INCOSE Healthcare Working Group

4th Annual Systems Engineering in Healthcare Conference

Panel Session: Challenges in Computational Model V&V for Systems Engineers

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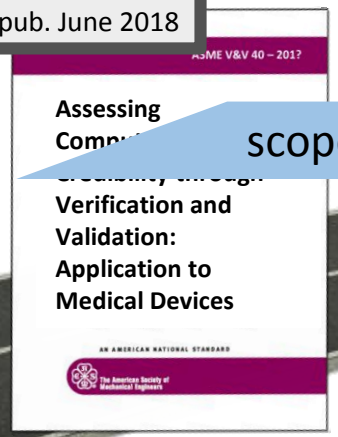
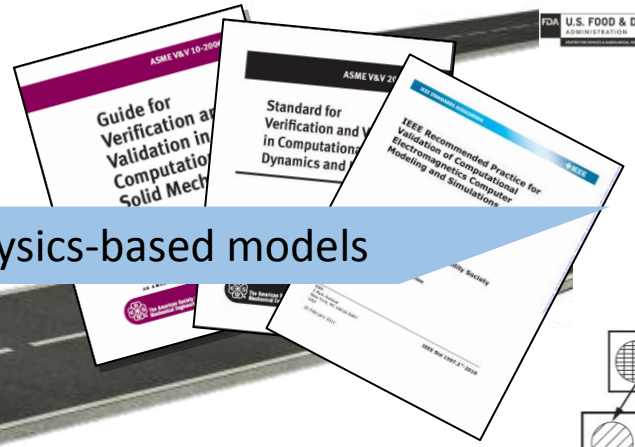
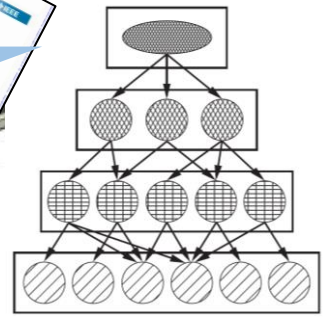
Regulatory Pathway for Computational Modeling

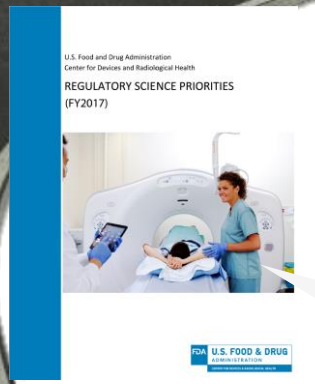
expected pub. June 2018

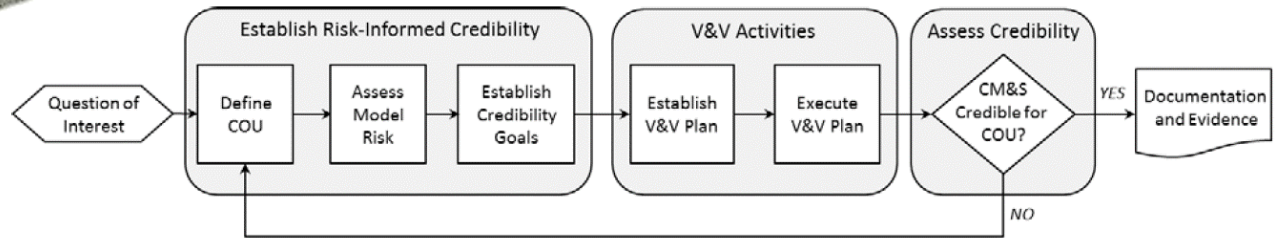




scope = physics-based models





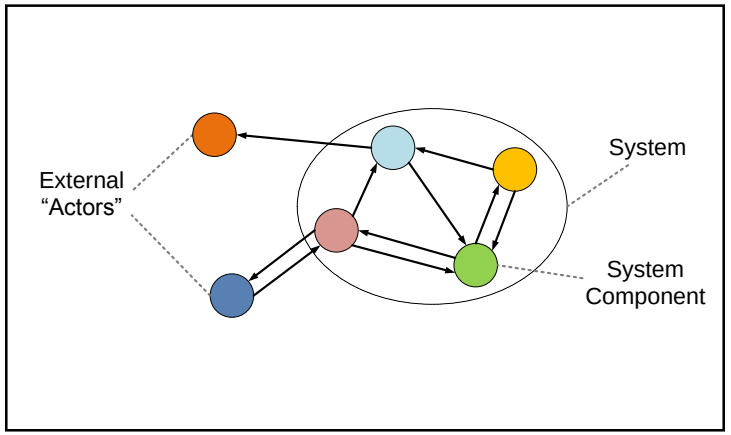


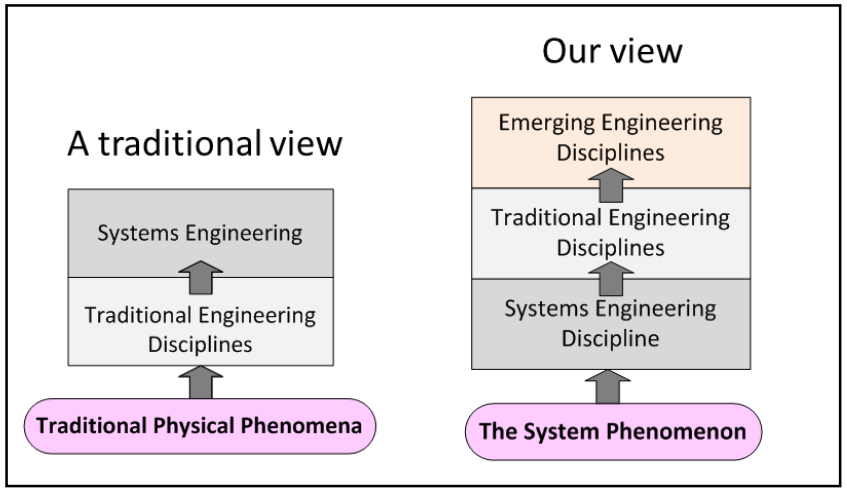
"Develop computational modeling technologies to support regulatory decision-making"

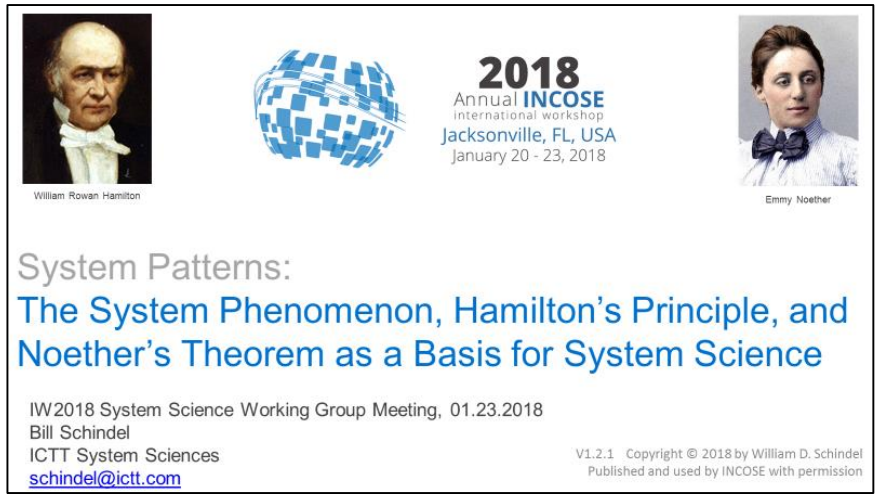
Challenges in Computational Model V&V for Systems Engineers

Bill Schindel

There is a (mis)perception that “computational models” in mechanics and other phenomena must be different than “system models” familiar in INCOSE. Some of this is a matter of historical origin; convergence greater than evident:







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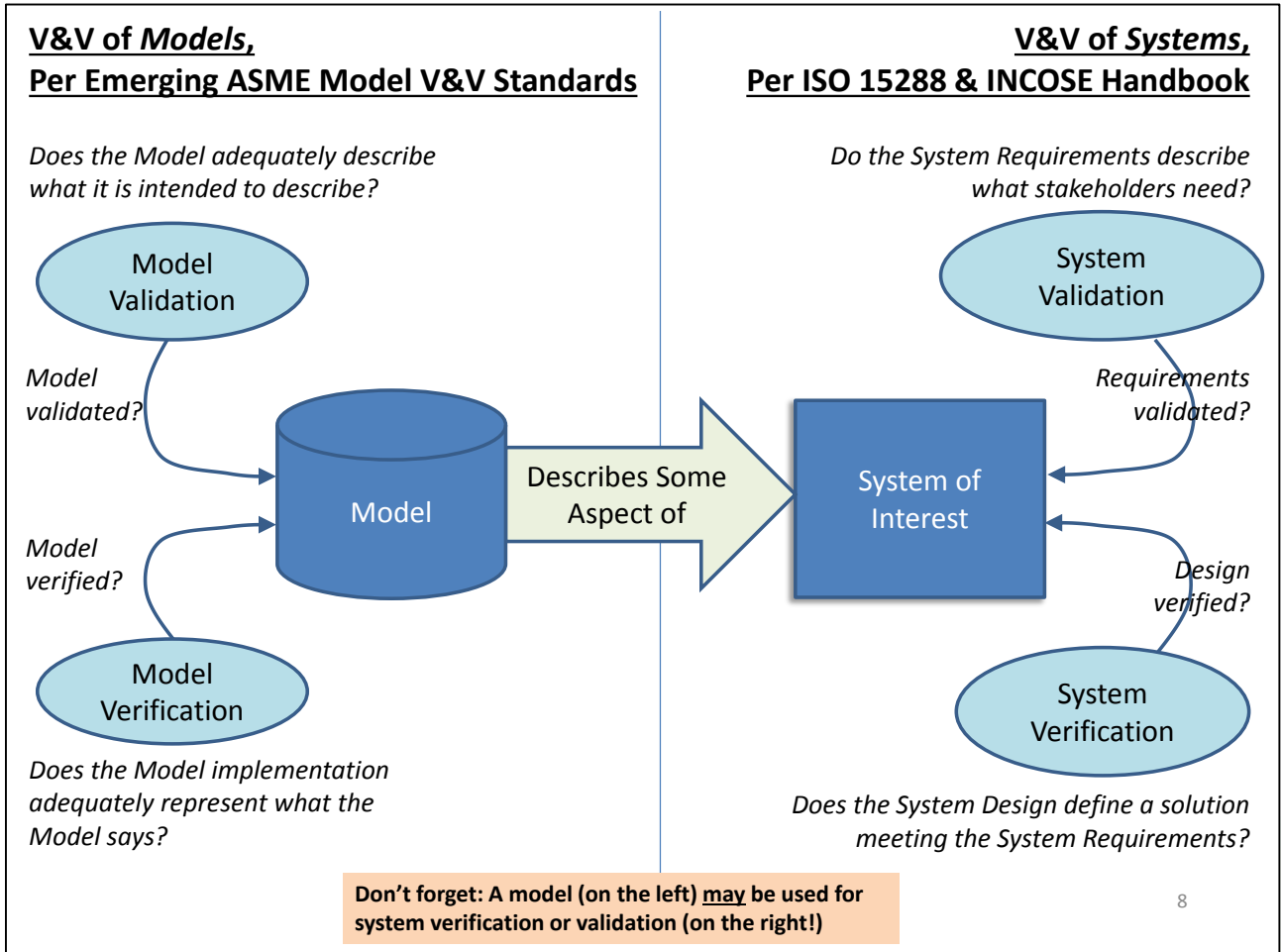
Challenges in Computational Model V&V for Systems Engineers

Bill Schindel

- One convergence aspect is attention to ***model credibility***.

- Computational modeling, physics-based and data-driven, brings historical attention to model credibility for intended uses--rooted in history of similar approaches to model credibility in physical sciences and mathematics.
- By contrast, credibility of "system" models has sometimes been treated as a more subjective question. The systems community focuses on "V&V of a target system", not always recognizing that the "V&V of models" describing it is different.



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Challenges in Computational Model V&V for Systems Engineers

Bill Schindel

- With increased interest in model compatibility, integration of simulations, and stronger theoretical foundations for systems science, the idea that there is a profound difference between something called a system model and other computational models is hereby questioned.
- INCOSE joining the ASME effort for model VVUQ standards has been a healthy way to pursue these issues. In return for a stronger model VVUQ framework, INCOSE has been able to offer system frameworks in which computational models are managed and exploited, including issues of model credibility.

V4 Institute
Virtual Verification Validation and Visualization Institute

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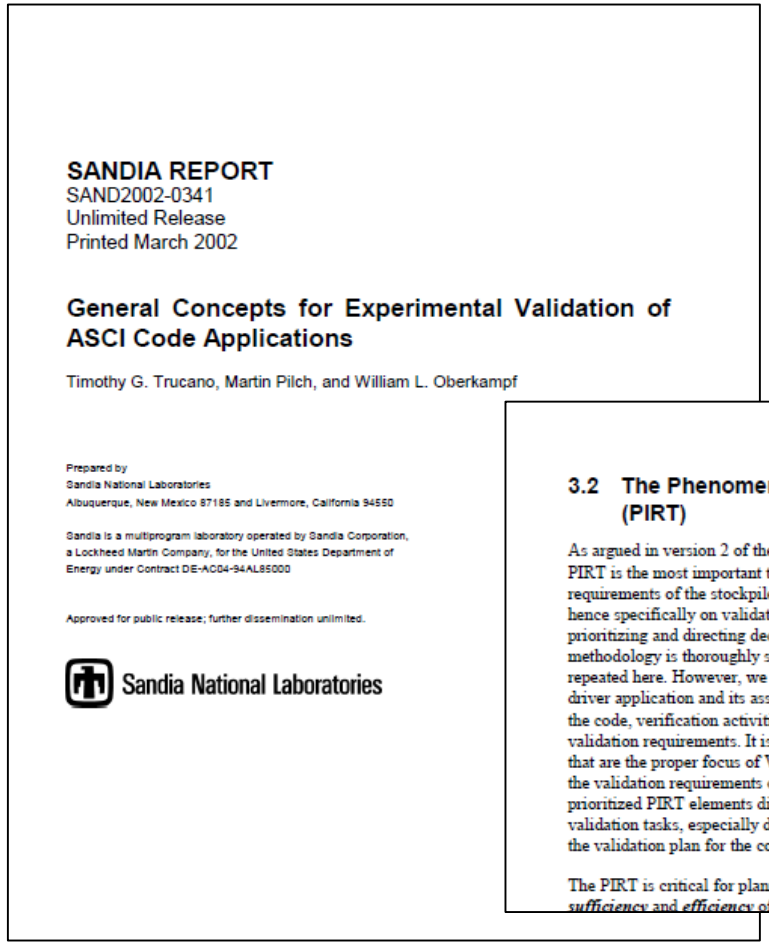
Challenges in Computational Model V&V for Systems Engineers

Bill Schindel



SANDIA REPORT
SAND2002-0341
Unlimited Release
Printed March 2002

General Concepts for Experimental Validation of ASCI Code Applications

Timothy G. Trucano, Martin Pilch, and William L. Oberkampf

Prepared by
Sandia National Laboratories
Albuquerque, New Mexico 87185 and Livermore, California 94550

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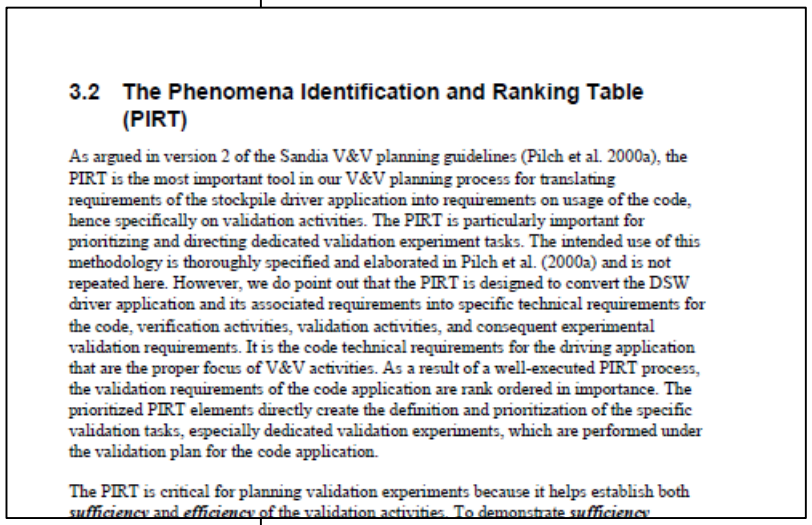
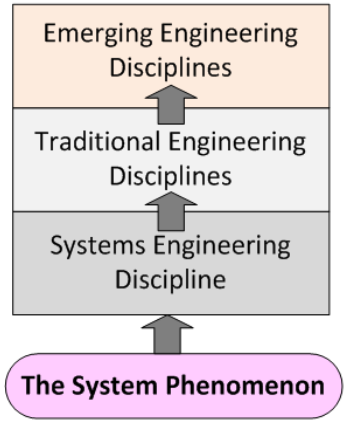
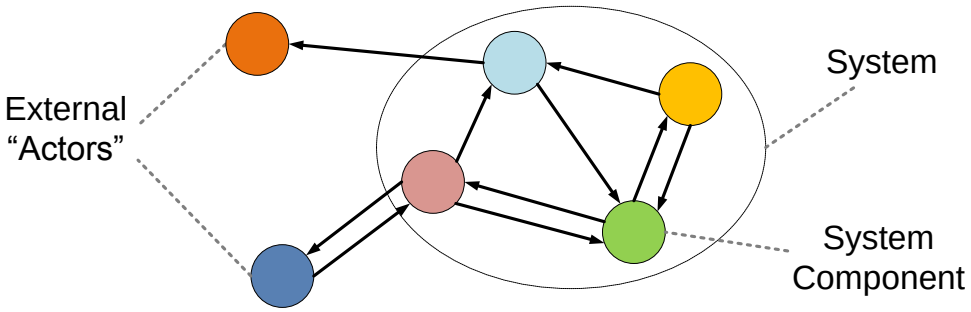


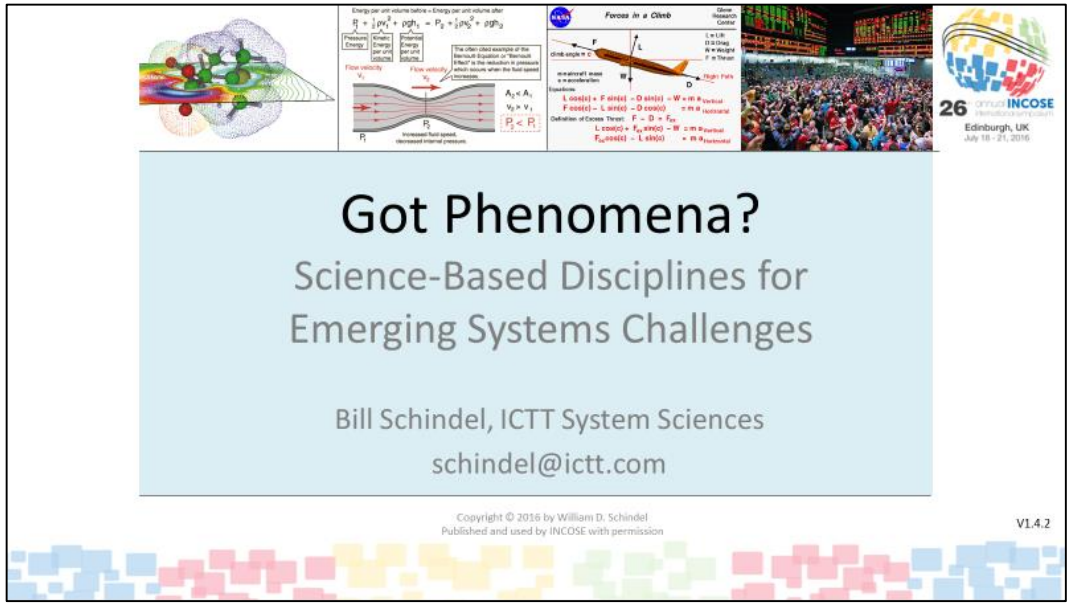
3.2 The Phenomena Identification and Ranking Table (PIRT)

As argued in version 2 of the Sandia V&V planning guidelines (Pilch et al. 2000a), the PIRT is the most important tool in our V&V planning process for translating requirements of the stockpile driver application into requirements on usage of the code, hence specifically on validation activities. The PIRT is particularly important for prioritizing and directing dedicated validation experiment tasks. The intended use of this methodology is thoroughly specified and elaborated in Pilch et al. (2000a) and is not repeated here. However, we do point out that the PIRT is designed to convert the DSW driver application and its associated requirements into specific technical requirements for the code, verification activities, validation activities, and consequent experimental validation requirements. It is the code technical requirements for the driving application that are the proper focus of V&V activities. As a result of a well-executed PIRT process, the validation requirements of the code application are rank ordered in importance. The prioritized PIRT elements directly create the definition and prioritization of the specific validation tasks, especially dedicated validation experiments, which are performed under the validation plan for the code application.

The PIRT is critical for planning validation experiments because it helps establish both *sufficiency* and *efficiency* of the validation activities. To demonstrate *sufficiency*







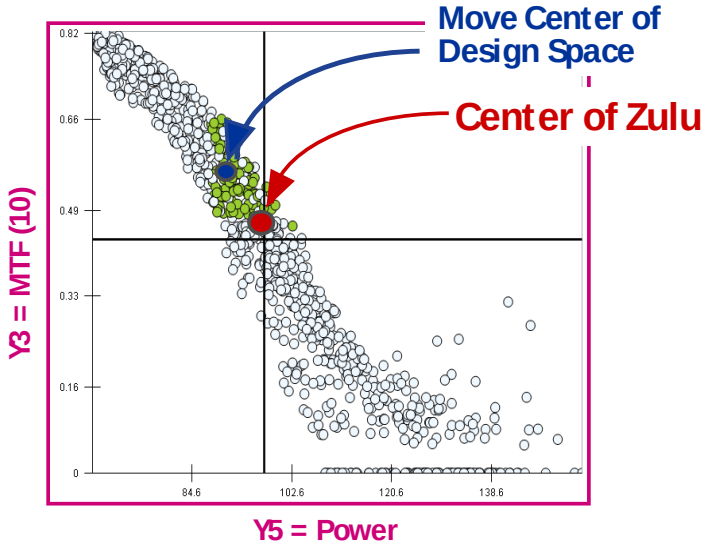
Challenges in Computational Model V&V for Systems Engineers

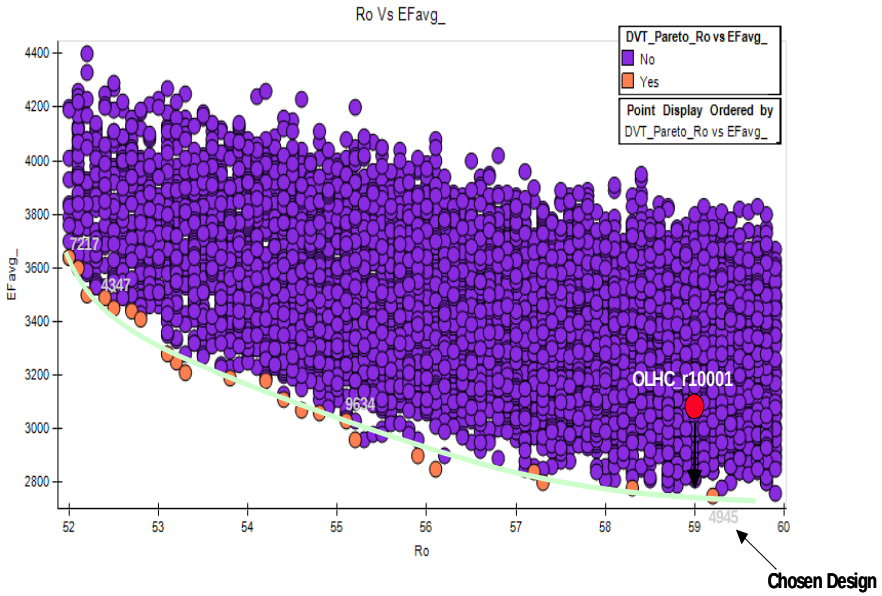
Chris Unger

- GEHC extensively uses modeling in our program development, with quite effective results. But from time to time we have had failures.
- Those failures were mostly due to a belief “modeling is good” and not thinking through the relative value of modeling vs. just testing…and whether a model could realistically meet the expectations for its use.

Challenges in Computational Model V&V for Systems Engineers

Monte Carlo Simulation of XR Tube Performance

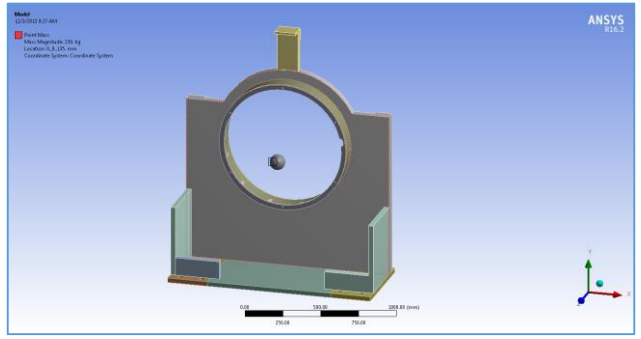




- Extensively explored design space
- Identified opportunities for increased production margin (design robustness)
- Helped save iterations…several further iterations were planned…full design verification

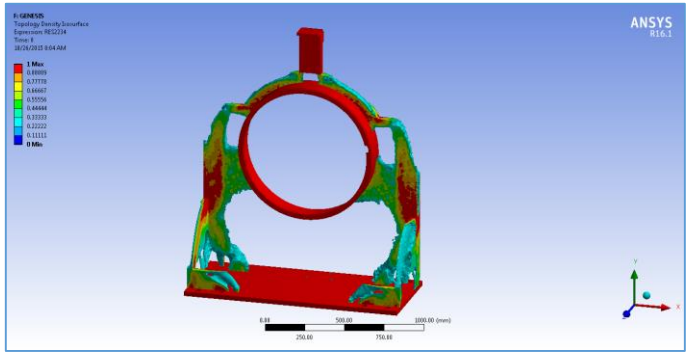
Challenges in Computational Model V&V for Systems Engineers

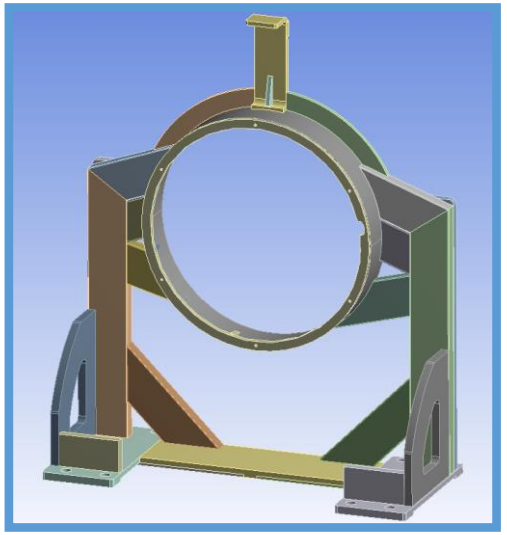
CT Mechanical Optimization



Define the Design Space
(Where Material <u>Could</u> Be)

Determine the Theoretical Optimized Shape that Meets Requirements





Use theoretical optimized shape as input to final design

- Cycle time: Months → Weeks → 3 days
- Full final design cycle to verify results

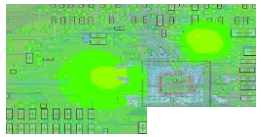
Challenges in Computational Model V&V for Systems Engineers

Baby Incubator…some predictability issues

An incubator maintains a safe environment (heat, humidity, O2…) for a Infant.

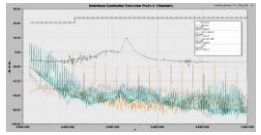
Goal - To develop multi-physics, control & system model that will reduce design iterations

Electrical Result:



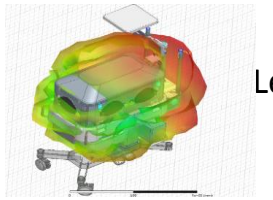
Level 1: PI SI wave

Complete



Level 2: PI/RE SI wave + Cir

Partial



Level 3: PI/RE SIwave + Cir +HFSS

Not Complete

EMC Result

Near field simulation: reasonable results

Far field simulation: poor results

Total effort exceeded the cost of building a local screen room

No analysis of the design margin (very small) compared to modelling error (very large)

Detailed Goals:

Thermal: Build system CFD model and downselect 2 options for further physical prototyping and CFD; develop ROM for further control loop development

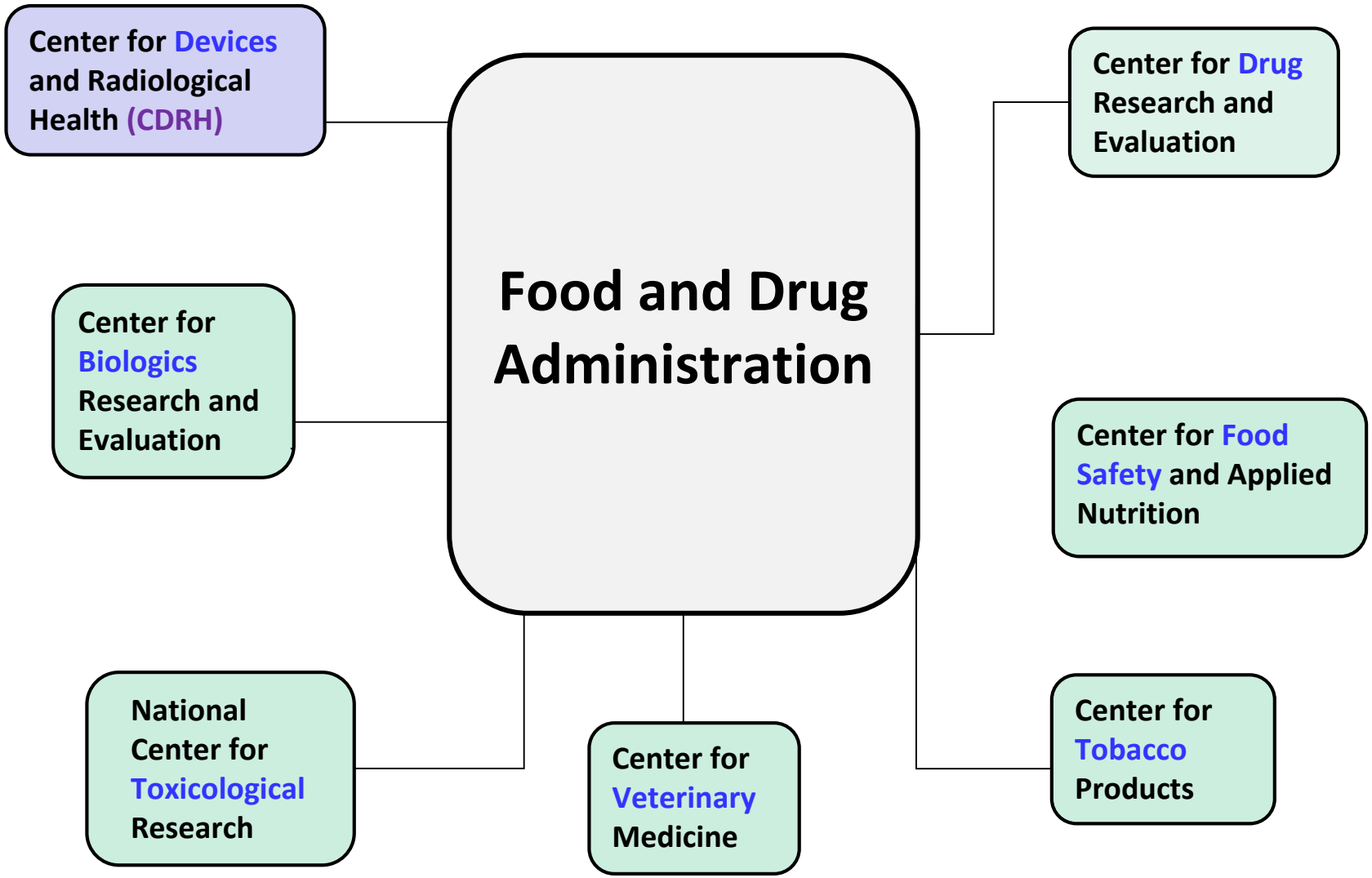
Electrical: Reduced board spins

EMI/EMC: Eliminate the need for screen room testing

- Team overcommitted
- Process lacked effective global review with US experts

Challenges in Computational Model V&V for Systems Engineers

Pras Pathmanathan



Challenges in Computational Model V&V for Systems Engineers

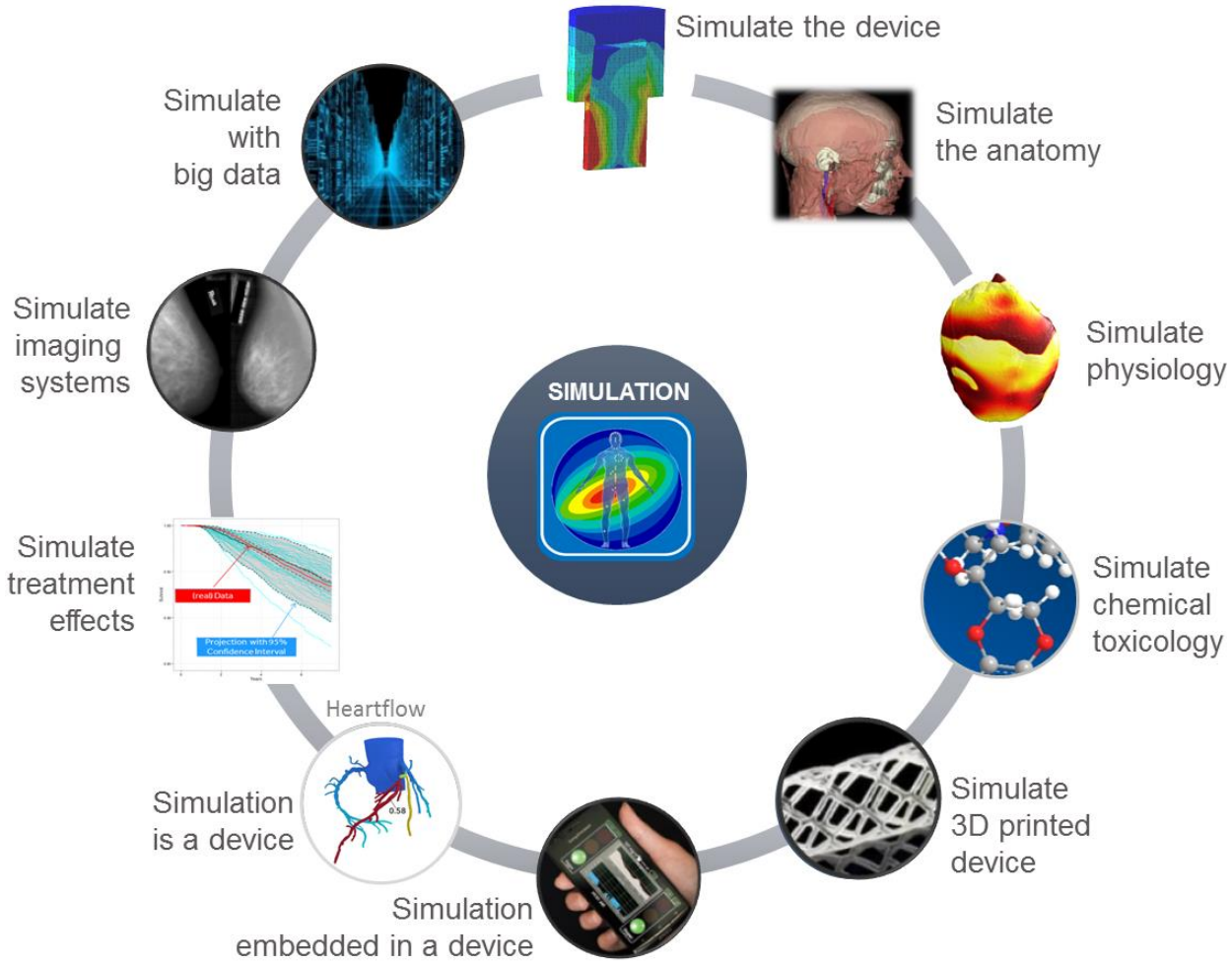
Pras Pathmanathan

From FDA's Strategic Policy Roadmap 2018:

Modernizing our Regulatory Toolbox:
[..]
Towards these goals, among the many steps FDA will take: The Agency will embrace advances like predictive toxicology methods and computational modeling across our different product areas

Crucial to develop methods and best practices for rigorously **demonstrating credibility** of biomedical computational models

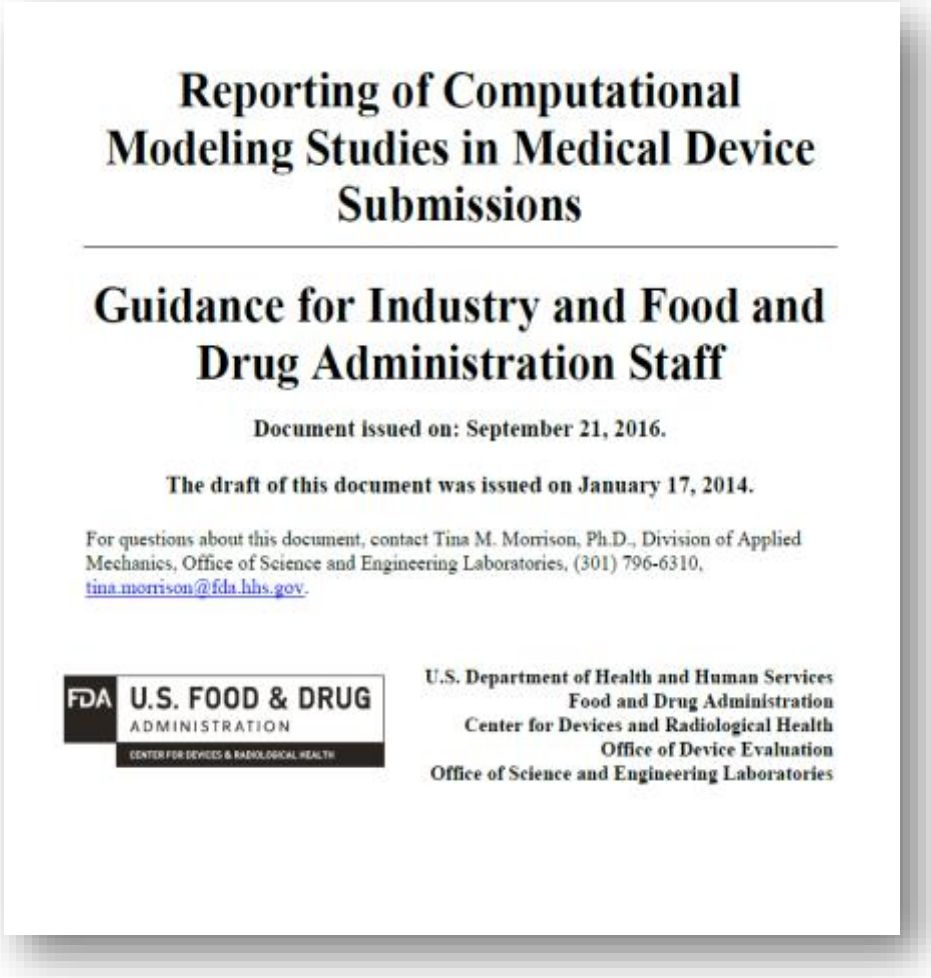
- Can draw from approaches and successes in traditional engineering fields (e.g. VVUQ)
- However, there are **unique challenges**



Challenges in Computational Model V&V for Systems Engineers

Pras Pathmanathan

- **CDRH Guidance on Reporting of Modeling and Simulation Studies**
- ASME V&V40 Standard (to be published summer 2018)
- MDIC "Virtual Patient"
- CDRH research output
- FDA's Modeling and Simulation Working Group



Reporting of Computational Modeling Studies in Medical Device Submissions

Guidance for Industry and Food and Drug Administration Staff

Document issued on: September 21, 2016.

The draft of this document was issued on January 17, 2014.

For questions about this document, contact Tina M. Morrison, Ph.D., Division of Applied Mechanics, Office of Science and Engineering Laboratories, (301) 796-6310, tina.morrison@fda.hhs.gov.

FDA U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR DEVICES & RADIOLOGICAL HEALTH

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
Office of Science and Engineering Laboratories

Google "FDA modeling reporting guidance"

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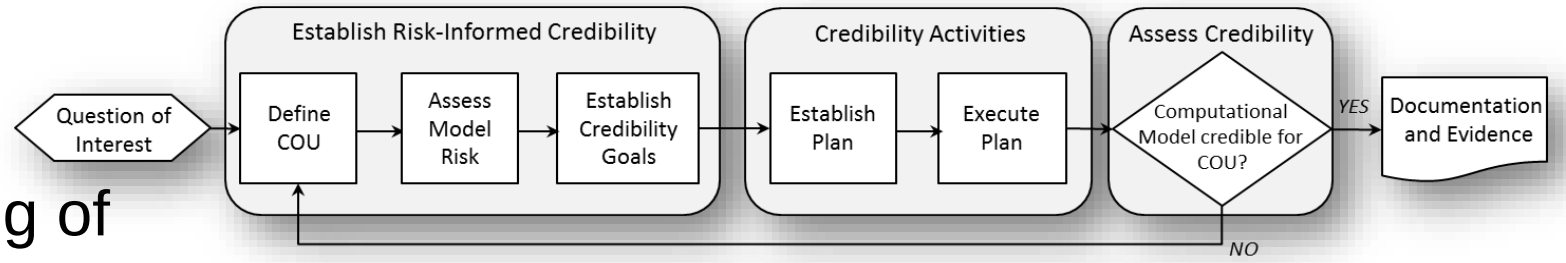

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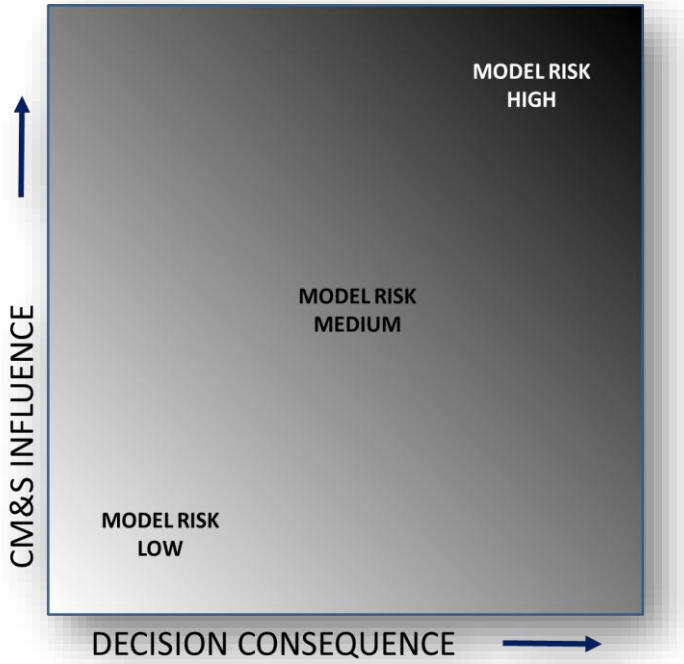

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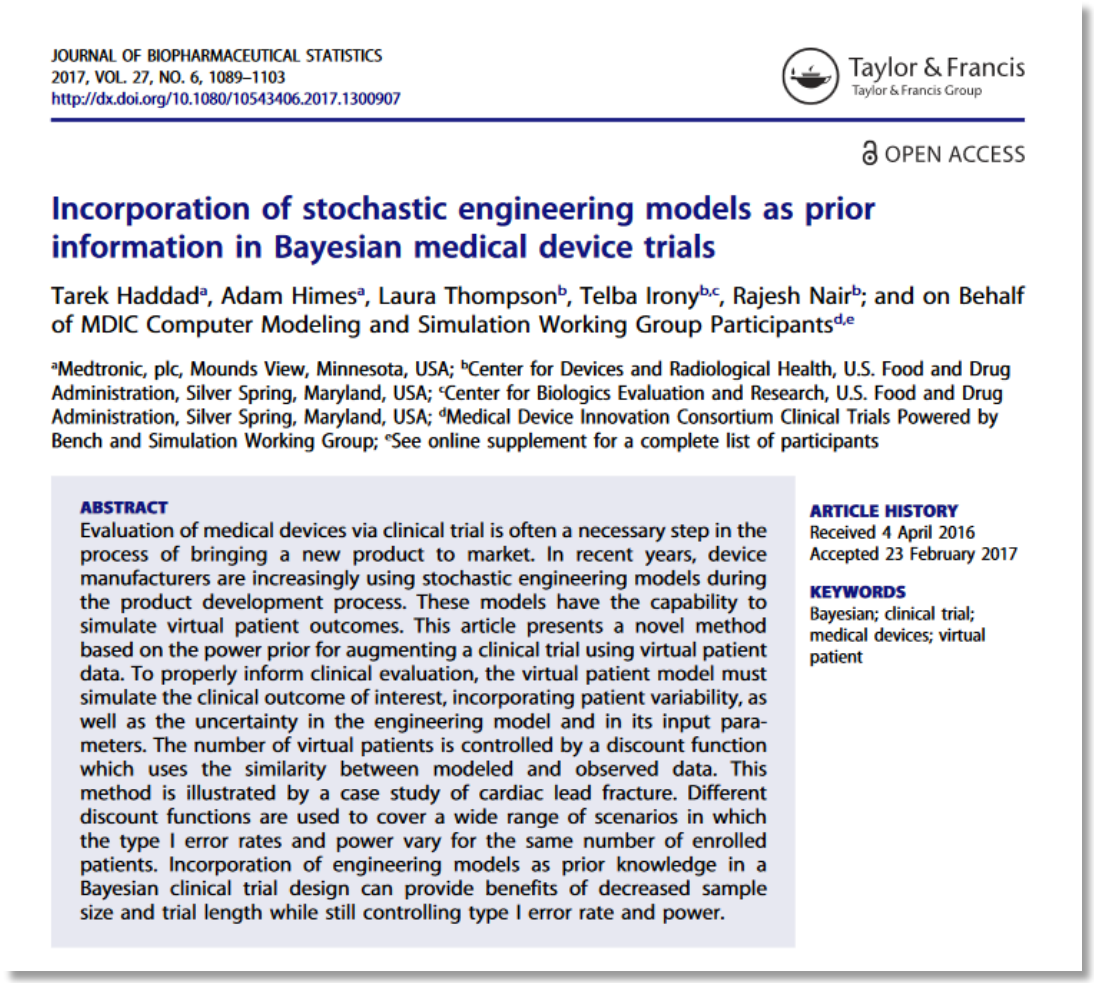

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Incorporation of stochastic engineering models as prior information in Bayesian medical device trials

Tarek Haddad[a], Adam Himes[a], Laura Thompson[b], Telba Irony[b,c], Rajesh Nair[b]; and on Behalf of MDIC Computer Modeling and Simulation Working Group Participants[d,e]

[a]Medtronic, plc, Mounds View, Minnesota, USA; [b]Center for Devices and Radiological Health, U.S. Food and Drug Administration, Silver Spring, Maryland, USA; [c]Center for Biologics Evaluation and Research, U.S. Food and Drug Administration, Silver Spring, Maryland, USA; [d]Medical Device Innovation Consortium Clinical Trials Powered by Bench and Simulation Working Group; [e]See online supplement for a complete list of participants

ABSTRACT

Evaluation of medical devices via clinical trial is often a necessary step in the process of bringing a new product to market. In recent years, device manufacturers are increasingly using stochastic engineering models during the product development process. These models have the capability to simulate virtual patient outcomes. This article presents a novel method based on the power prior for augmenting a clinical trial using virtual patient data. To properly inform clinical evaluation, the virtual patient model must simulate the clinical outcome of interest, incorporating patient variability, as well as the uncertainty in the engineering model and in its input parameters. The number of virtual patients is controlled by a discount function which uses the similarity between modeled and observed data. This method is illustrated by a case study of cardiac lead fracture. Different discount functions are used to cover a wide range of scenarios in which the type I error rates and power vary for the same number of enrolled patients. Incorporation of engineering models as prior knowledge in a Bayesian clinical trial design can provide benefits of decreased sample size and trial length while still controlling type I error rate and power.

ARTICLE HISTORY
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KEYWORDS
Bayesian; clinical trial; medical devices; virtual patient

Google "MDIC virtual patient"

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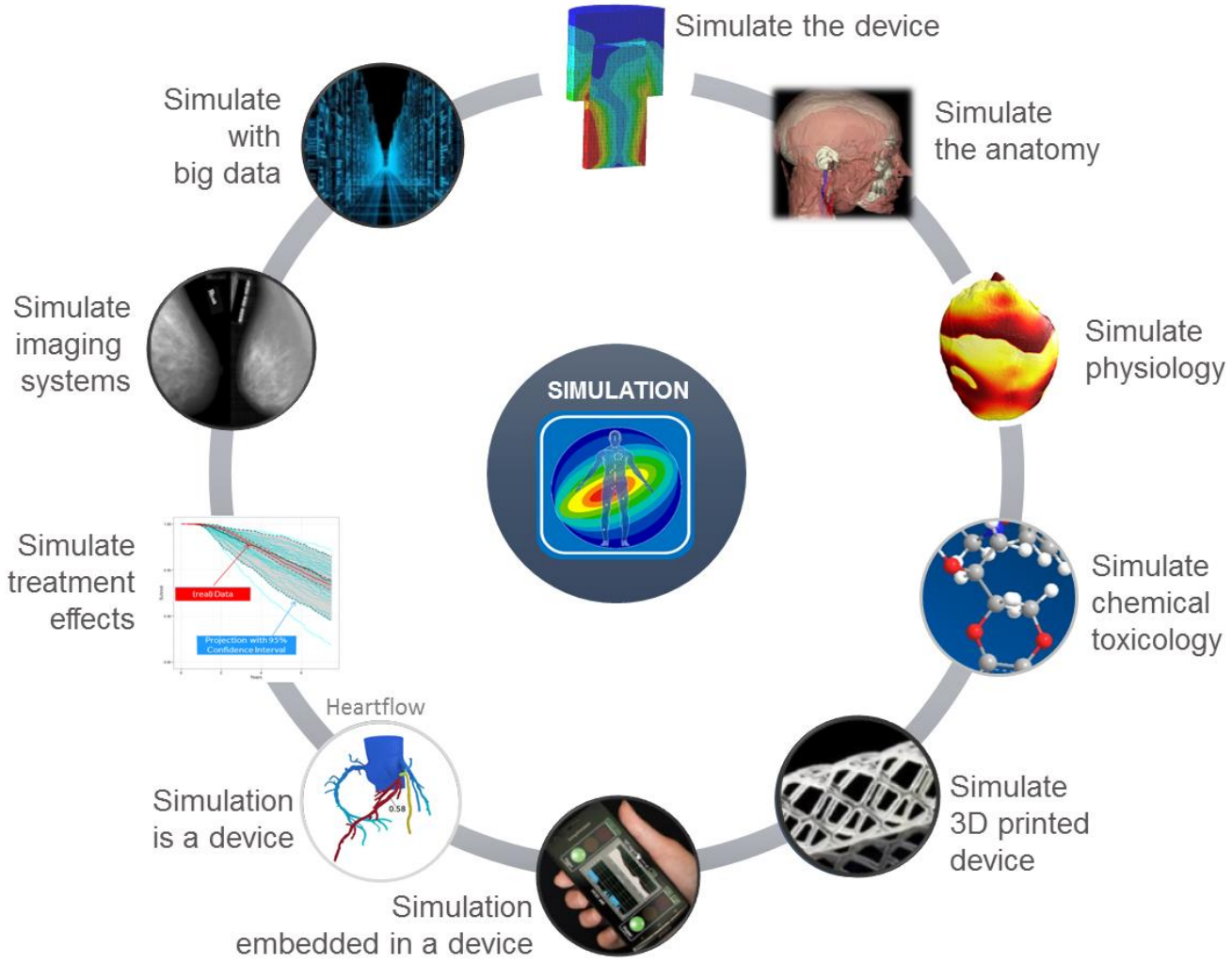

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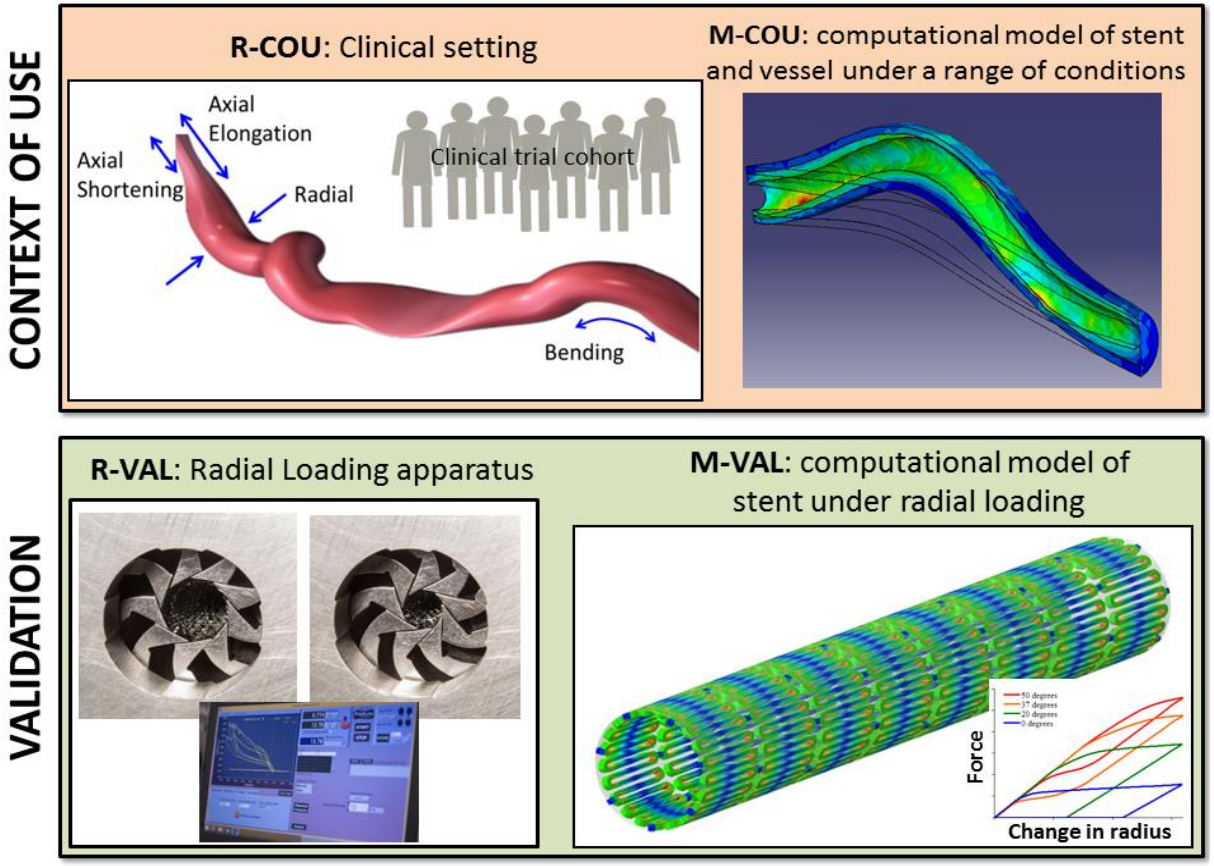

Pathmanathan et al. J. VVUQ, 2017

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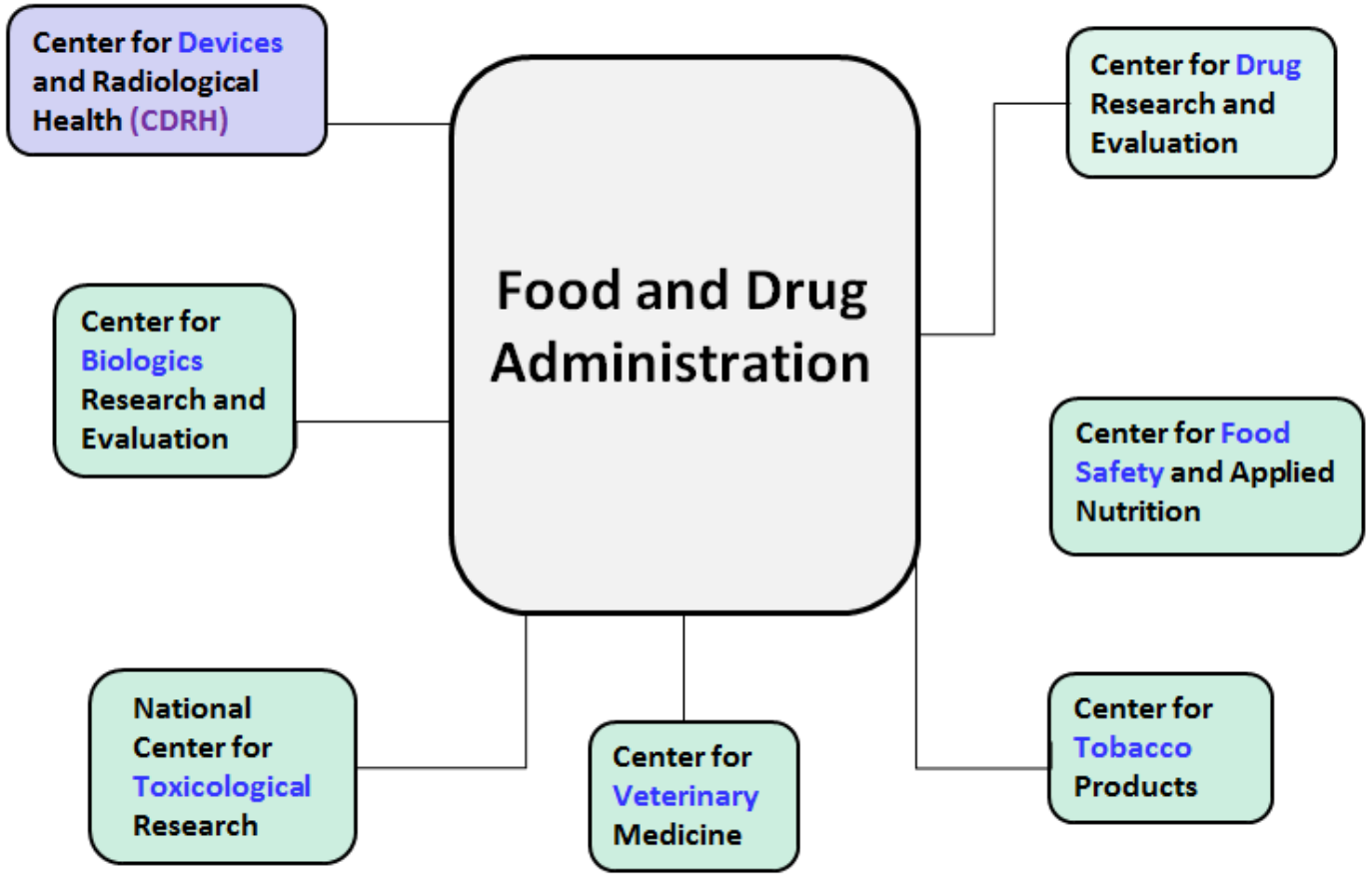

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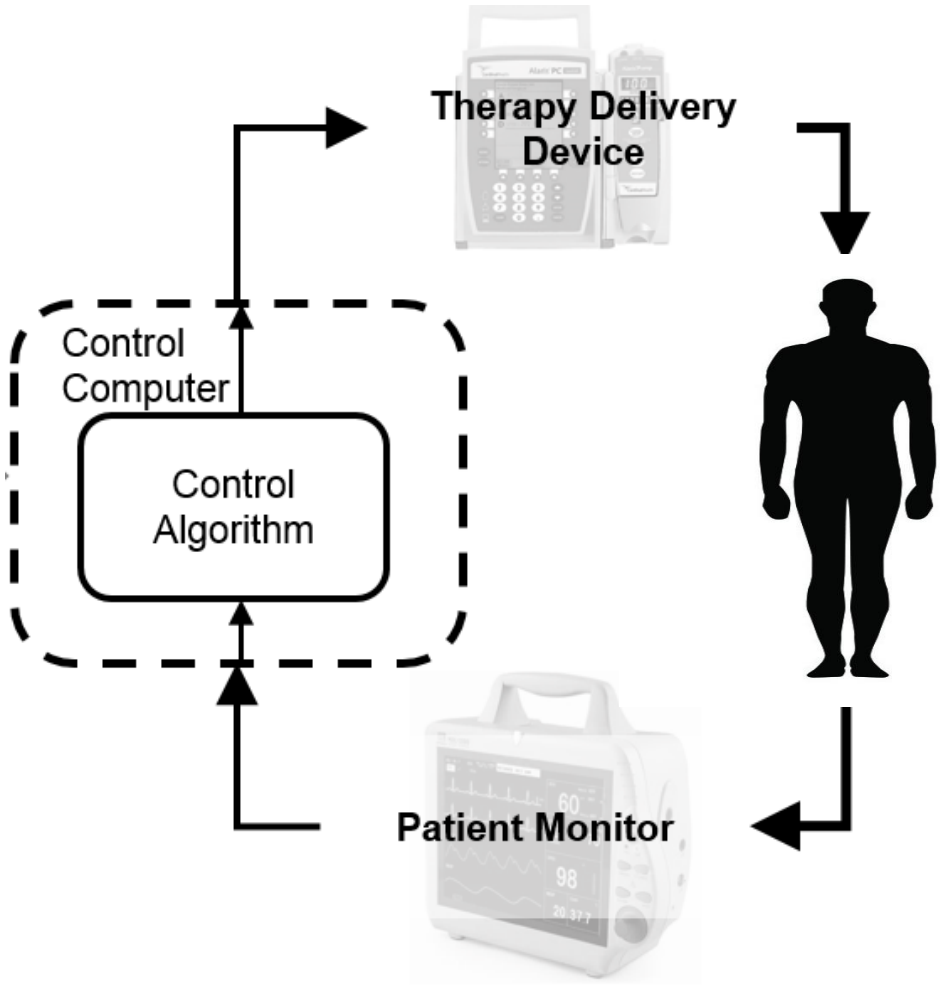

"Context of Use" based evaluation (e.g. design of controller vs evaluation of controller)

Physiological variability

Complexity of systems modeled
Complexity of model needed

Multiple sources of validation (or credibility) evidence

Experimental (clinical) validation difficulties

Q&A