Pathological Test for Cardio/cerebrovascular diseases: Platelets dynamics and Approximate Bayesian computation

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According to World Health Organization (WHO) report on 2015 Cardio/cerebrovascular diseases (CVD) have become one of the major health issue in our societies. But recent studies show the clinical tests to detect CVD are ineffectual as they do not consider different stages of platelet activation or the molecular dynamics involved in platelet interactions. Further they are also incapable to consider inter-individual variability. Recently, Chopard et al., (2017) introduced a physical description of platelets deposition, by integrating fundamental understandings of how platelets interact in a numerical model of platelets deposition, parameterized by 5 parameters (eg. *adhesion and aggregation rates).* Our main claim is that those parameters are precisely the information needed for a pathological test identifying CVD captured through the numerical model and also these parameters are capable to capture the inter-individual variability. Following this claim, our contribution is two-folds: we devised an inferential scheme for uncertainty quantification of these parameters using Approximate Bayesian Computation and High Performance Computing and finally tested the claim and efficacy of our methodology through an experimental study.

In Dutta et. al. (2018), we devised a Bayesian inferential scheme for estimation of these parameters, using experimental observations, at different time intervals, the average size of the aggregation clusters, their number per mm^2 , the number of platelets and the ones activated per µl still in suspension. As the likelihood function of the numerical model is intractable due to the complex stochastic nature of the model, we use a likelihood-free inference scheme approximate Bayesian computation (ABC) to calibrate the parameters in a data-driven manner. As ABC

requires the generation of many pseudo-data by expensive simulation runs, we use a high performance computing (HPC) framework for ABC to make the inference possible for this model. To verify our claim and whether the proposed methodology provides us with a diagnostic tool for CVD, we performed an experiment divided into three stages.

Stage 1: Experimental design for collection of blood or platelet from patients: We plan to analyze healthy volunteers and 4 groups of patients affected by different blood related diseases (eg. Diabetes, Hypertension and dyslipidemia) and recruited volunteers/patients for each of the group through consultations at the hospital and collected their blood sample for testing.

Stage 2: Study the deposition patterns observed in the Impact-R of platelet collected for each patients: The Impact-R is a well-known platelet function analyzer. It is a cylindrical device filled in with whole blood from a donor. Its lower end is a fixed disk, serving as a deposition surface, on which platelets adhere and aggregate. The upper end of the Impact-R cylinder is a rotating cone, creating an adjustable shear rate in the blood. Due to this shear rate, platelets moves towards the deposition surface, where they adhere or aggregate. Platelets aggregate next to already deposited platelets, or on top of them, thus forming clusters whose size increase with time.

Stage 3: Estimation of the *adhesion and aggregation rates* using Approximate Bayesian Computation given observed deposition patterns for each patient: Finally, to verify whether our claim is true, we investigate whether the estimated parameter values of the *adhesion and aggregation rates* for each of the patients by our methodology also clusters according to the grouping, showing the success of our methodology and proposing a personalized clinical test for early detection of CVD. In our view, this will open up an unprecedented opportunity of personalized pathological test for CVD detection using numerical modeling of platelet deposition, Bayesian uncertainty quantification and High performance computing.

Reference:

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