Abstract Submitted
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Measuring the DNA Cargo of Viruses Using Nanofluidics[1] IRIS E. HWANG, GEORGIOS KATSIKIS, SHA SHA, MIT, VINCENT AGACHE, Universite Grenoble Alpes, CEA, LETI, PAUL W. BARONE, JACQUELINE WOLFRUM, STACY C. SPRINGS, ANTHONY J. SINSKEY, RICHARD D. BRAATZ, SCOTT R. MANALIS, MIT — Adeno-associated viruses (AAVs) are engineered to deliver therapeutic DNA for gene therapy. However, AAV manufacturing is far from perfect, producing only a small portion of full viruses with the therapeutic gene. Real-time quality control in continuous AAV manufacturing requires characterizing the ratio of full to empty viruses. Here, we developed a nanofluidic approach for distinguishing full from empty viruses by measuring mass. Our approach uses nanochannel resonators, which measure nanoparticle mass from a proportional change in the device's resonant frequency. Single AAVs weigh only a few attograms, producing too low of a signal-to-noise ratio; we thus measure the average mass of AAV populations. We theoretically derived the relationship between the average AAV mass of a tested solution and the variance in resonant frequency. Using this relationship, we experimentally measured AAV mass, producing results consistent with standard, yet slower, biochemical methods. Using Monte-Carlo simulations of AAVs advecting and diffusing within the nanochannel, we gained additional insight into our measurements. With our approach, we aim to offer a real-time, high resolution characterization of AAV mass to enable quality control in continuous AAV manufacturing.

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