Interview with Dr. Souad Fehaili

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Dr. Souad Fehaili is our process engineering teacher. Thanks to this relationship, we could easily contact her as soon as the bioreactor idea came to our minds. Elaborating a confined bioproduction system is not an easy task, and requires multidisciplinary competences in various domains. That is why we were really lucky to get her precious technical and strategic advices on the subject.

Do you know any examples of bioreactors implemented outdoors? Would this system be considered as confined?

→ Of course, some bioreactors can be implemented externally. It is notably the case of photobioreactors, which need light to ensure the growth of photosynthetic micro-organisms.

In order to preserve the interesting property of our micro-organisms to respond to external temperature changes, the medium temperature inside the bioreactor should correspond to the outside air. Can we achieve this with an absence of heating or cooling system? Or metabolic reactions will heat up the medium by themselves?

→ You don't necessarily need to install your bioreactor outdoors to reproduce the outside air temperature inside the medium. According to me, it will be in fact far more convenient to put it in a contained facility given all the additional filtration, waste, recycling, and thermo-regulating systems you will have to connect. You can easily regulate the medium temperature according to the outside thanks to a thermal sensor set up outside and directly linked to a thermo-regulation system.

How could the medium temperature be regulated in this situation?

→ You will need a double envelope bioreactor. The thermal sensor will be connected to a water thermoregulation system, and activate either a cryostat to produce cold water, either a heater to produce hot water. The thermoregulated water will then circulate into the bioreactor external envelope in order to either cool or heat the medium. The advantage of a confined bioreactor is that you will be able to control the temperature and keep it at an optimal production value. When applying your microorganisms on the plants, they have to resist high temperatures.

We would like to use a continuous culture system in order to keep the autonomy of our self-regulating system. We found chemostats, which appeared well adapted for this objective. What do you think of this option?

→ A chemostat would perfectly fit your requirements. Two tanks need to be installed: a feed tank containing fresh medium, and a waste tank. The limitation is that at some point, you need to get rid off dead bacteria. You will then need to regularly empty the tank (every few weeks, but the precise interval could be determined by some tests), centrifuge the medium and eliminate the precipitated microorganisms. The entering and leaving medium flow rates will be regulated by some pumps. Since you are working with low volumes, volumetric pumps should be more suitable. In addition, they are also important to prevent the pressure loss due to internal frictions between the liquid and the wall. They restore the fluid energy and impose a flow.

What would be the best strategy to retain the microorganisms while letting the protectants of interest pass through to be disseminated? Are filters considered as containment systems?

→ The filtration system is a good idea. You will end with you different fluids: the fluid having passed through the filter is called filtrate, and will contain water, protective compounds and medium elements. The retained portion, containing bacteria, is called retentate. Decantation can turn out to be another interesting separation technique for your project. It could be advantageous if you want to limit the need for cleaning, as bacteria will end clogging the filter. The assessment of the best separation technique would require some tests at small scale. What could be interesting is to find a way to concentrate the filtrate after having passed through the filter. This would allow your product to be competitive by lowering the water consumption.

Based on our culture and filtration systems, can we consider our entire device as confined?
→ Filters can certainly be considered as containment systems as long as they are certified by an accreditation body. You could try to contact experts in this domain to get more precise information about the required certifications. In the same way, the entire equipment materials will be hermetic. However, there will still be a need to maintain the continuous culture and to clean the different parts. For this, filters will need to be transiently and exceptionally removed and the culture tank opened.

As the medium temperature will not be constant, should we find a way to modulate the microorganism and medium entry in function, as the growth rate will probably change?

→ Ideally you should. But unfortunately, precisely regulating the flow rate of entering medium according to the growth rate resulting from changing temperatures would be difficult. The entering flow rate is usually constant.

What would be the best dispersion technique to use?

→ I would say you could mimic the classical aspersion method, but it depends on the liquid viscosity. If too viscous, this technique will not be adapted.

Do you have other remarks?
→ You should contact an automation specialist regarding the whole aspect of the bioreactor automated regulation. It is important that you highlight precisely what would be the added value compared to the initial project idea, but also to already existing plant protection techniques. What is important is also to determine if your microorganism will survive after the filtration step. If it is the case, you will be able to add a recycling loop and make the retained microorganisms re-enter the culture tank. If not, they will have to be dropped into the waste container.

We are really grateful to Souad Fehaili, without whom we would not have been able to push our very fledgling idea so far !

The iGEM IONIS Team.