

Biosensors 2018: Automation of biotechnological bioreactor production processes: Tom Zimmermann- Michigan State University, USA**Tom Zimmermann***Michigan State University, USA*

The change of health care towards personalized medicine requires an adaptation of the biomedical and pharmaceutical production. The demand for sophisticated and customized products, including monoclonal antibodies, therapeutic proteins and vaccines, is ever growing. At the same time, high efficiency and product quality are key requirements. A personalized and affordable medicine requires low volume and highly parallelized production methods, frequently realized in single-use bioreactors. Complexity and requirements of strictly controlled bioreactor processes are increasing rapidly. A continuous measurement of relevant process parameters and full automation of biotechnological production processes are critical to a high process yield and productivity. Parallel realtime in-situ monitoring of a variety of parameters in complex fluids can be realized by suitable multi-sensor systems (Fig. 1). Integrated disposable in-situ monitoring and control systems are not commercially available, yet. Required systems should control typical parameters of a cell culture in a bioreactor process and monitor various metabolic proteins and lactate, the nutrient glucose and cell density as well as the pH and the temperature. Integrated bioMEMS with a functionalized bioactive recognition layer shall be used to detect in-situ and in real-time most specifically on the biomolecular level bioanalytes of interest in highly complex bioreactor environments. Key for a stable, reliable, and robust in-situ sensor- and actor-system with low biofouling property might be the use of highly biocompatible diamond and carbon material systems.

The exhibition of bioreactors isn't just dictated by profitability yet additionally by process quality, which is for the most part controlled by changes in the process factors. As vacillations in these amounts legitimately influence the inconstancy in the item properties, combatting bends is the principle assignment of reasonable quality confirmation. The

clear method of decreasing this fluctuation is monitoring the item arrangement process firmly. Reason for this keynote is to show that there is sufficient proof in writing demonstrating that the exhibition of the aging procedures can essentially be improved by criticism control. A large portion of the as of now utilized open circle control methods can be supplanted by generally straightforward input strategies. It is appeared by viable models that such a retrofitting doesn't require noteworthy changes in the settled gear. It's the time since producers follow the advancements in most different ventures and improve process quality via programmed criticism control.

High speed downstream process development

The significant expenses of downstream handling in bioprocessing have made advancement of streamlined downstream procedures basic for business feasibility. Downstream handling alone can represent more than 85 percent of all out creation costs in numerous bioprocesses. All things considered, mechanized high-throughput procedures are getting progressively adequate in downstream procedure improvement, moving endlessly from conventional experience-based consecutive procedure structure. High-throughput screening (HTS) permits an a lot bigger number of factors to be researched inside a financially applicable time period, offering unquestionably increasingly complete portrayal and, along these lines, advancement of downstream procedures before scale-up.

Scaling down of individual unit activities has definitely prompted improvement of complete mechanical procedures at the microscale. Improvement of pilot-scale preparing plants can altogether upgrade process execution and diminish creation costs. Such downsized models empower quick and extensive mechanized portrayal of proposed forms before pilot-scale acknowledgment.

To satisfy quickly extending need for scaled down HTS preparing, a few makers are currently offering

items explicitly custom fitted to these applications. GE Healthcare's PreDicator plates are one such model, supporting high-throughput process advancement by permitting equal screening of chromatography conditions for official, washing, and elution. These 96-well channel plates are prefilled with bioprocess chromatography media (GE Healthcare) and offer mechanization of particle trade and immunizer fondness chromatography.

In process quality control

In process quality control (IPQC) is a procedure of observing basic factors of assembling procedure to guarantee a nature of the last item. In process fabricating controls are built up and archived by quality control and creation work force to guarantee that nature of the item is inside the satisfactory administrative range. Utilization of computerization to quicken test groundwork for investigation offers huge time reserve funds contrasted and manual example planning even it offers critical reproducibility. As well as permitting fluid dealing with errands to be performed quickly, robotization can be utilized to build up fast procedure examination for both procedure structure and IPQC applications.

The adaptability of the workstation permits joining of QC devices onto the stage, offering an a lot higher throughput limit with regards to bioprocess streamlining. Consolidating short trial times with low material necessities empowers examination of a wide assortment of factors, diminishing expenses related with manual procedures and improving procedure understanding.

At present, IPQC are constrained to fundamental screening procedures in bioprocessing and regularly utilizing just a couple of information created by High throughput screening stages. In spite of the fact that they have been utilized effectively to decrease bioprocess advancement times and improve yields, a great part of the information are adequately "squandered." Integration of very good quality diagnostic advances, for example, - mass spectrometry (MS), surface plasmon reverberation (SPR), and slender electrophoresis (CE) - onto robotized HTS stages will offer more noteworthy knowledge into bioprocessing responses. Coupling such procedures with information mining should offer propelled, high-

throughput process examination, improving DoE plan without huge extra example necessities.

Single use or multiple use facilities

The bioproduct maker expected to conclude whether to take a risk on a totally expendable (single-use) office or put resources into a customary hardened steel based one or go for a half and half alternative at the 200-L scale. Table 1 records key money related and operational models we thought about important. We fused milder worries notwithstanding process-monetary contemplations. It is reasoned that the less cleaning approval examines required by dispensable offices. Such endeavors can be critical with films and chromatography gums specifically, for which the quantity of cycles over which materials can be utilized with certainty (with no weakening in execution) must be illustrated. Another concerned we can not disregard is requirement for extra approval contemplates expected to evaluate the impact of extractables drained from expendable materials and to show the honesty of such materials.

To effectively execute single use and additionally hardened steel fabricating procedures, maker's must build up their own basis to produce lower costs and smooth out tasks. Single-use frameworks offer numerous points of interest over regular tempered steel frameworks and have properly increased wide acknowledgment in the biopharmaceutical business. Focal points, for example, increments in group achievement rate, end of expected cross pollution, progressively fast changeover between crusades, decreases in water and waste water prerequisites, and ends of clean set up (CIP) and steam set up (SIP) approval all have been referred to as purposes behind utilizing single-use frameworks. Albeit a few points of interest are no longer as solid as foreseen a few years back, the need to diminish venture cost and time keeps on being one essential driver for actualizing expendable frameworks.