

# Analysis of fluorescein release through a hydrogel diffusion barrier

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## Introduction

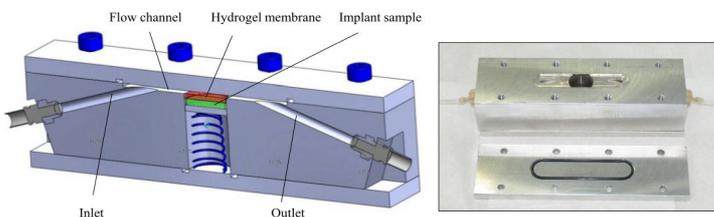
- Implant-associated infections are a serious condition mostly caused by bacteria, which are introduced during surgery [1].
- In extreme cases the implant needs to be surgically replaced (so called *revision*).
- Possible ways to address these problems include the use of drug-eluting implants [2, 3] or bone cements [4, 5].
- Before a drug-eluting implant can be placed on the market, a thorough assessment of the drug-release kinetics both in-vitro and in-vivo is required [4].
- The most common in-vitro method is the so called paddle apparatus [6]. It is very simplistic and shows poor correlation with clinical trials and animal tests.
- *In-vivo* studies are expensive, time-consuming and often ethically questionable.

## Objective

- To develop a phenomenological in-vitro model for continuous monitoring of the drug-release kinetics from orthopedic implants.
- This method is aimed at reducing the number of animal tests in the early stages of the development of new drug-eluting implants by providing the manufactures of such implants and alternative in-vitro method.

## Material and methods

- Emulation of a diffusion barrier:

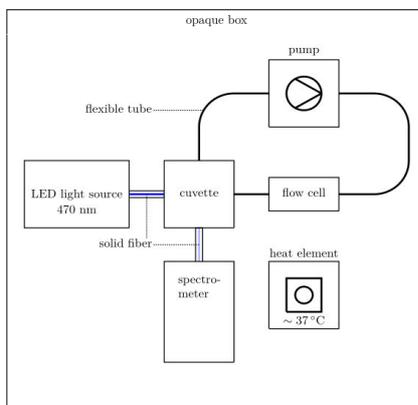


- The membrane serves as a diffusion barrier. The characteristics of the hydrogel membrane can be controlled by changing its composition and thickness (1-4 mm) and depends on the biological tissue which should be emulated.

- Measurement setup:

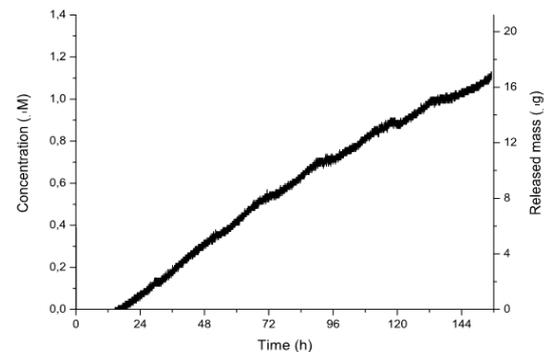
The blood substitute circulates in circle past the hydrogel membrane.

The analysis of the medium takes place in form of online spectroscopy. The temperature regulation ensures constant a constant temperature of 37 °C inside the opaque box.



## Results

- Release study of 40 µM Fluorescein sodium aqueous solution (no implant model).



- First detectable dye concentrations measured after 12 hours.
- Concentration in the main flow circuit after one week was 1.1 µM, which equals an amount of released drug of 16.6 µg (40 % of the available amount in the reservoir).
- Small oscillations ( $\pm 10\%$ ) due to the night and day temperature fluctuations can be observed on the curve.

## Outlook

- First tests have shown that the proposed method can be used for continuous monitoring of the drug release process.
- Future measurements will be carried out with implants being coated with Fluorescein labeled Gentamicin and multilayer hydrogel membranes.
- Parameters like membrane thickness or flow rate should then be tuned to match in-vivo data reported in the literature.
- In a next step the results have to be compared with results from establish methods like the paddle apparatus to provide an alternative for in-vivo studies.

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GEFÖRDERT VOM

