed high adsorption rate of NSV virions to cells, represents a strategy to ensure their survival in the resource-limited marine environment.

In sum, this study identifies a new group of marine viruses that infects mesophilic AOA hosts, exhibits a chronic infection cycle and has an impact on global nitrogen cycling.

Andrea Du Toit

ORIGINAL ARTICLE Kim, J.-G. et al. Spindle-shaped viruses infect marine ammonia-oxidizing thaumarchaea. *Proc. Natl Acad. Sci. USA* https://doi.org/10.1073/pnas.1905682116 (2019)

by only one daughter cell, and the other cell is thus irreversibly differentiated from its sibling. The authors constructed a circuit based on the chromosome partitioning system (*par*) of *Caulobacter crescentus* for APP in *E. coli*. Two *par* elements (a centromere-like *parS* site and the *parS*-binding protein ParB) were cloned into 'target' and 'regulatory' plasmids, respectively. When expressed, ParB sequestered target plasmids into a single cluster, which was inherited by one daughter cell only. Importantly, cells underwent multiple rounds of APP.

Next, the authors used this system to physically separate genetically distinct cells by linking motility to the presence or absence of a target plasmid encoding a repressor that downregulates *motA* (a gene required for motility). During APP in mutant *motA* cells, the target plasmid is lost, leading to *motA* expression and motility. Last, the authors produced cells with four distinct differentiated states by introducing a second APP circuit.

In a second study, Mushnikov et al. engineered fusions of *C. crescentus* PopZ (a cell pole organizing protein that is stably maintained at single cell poles over multiple generations) and a phosphodiesterase into *E. coli*, which degrades the signalling molecule cyclic di-GMP (c-di-GMP). In their system, expression of the PopZ fusion is induced through either the introduction of a small molecule or light, using optogenetics. When expressed, the PopZ fusion accumulated at single cell poles, which were asymmetrically inherited, resulting in two distinct cell types that have either high or low c-di-GMP levels. The differences in c-di-GMP levels were used to drive differential gene expression patterns in daughter cells, resulting in cells expressing different biosynthetic enzymes or motility phenotypes.

Together, these two studies show that complex multicellular synthetic bacterial populations can arise from simple genetic circuits, with potentially useful applications.

Ashley York

ORIGINAL ARTICLES Molinari, S. et al. A synthetic system for asymmetric cell division in *Escherichia coli*. *Nat. Chem. Biol.* **15**, 917–924 (2019)| Mushnikov, N. V. et al. Inducible asymmetric cell division and cell differentiation in a bacterium. *Nat. Chem. Biol.* **15**, 925–931 (2019)

IN BRIEF

BACTERIAL PHYSIOLOGY

The search for persistence mechanisms continues

Several different mechanisms have been suggested to underlie antibiotic persistence, which is the ability of a subpopulation of bacterial cells to tolerate antibiotic treatment without being resistant. Specifically, toxin–antitoxin systems, (p)ppGpp production and ATP depletion have all been linked to persistence, although with contradictory results in different studies and different bacteria. A new study by Pontes and Groisman now finds that *Salmonella enterica* subsp. *enterica* serovar Typhimurium can produce persister cells independently of the specific factors listed above and that slow growth alone can explain persistence in their experiments, leading the authors to conclude that there is no dedicated genetic programme that induces persistence, but rather that slowdown of core processes, including those targeted by antibiotics, explains persistence.

ORIGINAL ARTICLE Pontes, M. H. & Groisman, E. A. Slow growth determines nonheritable antibiotic resistance in *Salmonella enterica*. *Sci. Signal.* **12**, eaax3938 (2019)
RELATED ARTICLE Balaban, N. Q. et al. Definitions and guidelines for research on antibiotic persistence. *Nat. Rev. Microbiol.* **17**, 441–448 (2019)

PHAGE BIOLOGY

Pairing phages with their hosts in the human gut

Hugenholtz and colleagues adapted the recently developed technique of viral tagging to determine phage–host bacteria pairs in faecal samples from healthy humans. Briefly, they extracted viruses and stained them fluorescently. After binding to bacterial cells, this 'tag' was used to single sort and sequence pairs (that is, the bacterial cell and its attached fluorescent phage cargo). The authors identified 363 unique pairs, including some with previously unknown phages. Interestingly, the majority of phages could not bind more than one host species, making them unlikely agents of horizontal gene transfer between species in the human gut. However, phages from one donor could target over 40% of bacterial cells from another donor despite microbiome differences between the donors, which has implications for faecal microbiota transplantation.

ORIGINAL ARTICLE Džunková, M. et al. Defining the human gut host–phage network through single-cell viral tagging. *Nat. Microbiol.* https://doi.org/10.1038/s41564-019-0526-2 (2019)
RELATED ARTICLE Mirzaei, M. K. & Maurice, C. F. Ménage à trois in the human gut: interactions between host, bacteria and phages. *Nat. Rev. Microbiol.* **15**, 397–408 (2017)

ENVIRONMENTAL MICROBIOLOGY

The culture debate

Advances in cataloguing and culturing global microbial diversity have renewed the interest in so far uncultured taxa. The often-cited assumption that only 1% of all microorganisms can be cultured has been challenged by previous work suggesting that a high proportion of bacteria across different environments has been cultured already. However, Thrash and colleagues now revisit these and additional data and point out technological and conceptual pitfalls that might lead to an overestimation of the cultured proportion, for example, primer and database biases. They conclude that the majority of bacteria and archaea is still uncultured and argue "that it is impossible to know whether a microbe is culturable until it has been cultured" and that the term 'unculturable' should be avoided. The authors note that there are a few studies and environments such as the human gut in which culturing efforts have yielded higher proportions, and thus culturing uncultured taxa remains a priority.

ORIGINAL ARTICLE Steen, A. D. et al. High proportions of bacteria and archaea across most biomes remain uncultured. *ISME J.* https://doi.org/10.1038/s41396-019-0484-y (2019)
RELATED ARTICLE Lagier, J. C. et al. Culturing the human microbiota and culturomics. *Nat. Rev. Microbiol.* **16**, 540–550 (2018)