Hartmut Grammel et al., J Bioproces Biotechniq 2014, 4:6
http://dx.doi.org/10.4172/2155-9821.C1.006

OMICS International
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3rd International conference on

Bioprocess and Biosystems Engineering

September 14-15, 2015 Baltimore, USA

A fermentation strategy for industrial application of purple bacteria, based on computational modeling

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The high potential of anoxygenic photosynthetic bacteria to produce a range of important compounds such as photosynthetic pigments (porphyrines, carotenoids), coenzymes (Q10), biohydrogen and recombinant membrane proteins is well known since many years. Most of these products are associated with intracytoplasmic photosynthetic membranes (PM) which are induced to maximal levels under anaerobic conditions and low light intensities. However, the industrial large-scale application is so far limited by the requirement for light, which inevitably becomes a limiting factor when cell densities become very high. For the purple non-sulfur bacterium *Rhodospirillum rubrum*, we developed a process for large scale production of PM and associated products completely separated from the availability of light at microaerobic dark conditions in common bioreactors. The cultivation system was successfully employed in an industrial environment for producing phototoxic pigments for photodynamic tumor therapy. A major challenge for process control is that the term microaerobic is not well defined and cannot be reached by conventional oxygen control using amperometric dissolved-oxygen probes. It is therefore particularly useful that *R. rubrum* is exceptionally well accessible by optical spectroscopy for determination of various cellular redox components. By coupling fibre optic UV/Vis/NIR and fluorescence spectrometers to a bioreactor, *in situ* online spectroscopy was established for monitoring of the oxygen response of pyridine nucleotides, cytochrome C, photosynthetic complexes, membrane potential as well as cell growth. Different levels of computational modeling such as metabolic network analysis, and kinetic process modeling contributed to the development of a robust fermentation process for semi-aerobic high-level expression of photosynthetic genes and associated products in the dark. To meet a major requirement for industrial fermentation processes, kinetic process modeling was applied for fed-batch high cell density cultivation yielding 60 g/L cell dry weight. To our knowledge this value represents the highest cell concentration achieved with a phototrophic bacterium so far.

Biography

Hartmut Grammel, microbiologist completed PhD on antibiotics production with bacteria at the Institute for System Dynamics and Control, University Stuttgart, Germany. He was a founding member of the Max Planck Institute for Dynamics of Complex Technical Systems, Magdeburg, Germany in 1996. From 2007-2012, he headed a Forsys (research units in systems bioloy) research group funded by the German Federal Ministry of Education and Research (BMBF), Germany. In March 2012, he was appointed as Professor for Industrial Microbiology at Biberach University of Applied Science, Biberach, Germany. His current research focuses is on carbon dioxide fixing enzymes from phototrophic bacteria funded by BMBF.

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