CONTINUOUS VIRUS INACTIVATION USING A PACKED-BED REACTOR

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A critical unit operation in integrated continuous biomanufacturing is continuous virus inactivation. These reactors must provide sufficient minimum inactivation time and must have a narrow residence time. The narrow residence time is required to avoid a too short or too long incubation. Too short incubation may result in insufficient inactivation, too long may result in partial product destruction. We have developed a packed-bed continuous virus inactivation reactor (CVIR, Figure 1) with significant advantages over other continuous processing approaches, namely scalability, ease of operation and being truly continuous with undisrupted mass flow. The residence time distribution of our reactor is smaller compared to a coiled flow inverter or a jig in a box reactor.

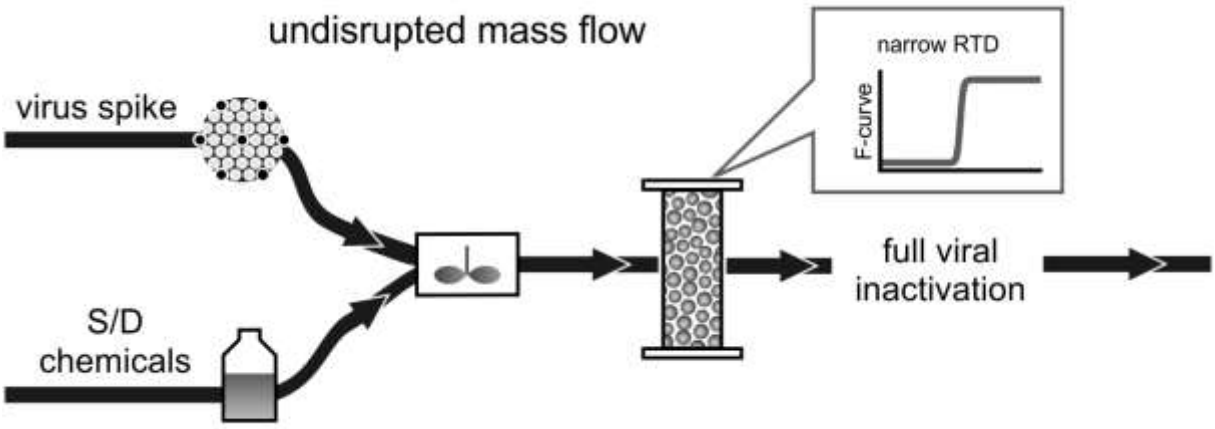

Figure 1: Overview of the continuous virus inactivation setup. The setup consists of a two independent stepper-motors syringe pump, a 2-chamber in-line mixer and the packed-bed CVIR.

Two industry-relevant virus models (X-MuLV and BVDV) were used to demonstrate the effectiveness of the CVIR for solvent/detergent treatment (S/D) unit operation. The CVIR achieved the same virus clearance performance as the traditional batch operation – a requirement for regulatory acceptance. An extensive array of controls proved that the observed virus inactivation was due to the S/D inactivation and not induced by the system. The S/D critical process parameters were subject of independent confirmation. Comparison against batch data showed that the virus inactivation capacity of the solvent detergent step using the packed-bed CVIR is as effective as batch operation and delivered comparable logarithmic reduction values (LRV). A 10-L column can process a stream of 85 L within 24 h.