Title:
Discovery of novel antidefense strategies in phages infecting stream biofilm bacteria

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Abstract (300 words maximum): :
Bacteria and their viruses (phages) have evolved numerous defense and counter-defense strategies in an evolutionary arms race. The bioinformatic discovery of bacterial defense against phage infection has accelerated in recent years. Defense islands – clusters of defense genes on host genomes – emerge as a key property to identify new potential defenses. In contrast, the discovery of viral counter-defense mechanisms lagged behind, long limited to anti-CRISPR proteins. A first bioinformatic tool to identify antidefense genes in viral genomes and metagenome-assembled genomes (vMAGS) was only published in 2024 and comprises 156 antidefense systems. The surge in studies on defense and antidefense mechanisms suggest we are just beginning to uncover their vast arsenal. Hitherto unknown defense and counter-defense strategies are expected to occur in understudied environments, such as stream biofilms. Stream biofilms are especially promising because phages have to overcome the extracellular matrix and deal with bacterial defense systems. Indeed, previous work showed that depolymerases are commonly found in phages infecting biofilm-dwelling bacteria. Yet, the arsenal of viral counter-defense of phages infecting stream biofilm bacteria remains unknown. Here, we outline the discovery of unknown viral counter-defense strategies using vMAGs obtained from stream biofilms. We leverage the colocalization of antidefense proteins and early transcribed genes as well as the short length of antidefense proteins to establish a list of candidates. Antidefense proteins are prone to horizontal gene transfer and signatures of these transfers might also be used to uncover potential systems. Moreover, metagenomic sequence assemblers generate De Bruijn graphs as an intermediate step, preserving micro-diversity which is often lost in the final assembly. Bubbles in these graphs near assembled viral contigs reflect viral micro-diversity and serve as promising hotspots for the discovery of novel viral counter-defense strategies.