IGNORANT EMPIRICISM IN CELL CULTURE ENGINEERING: 30 YEARS OF EXPENSIVE LESSONS

Matt Croughan, Keck Graduate Institute, USA
croughanmk@aol.com

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Although cell culture engineering has generally been quite successful, the path forward was not steady, but instead has had many stalls and diversions. These have largely been due to approaches based upon ignorant empiricism --- i.e., "it just seems to work, but we don't know why". As it turns out, ignorant empiricism often goes hand-in-hand with performance barriers that are not identified and thus not overcome for years. Examples will be discussed such as early sparging, agitation, and cell line handling protocols that limited the impact of nutrient enrichment and modern medium development. Until such barriers were identified and overcome, industrial cell culture could not have met the cost requirements and market demands for monoclonal antibody therapeutics. Ignorant empiricism also led to the expensive development and testing of many creative but operationally complex and impractical bioreactor designs, as will be shown. It also led to both near and complete stock outs of life saving drugs as well as the failure and take-over of a major biopharmaceutical company. Lastly, it continues to lead to unexpected run failures, operational crises, and process performance variability, including unacceptable variability in product quality. This talk will cover 30 years of expensive lessons learned, including some being learned only now.