Investigation of effects of a hot-spot in bioprocess control

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Bioprocesses have dynamics in different time scales and comprise of liquid-gas transfer and reactor dynamics in the time scale of seconds, cell metabolism in minutes and cell growth in hours, roughly speaking. For operation and control design the reactor is usually considered as homogenous and is a reasonable simplification. For larger reactors and dependent on the micro-organism effects of in-homogeneities may play an important role also for control design. A recent interesting study in 100 m^3-scale is [1].

Here a two-compartment model of a standard description of yeast is used to illustrate effects of a zone around the substrate inlet with high substrate concentration compared to the rest of the reactor. Oxygen supply is assumed to be above limitations for simplicity. The approach has been studied experimentally by several research groups by connecting two lab reactors in series with re-circulation and adding substrate to one of the reactors [2] and in [3] plug flow reactor was used instead for a more well-defined hot-spot zone. The model structure with two similar reactors in series with re-circulation can easily be configured in the object-oriented Modelica library [4].

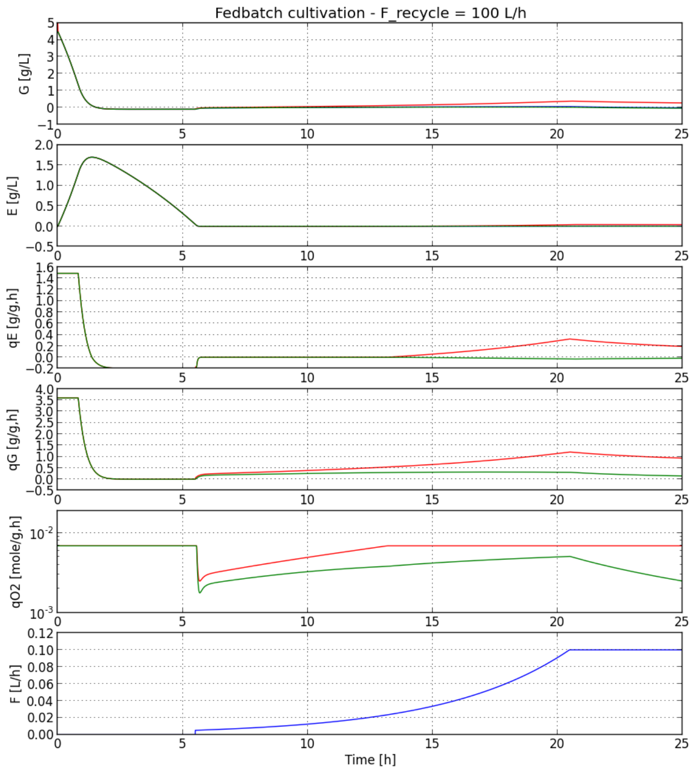

Figure 1. On-set of ethanol production/consumption at time 14 hours due to high substrate gradient around the substrate feed point. Simulation results. Larger reactor green line and smaller hot-spot reactor red line. G and E are glucose and by product ethanol concentration, and qG and qE are their specific consumption/production rate. Specific respiration rate is qO2 and finally F is the glucose substrate feed rate. The chosen F_recycle = 100 L/h corresponds to a space time of about 20 seconds for the hot-spot volume.

In Figure 1 the phenomena of simultaneous production of by-product ethanol in the smaller hot-spot reactor with substrate inlet and consumption of ethanol in the other larger main reactor. At time 14 hours the substrate supply reaches a level where ethanol is produced in the hot-spot and quickly consumed in the larger reactor, giving little overall accumulation of ethanol. The biomass yield drops however as seen in Figure 2.

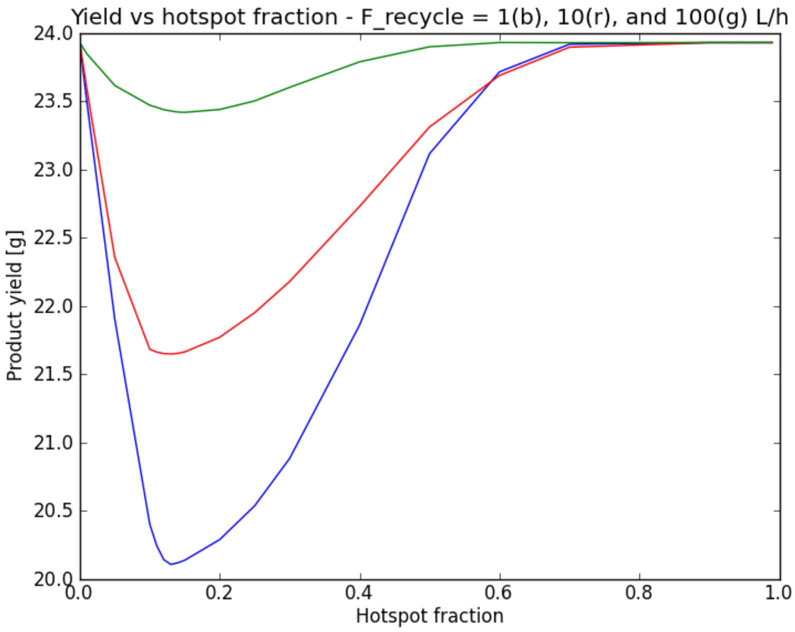

Figure 2. Biomass yield vs. hotspot fraction for different re-cycle flows. The hot-spot fraction is the size of the smaller reactor in percentage of the total volume of the two reactors.

Perturbations in feed rate around the optimal feed profile for the two-reactor setup is compared with results from a homogenous reactor. Implications for substrate control design are discussed.

The phenomena of simultaneous production and consumption of by-product is thought to be quite similar for different micro-organisms such as: *S. cerevisiae, E. coli* and *B. licheniformis*, although the by-product differs as well as the kinetic models.

References:

[1] Johnsson, O., ”Perturbation-based control of industrial fed-batch bioprocesses”, PhD-thesis, Department of Automatic Control, Lund University, 2015.

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[3] George, S., G. Larsson, and S.-O. Enfors, “Comparison of the Baker’s yeast process performance in laboratory and production scale”, Bioprocess Engineering, Vol 18, 1998.

[4] Axelsson, J. P., ”Modelica library for simulation of bioprocesses”, NPCW Copenhagen, 2012.