



# **GFP Whole Cell Microbial Biosensors: Scale-up and scale-down effects on biopharmaceutical processes**

*Frank Delvigne*

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Two strategies are usually considered for the optimization of microbial bioprocesses. The first one involves genetic or metabolic engineering of the target microbial strains in order to improve its production efficiency or its tolerance to adverse conditions. The second one is based on the chemical engineering improvement of the bioreactors and scaling-up rules. This work is more particularly dedicated to this second class of parameters. Recent developments in bioreactor technologies follow the scaling-out principle, i.e. carrying out several cultures in parallel with controlled conditions for screening purposes. Several mini-bioreactor concepts, i.e. bioreactor with working volume of 1 to 100 mL with controlling devices, have been developed following this principle. In general, chemical engineering similarities between conventional stirred bioreactors and their miniature equivalent are well characterized. However, the actual scaling-up rules are not able to cope with the complexity of the microbial stress response. Indeed, microbial stress response still remains not completely understood considering the process perturbations and the environmental fluctuations accompanying the scaling-up to industrial bioreactors. At this time, this kind of response can only be experimentally predicted by using scale-down bioreactors, i.e. lab-scale bioreactors designed in order to reproduce mixing imperfections that have to be expected at large-scale. However, the use of such an approach is time consuming and requires an experimented staff to elaborate the scaling-down protocols. Indeed, bioprocess development involves several steps which cannot be necessarily linked with each other considering the different cultivation equipment used.

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