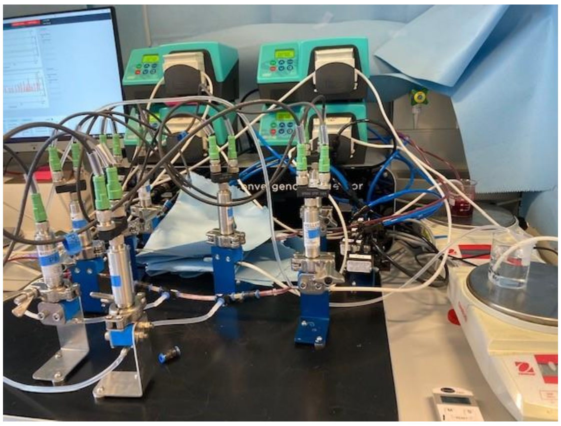
Problem statement

Kidneys have the crucial task of purifying our blood. Patients with only 10% kidney function left will get slowly poisoned, because by-products such as creatinine and urea are no longer or not sufficiently filtered from the blood anymore. Kidney failure could be innate or it could be due to an injury or unhealthy lifestyle (smoking, unhealthy diet, etc.). Due to an aging population and the prevalence of these risk factors the incidence of kidney failure is expected to rise.

The best treatment for kidney failure patients is a kidney transplantation, however, there are not enough donor organs available. Therefore, millions of patients depend on hemodialysis therapy worldwide. Unfortunately, hemodialysis has some disadvantages – even though it is a lifesaving therapy. First of all, patients need to go to the hospital three times a week to receive a dialysis session of usually four hours and this really limits their freedom and quality of life. Moreover, it takes a lot of time to remove toxins from patients' blood. Longer treatment times are therefore suggested, for example in the form of nocturnal dialysis, portable and wearable dialysis systems. However, dialysis filters are not suited for these prolonged applications yet. Research has namely shown that dialysis filters lose hydrophilic additives during dialysis treatment. Another major disadvantage of current hemodialysis systems is that the dialysis filters are not able to remove all kinds of toxins. Especially, the middle molecules and protein-bound toxins are difficult to filter from the blood. Finally, the carbon footprint and biological and ecological effects of the therapy are hot topics as well nowadays. Research focusing on these issues include, for example, the search for 'greener solvents' to be used for the manufacturing of the filters' membranes and ways to regenerate the therapy's dialysate solution [1-5].



'Mini dialysis set-up' (Convergence)

Ultimate goal

In order to improve hemodialysis, the following is needed:
A) a system that mimics the "healthy kidneys" and filters the blood for longer periods of time or continuously like in nocturnal dialysis or in a portable/wearable artificial kidney.
B) a system that can remove the middle molecules and protein-bound toxins.
C) a system that has a smaller carbon footprint.

Assignment goal

Up to now, our in-house developed filters for hemodialysis were tested using human plasma from healthy donors spiked with uremic toxins instead of using full human blood (containing red blood cells, platelets, etc.) which is of course a more complex fluid. To mimic a real dialysis therapy session, our dialysis filters should naturally be tested with full blood as well.

The goal of your assignment is to set up and improve an experimental protocol to test our in-house dialysis filters using full (porcine or human) blood. You will *prepare* 'mini dialysis filters' containing commercial hollow fiber membranes and in-house hollow fiber membranes, you will *perform* dialysis experiments with our dialysis set-up from Convergence, and you will *analyze* dialysis samples from the blood circuit and dialysate solution circuit to determine the filtering capacity of the hollow fiber membranes.

Research question: What is the best protocol for performing full blood dialysis experiments using a Convergence set-up?

Experiments & equipment

1. Preparation of mini-modules: dialysis filters containing commercial hollow fiber membranes and in-house developed hollow fiber membranes.
2. Characterization of the dialysis filters using the clean water flux (CWF) set-up, to determine the water permeance of the fibers.
3. Perform dialysis experiments (4h diffusion experiments) using full porcine blood and/or full human blood, spiked with:
    - → Indoxyl sulphate
    - → Hippuric acid
    - → Creatinine

4. Preparation and analysis of full blood samples and dialysate solution samples using high performance liquid chromatography (HPLC), to study the dialysis filters' toxin removal.
5. Perform long-term experiments (8h, 24h)

References

[1] Himmelfarb, J., et al., *The current and future landscape of dialysis*, Nature Reviews Nephrology, 16(10) (2020), p. 573-58.
[2] Dukhin, S., et al., *Outside-in hemofiltration for prolonged operation without clogging*, Journal of Membrane Science, 464 (2014), p. 173-178.
[3] Kim, D., et al., *High flux mixed matrix membrane with low albumin leakage for blood plasma detoxification*, Journal of Membrane Science, 609 (2020).
[4] Geremia, I., et al., *New mixed matrix membrane for the removal of urea from dialysate solution*, Separation and Purification Technology, 277 (2021).
[5] ter Beek, et al., *Hollow fiber membranes for long-term hemodialysis based on polyethersulfone-SlipSkin™ polymer blends*, Journal of Membrane Science, 604 (2020).