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## Sequential/parallel production of potential malaria vaccines – a direct way from single batch to quasi-continuous integrated production

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An intensification of pharmaceutical protein production processes can be achieved by the integration of unit operations and application of recurring sequences of all biochemical process steps. Within optimization procedures each individual step as well as the overall process has to be in the focus of scientific interest. This paper includes a description of the development of a fully automated production plant, starting with a two-step upstream followed by a four step downstream line, including cell clarification, broth cleaning with microfiltration, product concentration with ultrafiltration and purification with column chromatography. Recursive production strategies are developed where a cell breeding, the protein production and the whole downstream is operated in series but also in parallel, each main operation shifted by one day. The quality and reproducibility of the recursive protein expression is monitored on-line by golden batch and this is controlled by model predictive multivariate control (MPMC). As a demonstration process the production of potential malaria vaccines with *Pichia pastoris* is under investigation.

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