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Measuring phenotypic variability and plasticity in influenza A virus using multispectral viral strains[1]

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Despite relevance to human health, the mechanisms of enveloped virus assembly remain largely mysterious. This is particularly true of influenza A virus (IAV), which (unlike viral capsids with stereotyped shape and composition) forms heterogeneous particles whose assembly cannot be described in terms of equilibrium thermodynamics. Although the ability to assemble into particles with diverse size and composition could have important implications for infectivity, understanding how virion-to-virion differences arise and how they ultimately influence virus replication has proven challenging due to the lack of available tools for studying the assembly process. To address this challenge and establish a dynamic picture of how IAV assembles, we have developed virus strains that harbor small, non-disruptive fluorescent tags on each of the virus's five major structural proteins. Using these multispectral strains, we are able to quantify the protein composition and dynamics of virions as they assemble in live infected cells - measurements that have been previously inaccessible, and which reveal subpopulations of virus that favor either the binding or destruction of host receptors. The occupancy of these different subpopulations is malleable, shifting in response to environmental stimuli, including antiviral drugs that block receptor-destruction. In complex environments like the human respiratory tract, this phenotypic diversity could act as an evolutionary hedge.

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