Isotopic tracking of viral protein synthesis: new insights into nutrient biogeochemistry

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Isotopic tracers, particularly as applied to phage biology, lie at the heart of modern biochemistry and molecular biology, enabling such fundamental discoveries as the Hershey-Chase experiment's demonstration that DNA is the genetic material[1]. In the decades since, it has become clear that bacteriophages are not only useful laboratory tools, but also central players in the ecology and evolution of microbial communities. Viral lysis also has a unique biogeochemcial role, enhancing recycling through the microbial loop and shunting carbon and nutrients away from higher trophic levels [2]. Quantiative assessment of the impact of viruses on biogeochemistry has been hampered, however, by incomplete understanding of the sources of phage biomolecule constituents, and especially of the proportion of phage nutrients that derive from the pre-existing host cell biomass as opposed to being taken up from the extracellular medium after the infection begins[3]. Here we apply ^{15}N labeling and high-resolution proteomic mass spectrometry to determine the balance between host-derived and extracellularly-derived nitrogen for phage protein production. Using a model marine cyanobacterium-phage system, *Synechococcus* WH8102 and myovirus S-SM1, we observe that a substantial proportion of phage protein N is sourced from the medium post-infection, and that this proportion varies with host growth rate. We also document a shift from more host-derived to more-medium derived N over the course of infection, which manifests in distinct isotopic compositions of phage proteins expressed at different times during the protracted infection process. These observations provide key input to biogeochemical models of viral activity in global ecosystems, and change the boundary conditions often assumed to date to constrain nutrient budgets during infection processes.

[1] Hershey & Chase (1952), *Journal of General Physiology* 36, 39-56. [2] Jover, Effler, Buchan, Wilhelm & Weitz (2014), *Nature Reviews Microbiology* 12, 519. [3] Weitz, Stock, Wilhelm, Bourouiba, Coleman, Buchan, ... & Middelboe (2015), *ISME Journal* 9, 1352.