

AUTOMATED CONTROL OF OSMOLALITY IN A PERFUSION BIOREACTOR SYSTEM VIA *IN SITU* CONDUCTIVITY SENSORS

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Osmolality in mammalian cell culture systems has been shown to impact cell health and process performance. In intensified perfusion cell culture processes, osmolality can change greatly across a single bioreactor run as high biomass concentrations lead to significant nutrient consumption. To avoid negative impacts of varying osmolality, control of osmolality within a perfusion system is desirable. Our team has developed a novel approach to control culture osmolality by use of *in situ* conductivity sensors and single-sided feedback control with salt addition. Automated osmolality control resulted in a three-fold reduction in harvest phase osmolality variability. More consistent osmolality led to more uniform cell density profiles and has improved both inter and intra batch process consistency. After development of the technology at bench scale, automated osmolality control was demonstrated in a technical pilot plant and then transferred to a GMP manufacturing facility.