# COMPUTATIONAL MODELS OF PERITONEAL DIALYSIS

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## Introduction

Physiological *in silico* models play a critical role in improving patient-specific kidney replacement therapies and making them available to help patients with reduced kidney function. Peritoneal dialysis (PD) is one such therapy [1], that is used to supplement kidney function in 15% of the kidney patients in the Netherlands [2]. Myself and others have improved the mathematical models of kidney physiology, including amongst others sex-specific differences [3], solutes, drug and toxin transport [4] and their interactions [5], influence of tubular architecture [6], alongside models of the device itself, marking all important discoveries but what lacks is a benchmarking of the different models on the same clinical dataset. In this work, we look at some of the historical models of PD and benchmark the efficiency of the models in predicting time-dependent evolution of six solute dialysate concentrations (urea, creatinine, sodium, potassium, glucose and phosphate).

## Methods

We chose two mechanistic models (Graff et al. [7], Öberg et al. [8]) and two analytical models used in clinical practice (Garred et al. [9], Waniewski et al. [10]). The four models, in combination, encompass various mechanisms that are essential to PD (diffusion, convection, lymphatics). We collected experimental data from multiple dwell studies in one or two sessions ($n = 16$) performed in pigs. We trained each of the models by fitting the dialysate solute concentrations (in some of the dwell studies) to predict the mass transfer area coefficients (MTAC) of each solute. Using the fitted MTAC, we predict the dialysate solute concentrations in the rest of the dwell studies. We assessed the root mean square error (RMSE) and the physiological plausibility of the fitted MTAC to find the best performing benchmark model (table 1, figure 1).

Table 1 shows that model 7 (Öberg et al.) is the optimal model in terms of low error in solute concentration predictions, applicability of the model to multiple datasets (with different initial dialysate concentration), physiological MTAC values and reasonable ultrafiltration values in pigs. This model is also modular and has been applied to automated PD and continuous flow PD. In the future, we aim to extend this model to mimic a novel PD device with an adsorption chamber to help with detoxification [9]
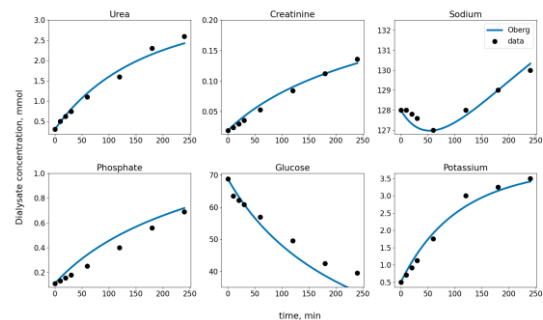


*Figure 1: comparison of predicted data by Öberg model with pig data.*

## References

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## Results and Discussion

| Model | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Graff1 | ✓ | | fixed | ✓ | ✓ | | ✓ | ✓ | ✓ | ✓ | |
| Graff2 | ✓ | fixed | ✓ | ✓ | ✓ | | | | ✓ | | |
| Graff3 | ✓ | ✓ | fixed | ✓ | ✓ | | ✓ | ✓ | ✓ | | |
| Graff4 | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | ✓ | |
| Graff5 | ✓ | fixed | fixed | ✓ | ✓ | | ✓ | ✓ | ✓ | ✓ | |
| Graff6 | ✓ | ✓ | ✓ | | | | | | | | |
| Öberg | ✓ | literature | literature | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Garred | ✓ | fixed | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | |
| Waniewski | ✓ | fixed | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | |

*Table 1: Is the model RMSE per solute ($<\pm3\%$), is the model applicable to all the datasets, are the predicted MTAC physiological? Graff model (model 1-6) is a comparison of six models with the convection and lymphatics mechanisms turned on and off. Column 1-3 represent diffusion, convection and lymphatics parameter whether fixed or fitted (✓) in the model. Column 4-6 represent the accuracy of predicting urea, creatinine, sodium, phosphate, glucose, potassium dialysate concentration. Column 10 represents generalisability of the model to different datasets and 11 represent plausibility.*