IMPLEMENTATION OF MODEL-BASED DESIGN OF EXPERIMENTS: APPLICATION OF COMPUTATIONAL MODELING TO SUPPORT HRP STUDIES

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Introduction

Ground-based Human Research Program (HRP) sponsored experiments are being used to investigate the effectiveness various countermeasures, such as those for Spaceflight Associated Neuro-ocular Syndrome (SANS). Computational models of the cardiovascular system, central nervous system, and ocular fluid system have been developed that can provide insight into physiological responses that cannot be ascertained directly from experimental observations. This study illustrates the concept of utilizing computational simulations to improve experimental efficiency using Model-Based Design of Experiments (MBDOE)[1].

Objective

- Develop a prototype MBDOE process (Fig. 1)
- Implement MBDOE procedures with the HRP developed computational models
- Investigate the potential to optimize a potential SANS countermeasure experiment

Methods

A published Head-Down Tilt (HDT) Experiment[2] was used to represent potential experimental data from an investigation to develop a countermeasure intended to achieve a target IOP. Implementation followed these assumptions and processes:

•HDT induces a head-ward bulk fluid shift as an analog to the fluid shift seen in microgravity and causes an increase in IOP
•IOP is measured at the eye at discrete time intervals
•IOP test data was artificially extended for to simulate the experimental process
•IOP measures generated for an initial test matrix of 1, 13, and 25 minutes at 60, 85, 110, 135, and 160 mmHg Mean Arterial Pressure (MAP) where MAP is assumed proportional to tilt angle.

The NASA-GRC Eye fluid balance model[3] provided the computational means to thoroughly investigate the experimental parameter space
•Lumped parameter numerical eye model to simulate IOP alterations in the eye during HDT
•Simulations reproduce HDT experiment predicting IOP at discrete time intervals

The implementation of the MBDOE process is described in Fig. 2, which illustrates the model parameter optimization step that improves model predictions with each iteration. This process assumes control parameters of time of the tilt testing (minutes) and the tilt angle assumed to be proportional to MAP.
•Compare current test data to model predictions
•Identify factors the cause target responses
•Repeat process – each iteration optimizes model parameters until predictions variance reach acceptable levels in the response region of interest

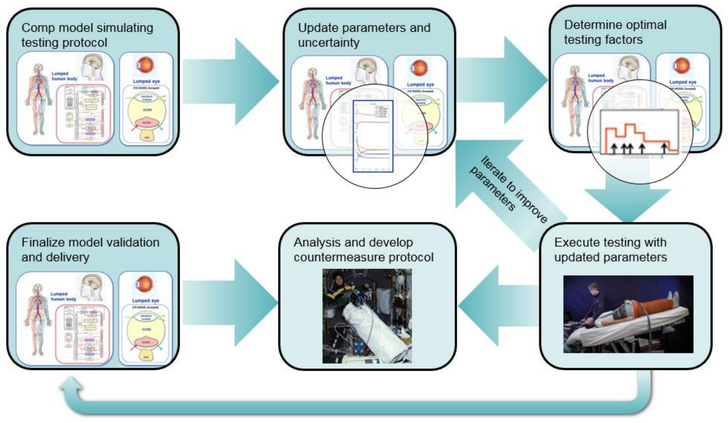

Figure 1: Illustration of MBDOE process optimizing countermeasure development. Shown here is model parameter improvement approach to reduce predictive uncertainty to inform experimental testing and model accuracy using tilt table experiments and cardiovascular, central nervous system and ocular simulation tools.

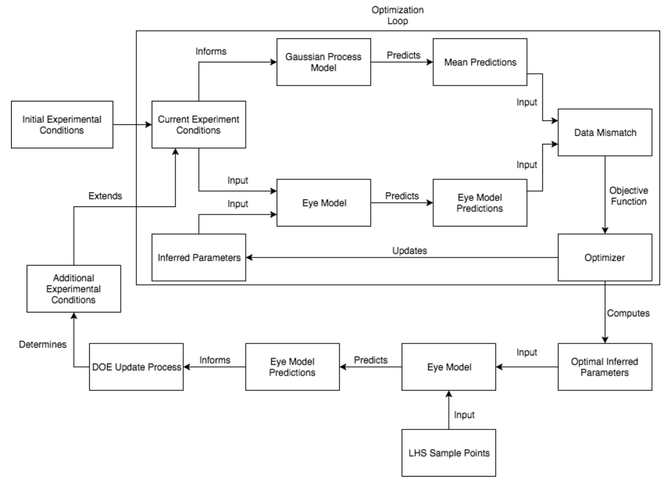

Figure 2. MBDOE process as implemented with GRC eye model. Note due to the artificial nature of the experimental data set, a Gaussian process smoothing was used with the data from Xu et al.[2].

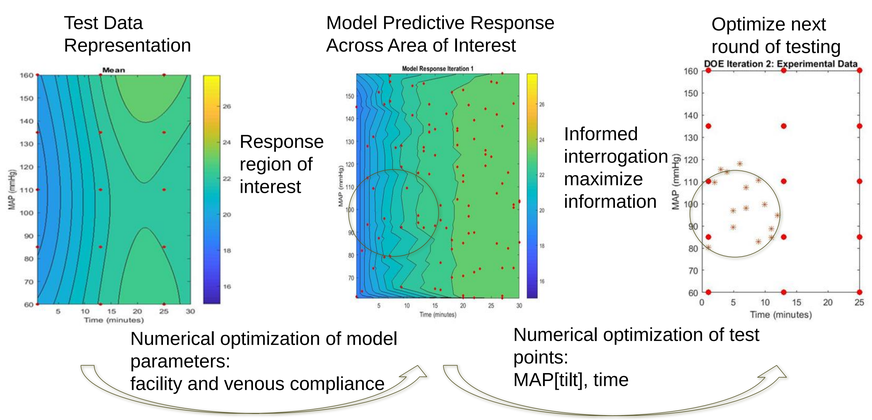

Figure 3: First iteration Experimental data representation (left), model response at optimized testing factors using LHS (center), informed testing based on model response (right).

Results

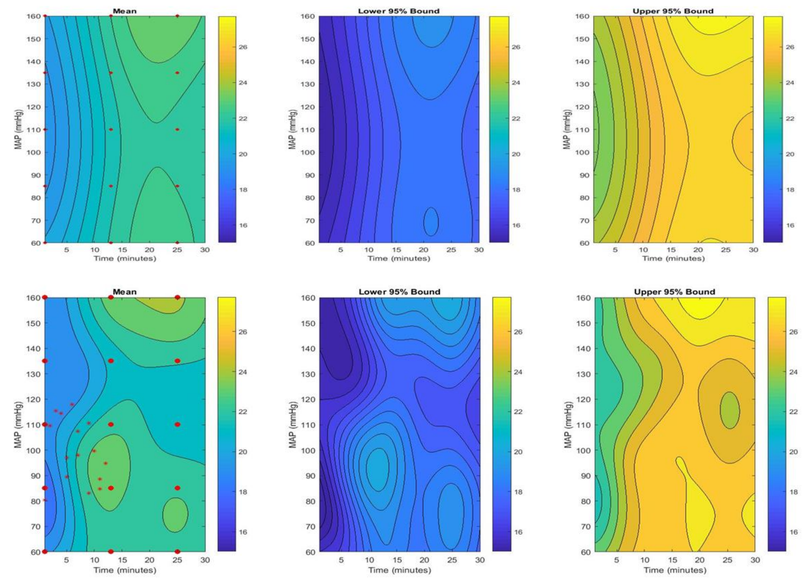

Figure 4: Test data mean IOP response (top left), minimum variance (top center), and maximum variance (top right) Following factor optimization and informed experimental testing at the region of interest (bottom left), minimum variance (bottom center) and maximum variance (bottom right) are reduced. Variance is represented using a Gaussian Process Regression.

Conclusions & Future Work

- After one iteration of the MBDOE process, local and system variance is reduced in the area of interest by approximately 13% (Fig. 4 and 5). More iterations of this process would further reduce variance and decrease uncertainty.
- Future work will include further development of these MBDOE processes to obtain a more systematic means of designing experiment parameters to minimize experimental uncertainty and establish closure criteria.

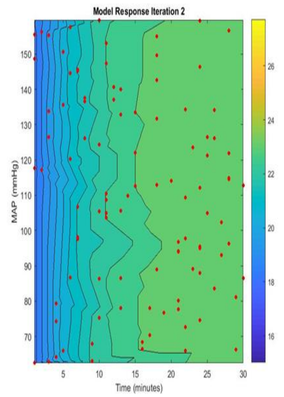

Figure 5: Decreased variance in IOP response following one MBDOE iteration.

References & Acknowledgements

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[2]Xu, X., Li, L., Cao, R., Tao, Y., Guo, Q., Geng, J., & Zhang, Z. (2010). Intraocular pressure and ocular perfusion pressure in myopes during 21 min head-down rest. Aviation, space, and environmental medicine, 81(4), 418-422.
[3]Nelson, E. S., Mulugeta, L., Feola, A., Raykin, J., Myers, J. G., Samuels, B. C., & Ethier, C. R. (2017). The impact of ocular hemodynamics and intracranial pressure on intraocular pressure during acute gravitational changes. *Journal of Applied Physiology*, jap-00102.