

## Biotechnology Congress 2015 : Transient physiologic states: Friend or foe? - Wieland Reichelt - Vienna University of Technology

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Progressively expiring patent protection brings forward generic drug industry and heats up competition for the most efficient and robust bioprocesses. While competition is intensifying, the FDA quality by design (QbD) initiative for increased process understanding is increasing demands concerning bioprocess development. These circumstances cumulate to the necessity of comprehensive process understanding and consequently highly efficient bioprocess development routines. For bioprocess development, literature has comprehensively proven the feeding strategy an especially promising target. Having mastered the feedback control of physiological rates by the use of soft sensors, the subsequent step of biotechnological development could lead towards controlled transient changes of physiological parameters. Whereas the majority of the scientific community has chosen the specific growth rate ( $\mu$ ) as target control parameter, we have invested extensive work in the control of the specific substrate uptake rate ( $q_s$ ). Hereby, the  $q_s$  control renders physiology accessible, substrate availability being upstream of physiological variables example  $\mu$ . We want to test the hypothesis that dynamic process control as  $q_s$  profiles in terms of ramps and oscillations constitute tools for efficient tweaking of physiology. By alternating the substrate availability in the reactor the physiologic state of E.coli shall be modulated between high metabolic load and recreational phases during induction. Focusing on product physiology interrelations, modeling and investigation of scale up effects is explicitly not in scope of our investigation. Hereby, we want to address specific questions as the impact frequency and amplitude for  $q_s$  oscillation of on physiology as well slope and orientation of  $q_s$  ramps. The amplitude of oscillation is of great interest can physiological limits be temporarily exceeded by granting periods of recovery? Whereas a high frequency of oscillation of the specific substrate uptake rate could be limited by technical constraints (example sampling capacities, error of measurement) a too long duration could fail to have any impact besides acetate formation. Provocative responses could be both valuable and negative to the mind, contingent upon qualities of their enactment in different phases of neurodegeneration. Gentle enactment of microglia and astrocytes as a rule uncovers neuroprotective impacts and improves early side effects of neurodegeneration; for example, discharged cytokines help keep up synaptic versatility and adjust neuronal sensitivity, and invigorated cost like receptors (TLRs) advance neurogenesis and neurite outgrowth. In any case, solid actuation of glial cells offers ascend to cytokine overexpression/dysregulation, which quickens neurodegeneration. Adjusted common guideline of

p53 protein, a significant tumor silencer, and NF- $\kappa$ B, the significant controller of aggravation, is by all accounts urgent for the move from useful to negative impacts of neuroinflammatory responses in neurodegeneration. Remedial mediation in the p53-NF- $\kappa$ B pivot and adjustment of TLR movement are future difficulties to adapt to neurodegeneration. In the focal sensory system (CNS), degenerative procedures are portrayed by morphological, anatomical, and useful changes that lead to ahead of schedule, constant, and dynamic neuronal misfortune. Constant neurodegenerative illnesses are characterized as innate, irregular, and protein misfolding maladies, which are normally described likewise by the decrease of intellectual capacities, especially learning and memory. These incorporate Alzheimer's sickness (AD) and different dementias, transmissible spongiform encephalopathies (TSEs), amyotrophic sidelong sclerosis (ALS), Parkinson's infection (PD), Huntington's malady (HD), and prion ailments. The causes related with neuronal degeneration remain ineffectively comprehended. For the most part realized hazard factors for most neurodegenerative illnesses are hereditary polymorphisms and propelled age. The overarching theory is that the protein totals or seeds ( $\alpha$ -synuclein, amyloid beta ( $A\beta$ ), lipofuscin, tau protein) trigger a course of occasions prompting neurodegeneration and neuronal apoptosis [1–3]. A few different instruments might be engaged with the pathogenesis of neurodegenerative issue, including constant aggravation, vascular components, oxidative pressure, and decreased accessibility of trophic factors in the cerebrum. Guideline of immuno-provocative control is one of the pertinent procedures associated with the pathogenesis of neurodegenerative issue. Intrinsic and versatile unsusceptible reaction in the mind are firmly controlled in connection with the outskirts. Safe actuation in the CNS consistently includes microglia and astrocytes, which, in non-neurotic conditions, contributes in the guideline of homeostasis of the mind tissue. Endothelia cells and perivascular macrophages are additionally critical to the translation and spread of incendiary signals inside the CNS [4]. In the CNS, microglia consistently examine the microenvironment by delivering factors that impact neighboring astrocytes and neurons, especially in light of disease or neuronal cell injury. This prompts the actuation of a provocative reaction that further draws in a transient, self-restricting reaction through the invulnerable framework and starts tissue fix. Under obsessive conditions, when the ordinary goals instruments fizzled, there is an irregular initiation and creation of fiery components, prompting incessant

neuroinflammatory state and movement of neurodegenerative changes. Interminable neuroinflammation is seen at generally beginning periods of neurodegenerative ailment. The referenced neurodegenerative components sway on glial capacity by overactivation of both microglia and astrocytes activating creation and discharging a lot of ace incendiary cytokines and receptive oxygen and nitrogen species (ROS, RNS). Incessant actuation of microglia is connected to the debasement of protein, the brokenness of mitochondria, and the imperfections of axonal vehicle and apoptosis, which detrimentally affect neuronal capacity and lead to cell passing. Besides, neuroinflammation brings about the ensuing invasion of insusceptible cells from the fringe to the CNS over the blood mind obstruction (BBB), which quickens neuroinflammation and neurodegeneration [5]. In this survey, we plan to address the job of microglia, astrocytes, and resistant reaction in the CNS in the improvement of neurodegenerative issue. The audit will introduce the "two appearances" of neuroinflammation, which can bring about the reclamation of mind homeostasis just as inception or/and quickening of neurodegenerative procedures. Irritation, Inflammation, and Neuroinflammation

Irritation is a complex organic reaction of the body to cell and tissue harms brought about by concoction (acids, soluble base), physical (ionizing radiation, attractive field, ultrasonic waves), and natural components (infections, microscopic organisms, parasites, exotoxins, and endotoxins) [6]. The sort and scope of provocative reaction rely upon the sort and force of the aggravation. Moreover, the tissue and organ opposition is additionally significant. The power of the aggravation and the hour of its effect on tissue decide the kind of provocative state, intense or constant. Irritation can be advantageous as an intense,

transient invulnerable reaction to destructive conditions, for example, tissue injury or an attacking pathogen.

### Biography

Wieland Reichelt is a Project Assistant in the Christian Doppler Laboratory for Mechanistic and Physiological Methods for Improved Bioprocesses at the Vienna University of Technology (VUT). He studied Biochemistry at the Karl Franzens University in Graz before doing his Master's thesis in the field of programmed cell death and aging. After a year of PhD research in the field of neurodegeneration (Parkinson), he transitioned to the field of bioprocess technology at VUT to acquire in-depth understanding of pharmaceutical bioprocess production process approaches. Within his PhD work, he is spanning applied to basic science by developing and employing physiological bioprocess control strategies to tweak industrial bioprocesses to maximum productivity. Hereby, the project unifying goal is to gain mechanistic insight into bioprocess physiology to ultimately achieve comprehensive bioprocess understanding and transferable platform knowledge.

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