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Beneficial effects of scale-up: toward a better integration of microbial physiology for bioprocess engineering

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Scale-up procedures are known to induce unwanted effect at the level of the microbial physiology [1]. Indeed, appearance of gradients due to mixing defects lead to the exposure of the microbial cells to environmental fluctuations. Since microbial cells are able to respond to these fluctuations by changing metabolic pathways or by inducing specific response proteins, global physiology can be significantly affected in large-scale bioreactors by comparison with lab-scale equipment. It is known at this level that productivity is reduced in large-scale environment. However, it is less known that robustness and fitness of microbial cells is promoted in fluctuating environment [2]. Since robustness and productivity are both needed in order to lead to efficient cell factories, large-scale fluctuations can be viewed as an innovative way for improving cell factories. This concept will be demonstrated in the case of *E. coli* for which both metabolic engineering and bioreactor design can be exploited in order to increase the efficiency of the corresponding bioprocess [3][4][5]. In a second time, this concept will be extended to two less common cell factories, i.e. *Bifidobacterium bifidum* [6] and *Yarrowia lipolytica* [7]. In conclusion, both metabolic engineering (and to some extent synthetic biology) and bioreactor design can be exploited in order to lead to more robust and innovative bioprocessing strategies.

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