

## Invertible neural networks for resolving the hemodynamic inverse problem

In medical diagnostics, where the health status of a patient is often determined with little or no intervention, measurands often obtained indirectly by solving a statistical inverse problem. Since variability in biological systems is typically large, the inverse problem is often ill-posed and uncertainty estimations are difficult. In recent years, efficient methods for uncertainty quantification for indirect measurements have been developed and applied [1]. To improve efficiency and computational speed, invertible neural networks (INNs) are successfully applied to estimate posterior distributions (distributions of the measurand) [2,3].

However, the state-of-the-art INNs do not account for measurement error models and estimates of significant hyperparameters, which leads to a systematic underestimation of obtained uncertainties (peak and multimodal distributions). First mathematical foundations for the treatment of multimodal posterior distributions were developed by Hagemann et al. [4].

In the proposed project, a general framework to determine uncertainties for Bayesian inversion for computational expensive systems using INNs will be developed. This includes the treatment of measurement errors, model errors and uncertainties caused by stochastic INNs.

The developed framework will be applied to hemodynamics (blood flow through the human body) to solve the statistical inverse problem from simulated and clinical data to provide more clinically relevant information for physicians from measurements.

The overall objective of the project is to develop a stochastic INN approach for dealing with measurement errors, model errors, hyperparameters, multimodal posterior distributions, and apply it to hemodynamics to obtain information of the cardiovascular system from blood pressure measurements for improved diagnosis.

The specific objects of the project are:

- Develop a stochastic INN approach for Bayesian inversion incorporating measurement and model errors.
- Develop tools to capture multimodal posterior distributions in the framework of stochastic INNs.
- Train stochastic INNs with virtual hemodynamics reference data and estimate physiological parameters and associated uncertainties from simulated measurement data.
- Determine distributions of cardiac and arterial parameters like elastic PWV, muscular PWV, elastic diameter, muscular diameter, heart rate, stroke volume and peripheral resistance for different cohorts from real data.

Work program is divided into 5 work packages (WP).

**WP1:** Extending the state-of-the-art INN approach to solve high dimensional statistical inverse problems by including measurement errors, model errors and hyper-parameter estimations.

**WP2:** Use appropriate Lipschitz constants to learn transport maps from multimodal Gaussian distributions to multimodal posterior distributions.

**WP3:** Train the developed stochastic INNs through databases consisting of simulated data for estimates of cardiac and arterial parameters. At least two databases of virtually adults are available to train the extended stochastic INNs. The databases contain cardiac and arterial parameters as well as pulse velocities, pressure curves and PPG [5,6].

**WP4:** Validation of the INN with simulated reference data.

**WP5:** Determine cardiac and arterial parameters and associated uncertainties for different cohorts from blood pressure measurements using pre-trained stochastic INNs near real time. Uncertainties include model errors, measurement errors and INNs uncertainties.

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