INCOSE Healthcare Working Group

4th Annual Systems Engineering in Healthcare Conference

Closing the Loop on Medical Device Systems Simulation

Marc Horner, Ph.D.

Technical Lead, Healthcare

ANSYS, Inc.

Outline

A. Healthcare Industry Overview
- Systems Engineering for Medical Devices
- Digital Systems Prototyping
- Regulatory Update

B. Insulin Pump Example
- Background
- Drug Delivery Sub-system Model
  - Kink Detection Modeling
  - Virtual Patient Modeling

C. Conclude

Healthcare Industry Overview

Today's Medical Devices are Increasingly

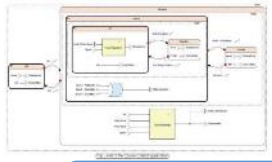
Electric	Smarter		Connected	
IVD devices	**Physiological Monitors**	**Mobile Medical Apps**	**Wearables**	**Capital Intensive Devices**
				
Blood Analyzers Immuno-assays Breast Biopsy Equipment HIV Detection Systems	Weighing scales Pulse Oximeter BP Meter ECG Ventilators Blood Glucose Meters Heart Rate Monitors	Medication Adherence Systems Dosage Calculation Systems	Activity Tracker Pedometer Sleep Apnea Detector	Implants Prostheses MRI/CT/ Ultrasound Scanners

* Cogizant, How the IOT is Transformng Medical Devices, May 2016

Components

Electronic Control

Actuators



Embedded Software

Sensors

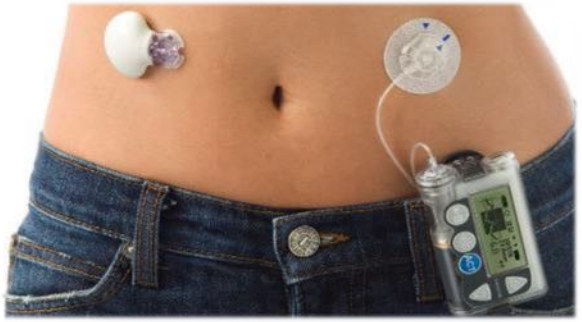
Domain-specific

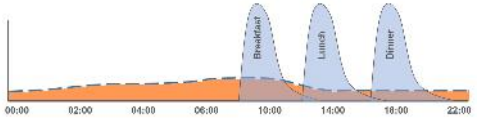
Component-centric

…are ultimately part of a system

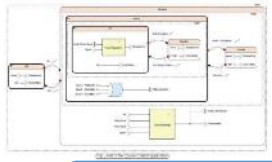
Electronic Control

Actuators

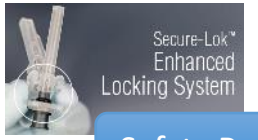




Operational Profiles



Embedded Software

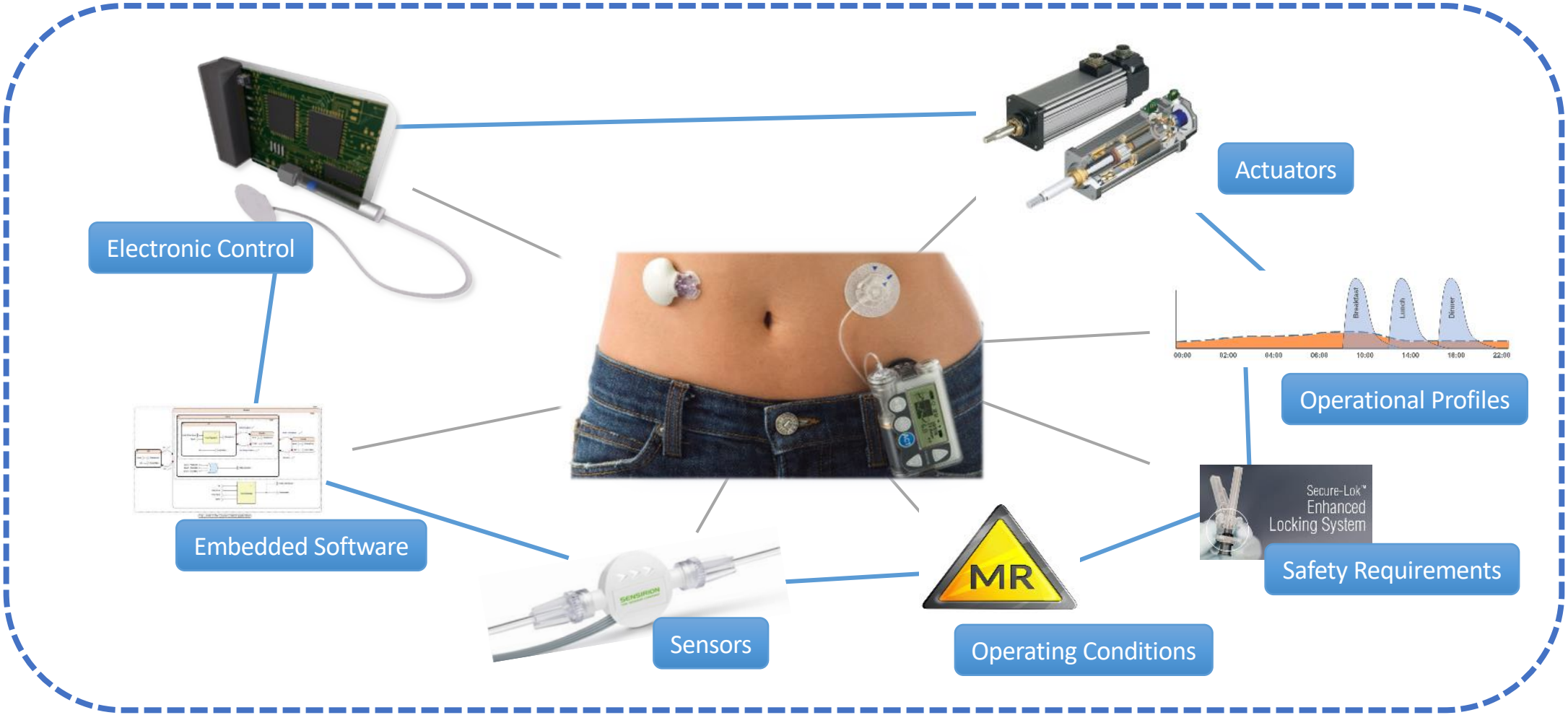


Safety Requirements

Sensors

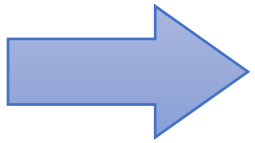
Operating Conditions

…with complex interactions.



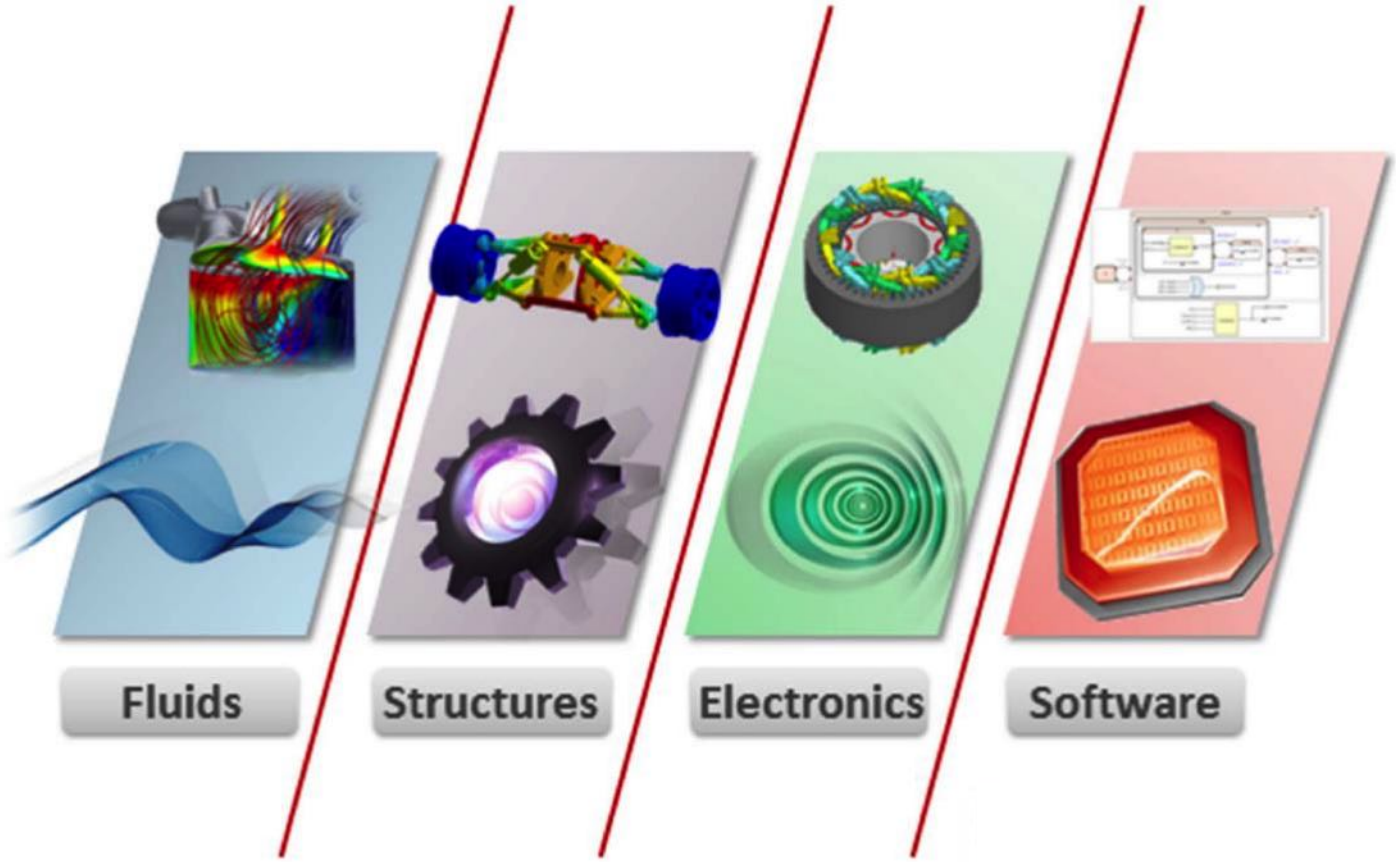
Challenge: System Complexity

- Understand and optimize performance
- Eliminate late-stage integration failures
- Improve collaboration among design disciplines
- Enhance or reduce physical testing
- Accelerate innovation



Digital System Prototyping

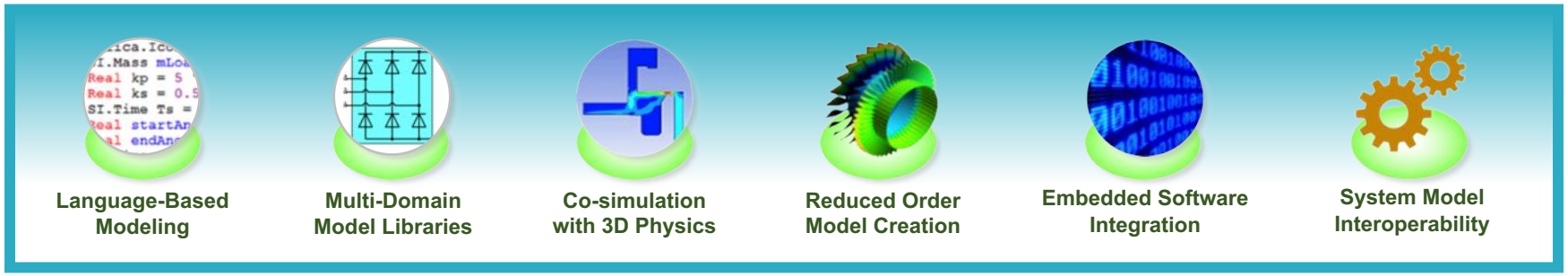
Design Still Happens in Silos



Each discipline has its' own set of tools, processes, and expertise.

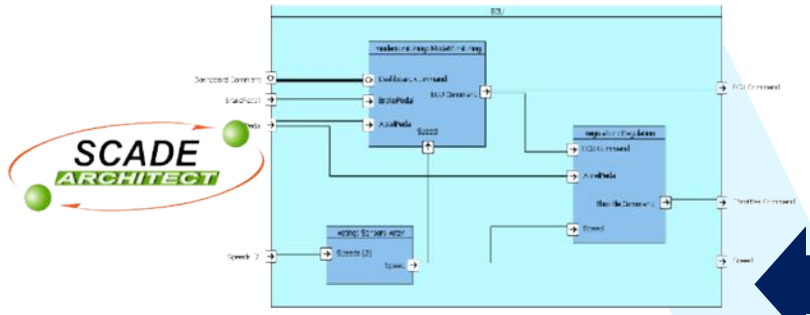
Systems Engineering: A Unifying Approach

Systems Modeling – Model Flexibility, Reusability, and Interoperability

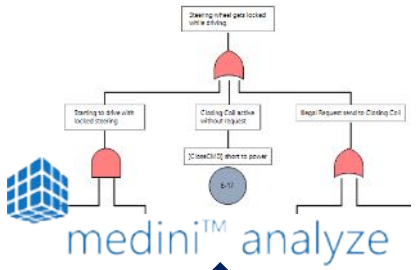


The ANSYS Portfolio

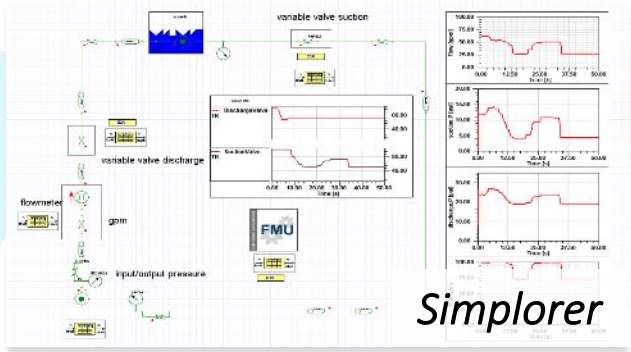
Model-Based Systems Engineering



System Safety Analysis



System Simulation & Digital Twins

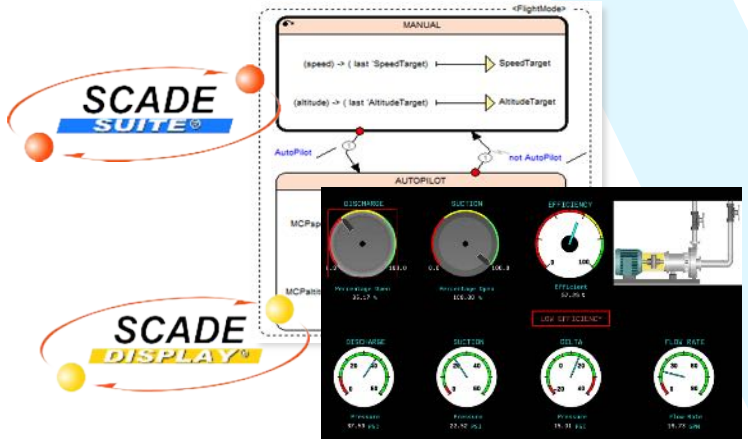


System Architecture

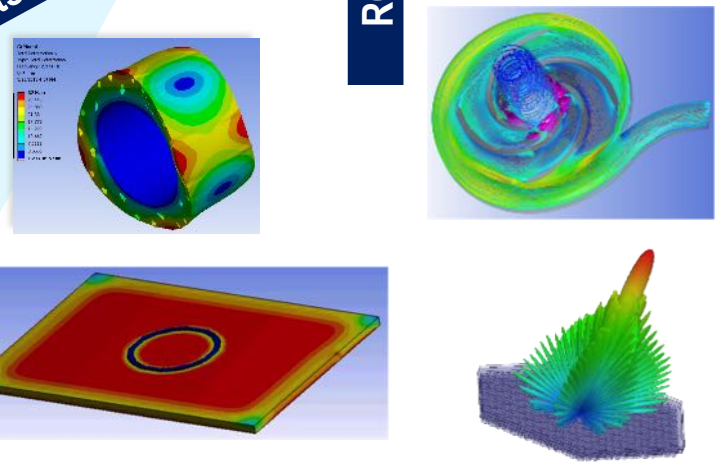
System/SW Architecture

SW Components (FMI)

ROM



Model-Based Software Engineering



3D Physics Simulation

FDA Analyses of Product Recalls

Exhibit 11: Recall case codes by root cause

Model recalls (case numbers), 2003-2009, N=4,391

>=15%
5-14%
1-5%

Confidential and Proprietary

	Design	Suppliers	Manufacturing	Postproduction & change ctrl	Other	Unknown	Total by product attribute
Hardware	15%	12%		2%			29%
Software	8%			7%			15%
Labeling	4%		3%	1%			8%
Packaging	1%		3%				5%
Process	3%	2%	18%	1%			24%
Regulation					1%		1%
Other					9%		9%
Unknown						9%	9%
Total by value stream	31%	14%	24%	12%	10%	9%	100%

Source: Data from RECS database

"failures in product design and manufacturing process control caused more than half of all product recalls"

Reasons for recalls

Recall causes assigned by FDA were tabulated for recalls classified during FY 2010 – FY 2012. These are listed in Figure 21 in decreasing frequency of use. Note that each recall has only one recall cause determination and uses FDA current terminology and processes.

Figure 21:

Recall reasons	Number
Nonconforming Material/Component	429
Software Design(Device)	429
Device Design	425
Process Control	266
Component Design/Selection	144

"The most frequent causes for recalls are related to device design, software, and non-conforming material or component issues."

1. *from FDA Report "Understanding Barriers to Medical Device Quality" (2011)*

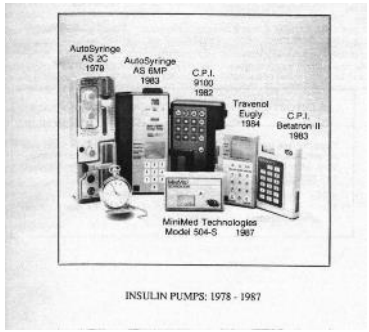
INCOSE Healthcare Working Group
4th Annual Systems Engineering in Healthcare Conference

Infusion Pump Safety

FDA NEWS RELEASE

For Immediate Release: April 23, 2010
Media Inquiries: Dick Thompson, 301 796 7566; dick.thompson@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

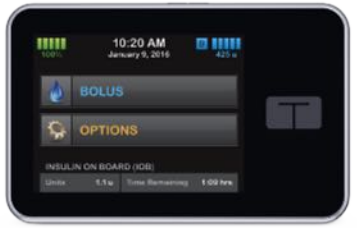
FDA Launches Initiative to Reduce Infusion Pump Risks
Agency calls for improvements in device design

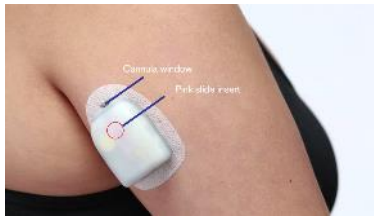


…infusion pumps also have been the source of persistent safety problems. In the past five years, the FDA has received more than 56,000 reports of adverse events associated with the use of infusion pumps. Those events have included serious injuries and more than 500 deaths. Between 2005 and 2009, 87 infusion pump recalls were conducted to address identified safety concerns, according to FDA data.

The most common types of reported problems have been related to:

- software defects, including failures of built-in safety alarms;
- user interface issues, such as ambiguous on-screen instructions that lead to dosing errors; and
- mechanical or electrical failures, including components that break under routine use, premature battery failures, and sparks or pump fires.





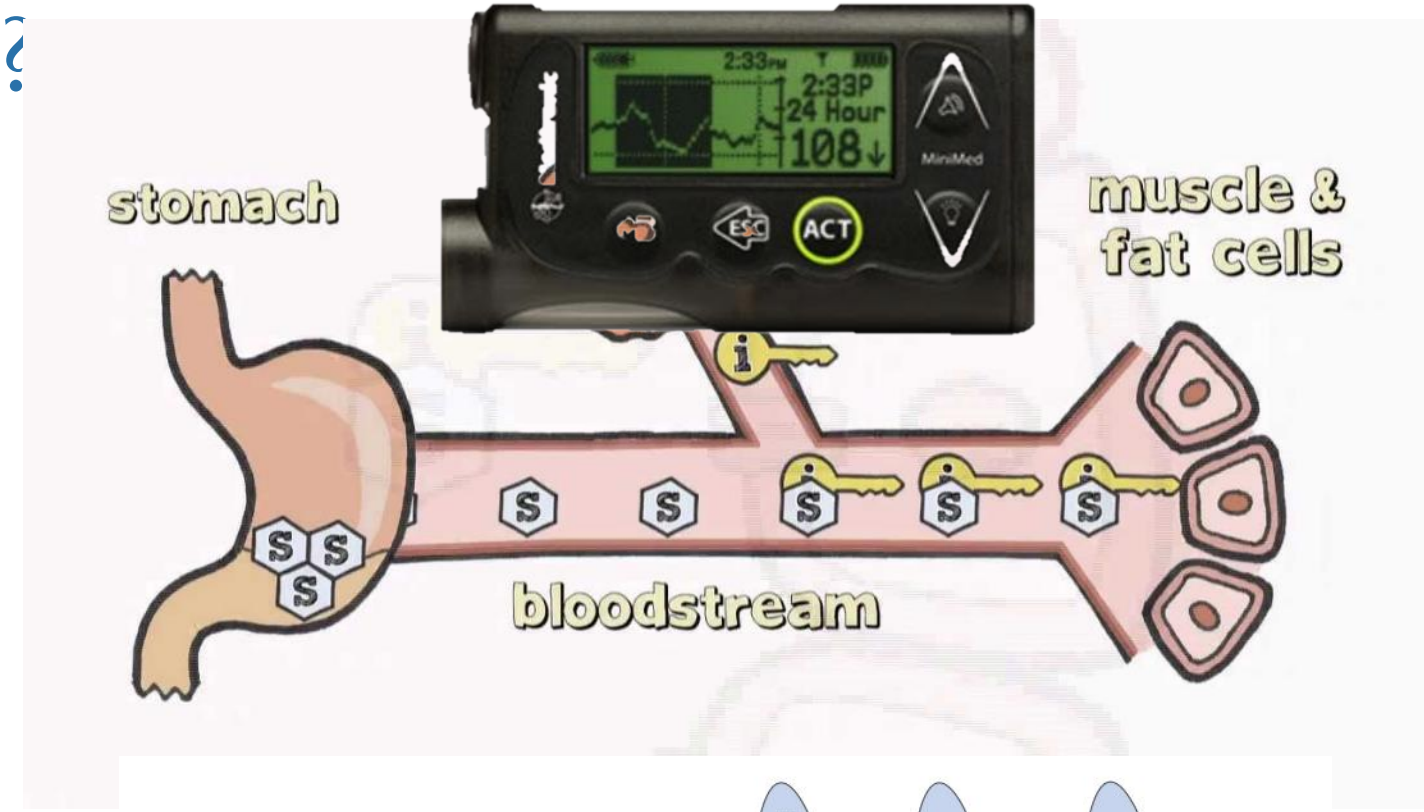
"many of the reported problems appear to be related to deficiencies in device design and engineering"

http://diyabetimben.com/diyabet-muzesi/

Insulin Pump Model

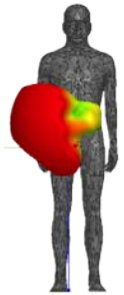
What is Diabetes?

- Insulin is a hormone created by the pancreas. It is required for sugar molecules (from the food you eat) to move inside cells. Patients with diabetes either do not produce insulin (Type 1) or do not use insulin the right way (Type 2).
- Insulin pumps replace the function of the pancreas by injecting insulin under the skin throughout the day.

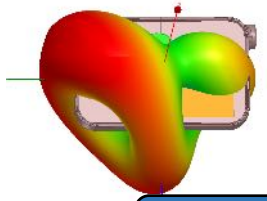


diabetes image from https://i.ytimg.com/vi/SCCb5GqhnrI/maxresdefault.jpg
Pump image from http://www.medtronicdiabetes.com/products/minimed-530g-diabetes-system-with-enlite

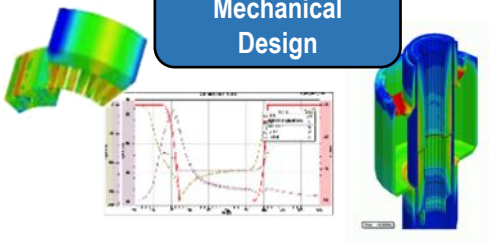
Components, Components, Components



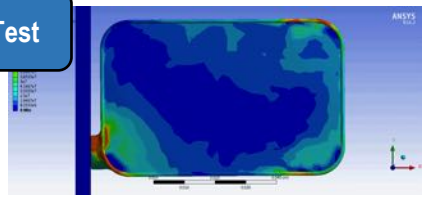
HBM EM



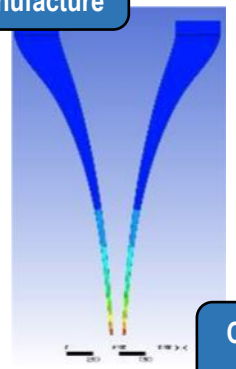
Antenna Design/Optimization



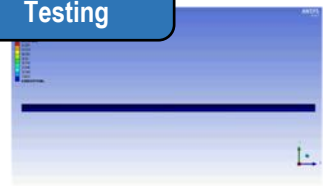
Electro-Mechanical Design



Drop Test



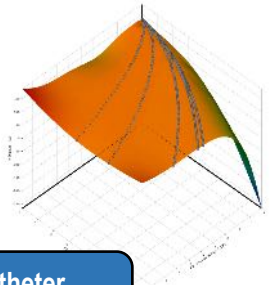
Catheter Manufacture



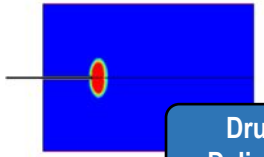
Catheter Kink Testing

Embedded Software - Display

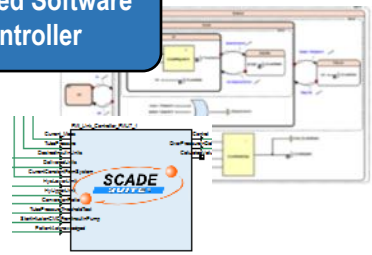
Catheter Pressure Testing



Catheter Occlusion ROM

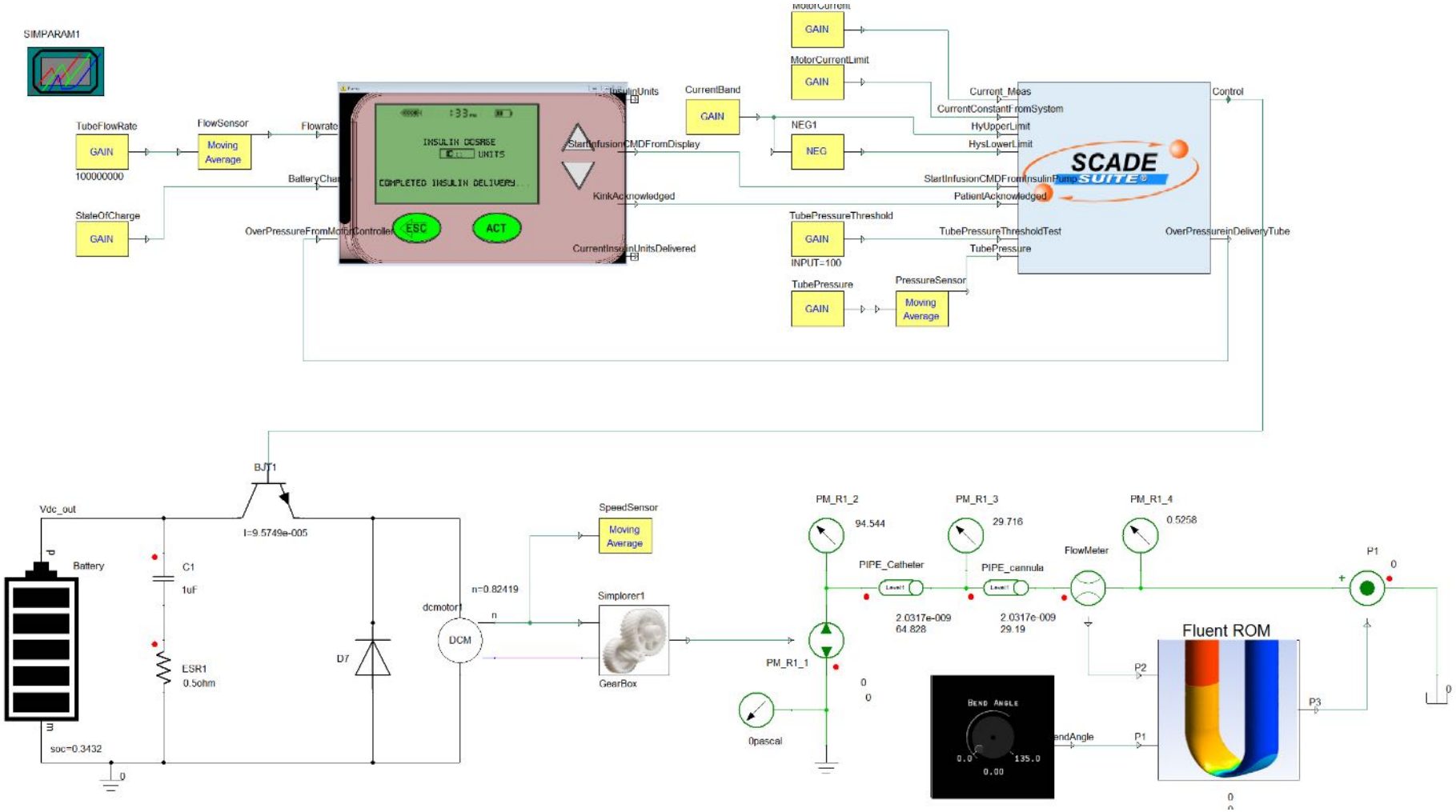


Drug Delivery



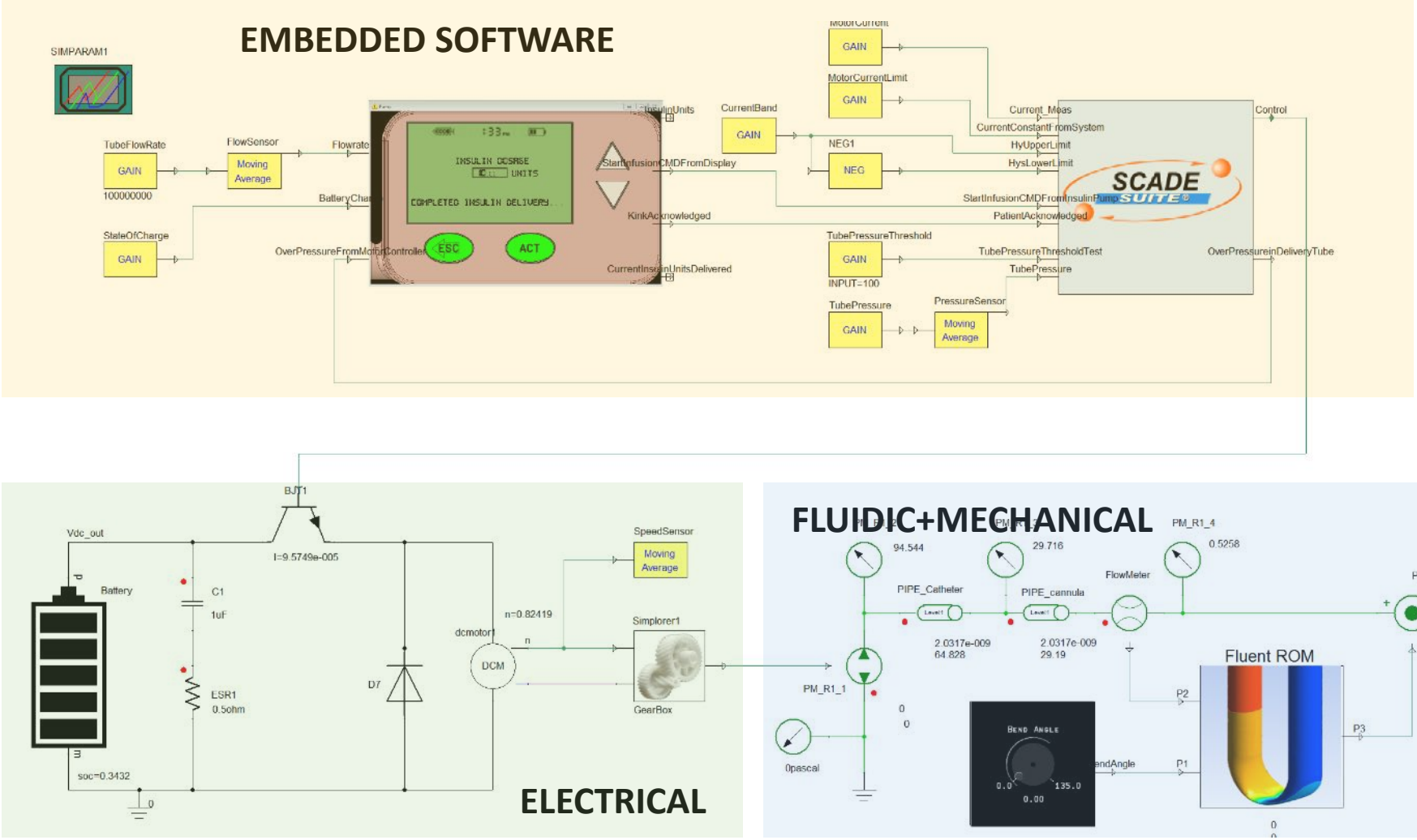
Embedded Software - Controller

Drug Delivery Sub-System



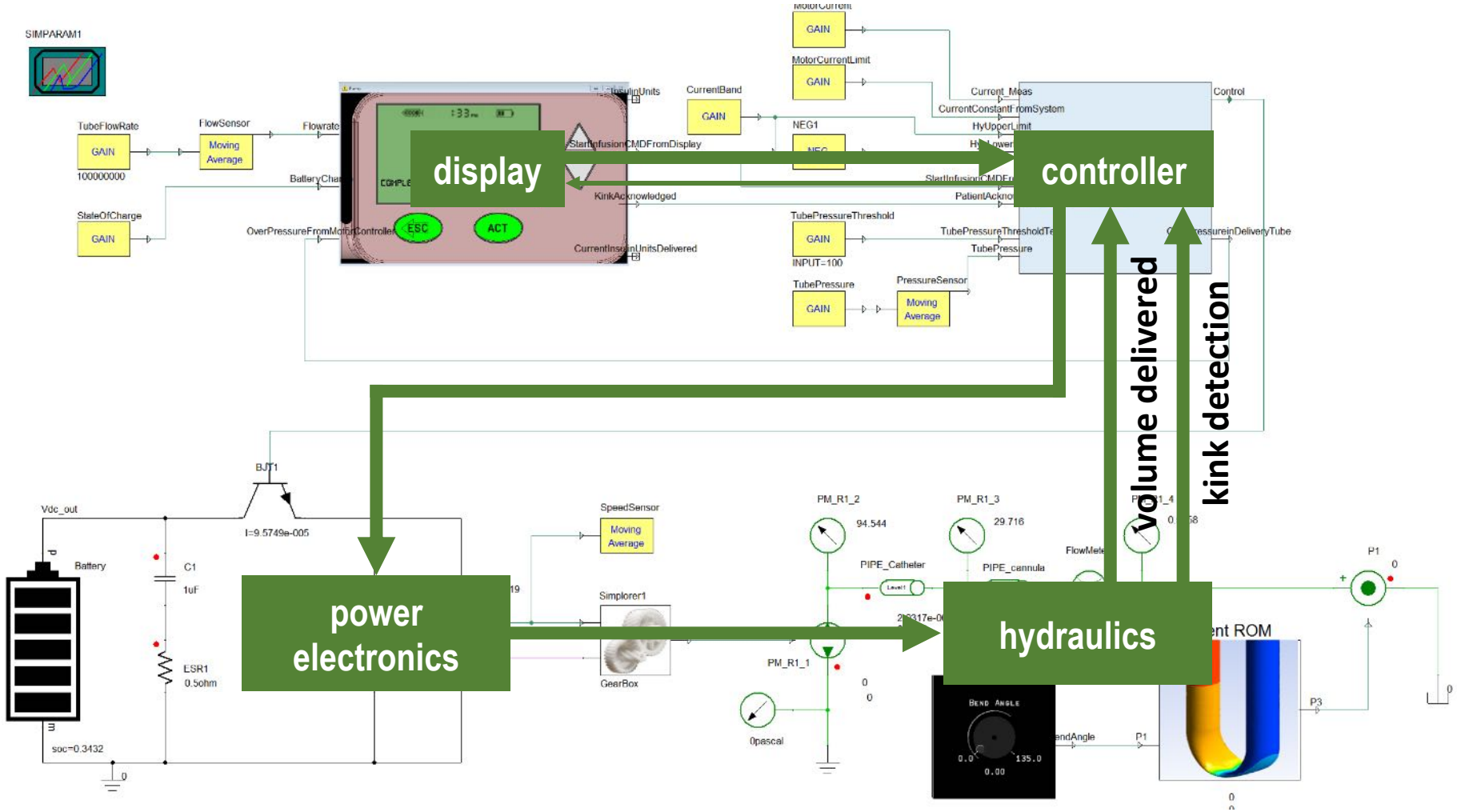
Drug Delivery Sub-System

MODEL DOMAINS

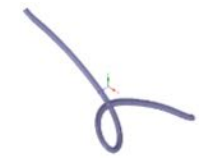
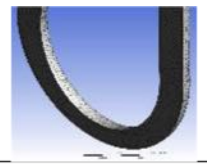
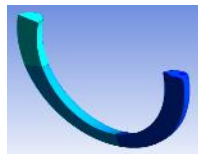
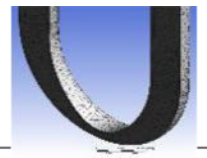
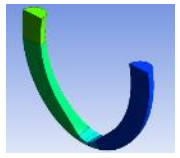
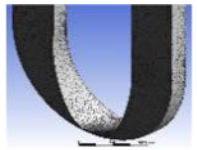
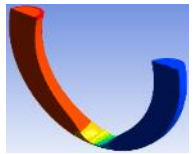


Drug Delivery Sub-System

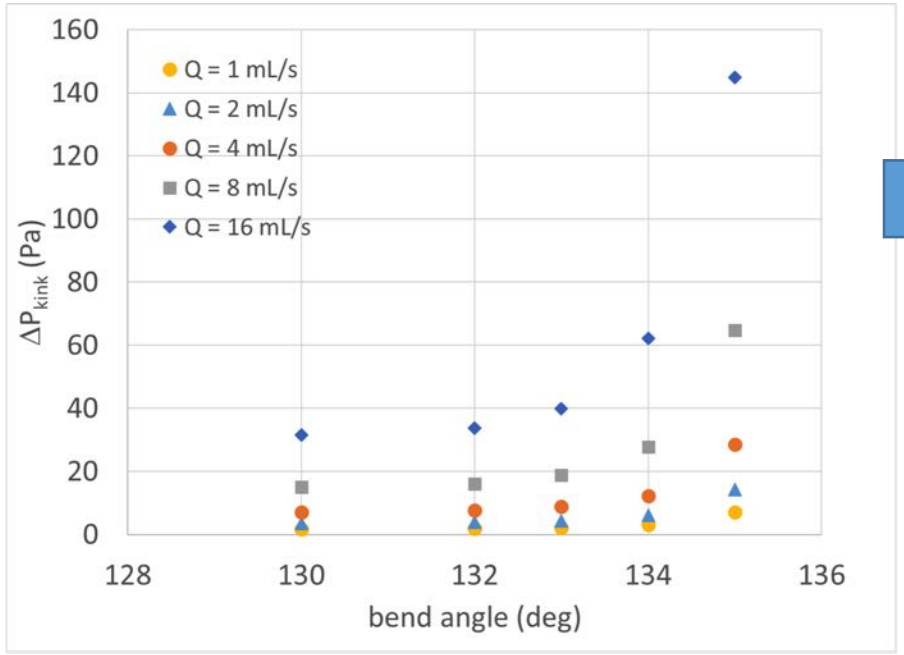
INFORMATION FLOW



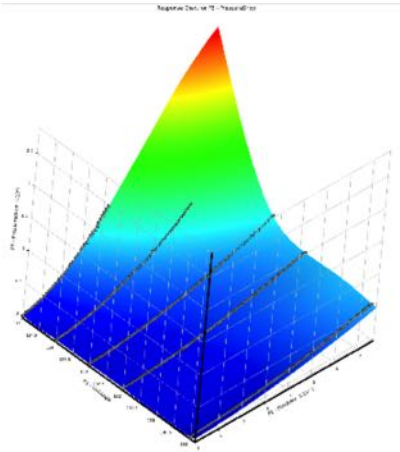
Pressure-Flow Analysis of Tube Bending

Non Linear Kink Prediction	Deformed Geometry Export	Fluid volume extraction of kinked model	Detailed Flow Simulation (kink angles & flow rates → pressure drop)
3D FEA	3D FEA → CAD	CAD → 3D CFD	3D CFD
			
			
			

Family of Structural Fluid Simulations

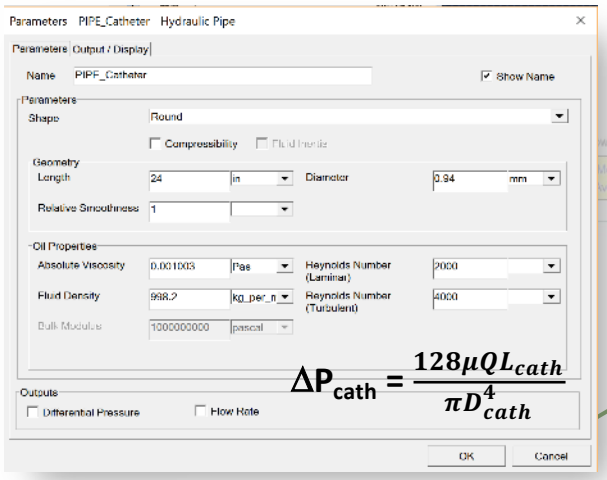


ROM

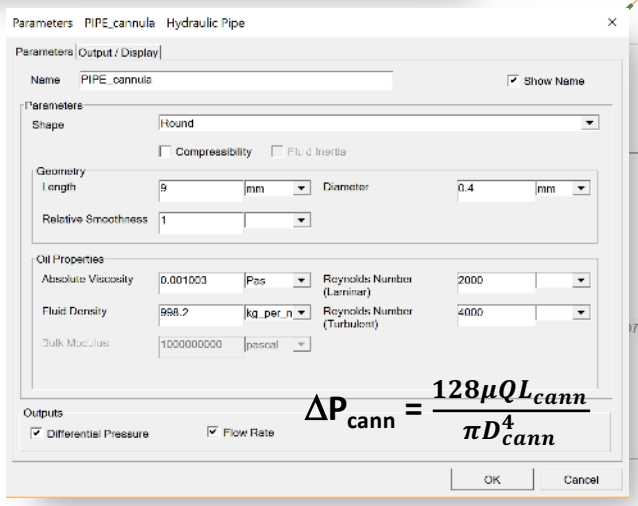


Insulin Pump – ROM Behavior

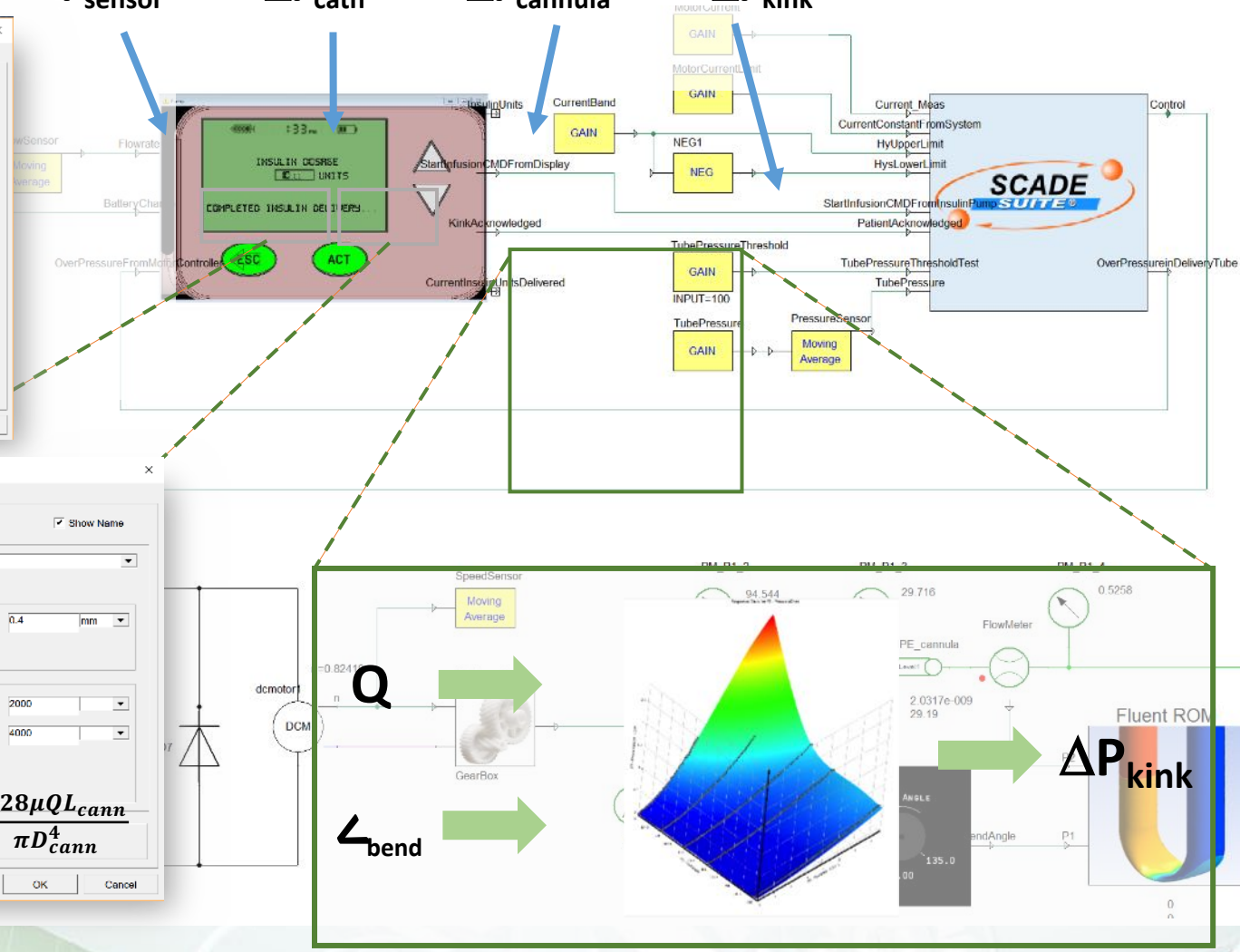
$$P_{sensor} = \Delta P_{cath} + \Delta P_{cannula} + \Delta P_{kink}$$



$$\Delta P_{cath} = \frac{128\mu Q L_{cath}}{\pi D_{cath}^4}$$



$$\Delta P_{cann} = \frac{128\mu Q L_{cann}}{\pi D_{cann}^4}$$



REQUIREMENT:

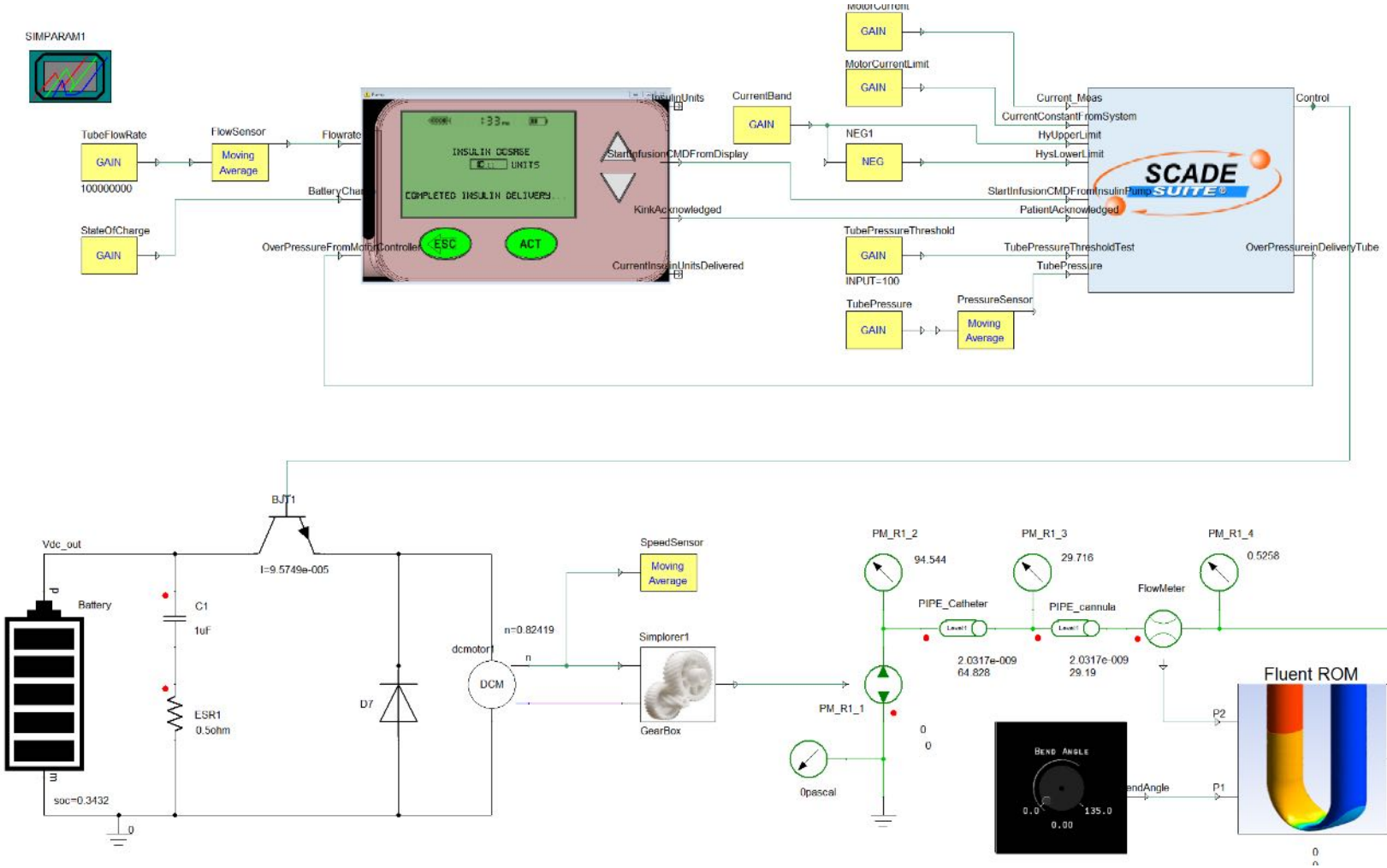
if $P_{sensor} > P_{threshold}$ then (

$i_{motor} = 0$;

warn patient;)

Drug Delivery Sub-System

VIRTUAL PATIENT



Couple the device model to a patient predictive model of glucose metabolism.

Virtual Patient Model

Two-compartment insulin model

$$\frac{dI_{SC}(t)}{dt} = -\frac{1}{\tau_1}\cdot I_{SC}(t) + \frac{1}{\tau_1}\frac{ID(t)}{C_I} \quad (1)$$

$$\frac{dI_P(t)}{dt} = -\frac{1}{\tau_2}\cdot I_P(t) + \frac{1}{\tau_2}\cdot I_{SC}(t) \quad (2)$$

Insulin effectiveness

$$\frac{dI_{EFF}(t)}{dt} = -p_2\cdot I_{EFF}(t) + p_2\cdot S_I\cdot I_P(t) \quad (3)$$

Two-compartment glucose model

$$\frac{dG(t)}{dt} = -\left(GEZI + I_{EFF}\right)\cdot G(t) + EGP + R_A(t) \quad (4)$$

$$R_A(t) = \frac{C_H(t)}{V_G\cdot\tau_m^{\,2}}\cdot t\cdot e^{-\frac{t}{\tau_m}} \quad (5)$$

- The patient model requires a **mathematical** representation of the relevant physics.
- The model should capture insulin metabolism as well as the ability of insulin to effect glucose uptake into cells.
- Researchers and industry typically rely on pharmacokinetic/pharmacodynamics (PK/PD) modeling to represent these processes.

*Kanderian et al., Identification of Intraday Metabolic Profiles during Closed-Loop Glucose Control in Individuals with Type 1 Diabetes, J Diabetes Sci and Tech , Vol. 3 (2009).

Virtual Patient Model

Two-compartment insulin model

$$\frac{dI_{SC}(t)}{dt} = -\frac{1}{\tau_1}\cdot I_{SC}(t) + \frac{1}{\tau_1}\frac{ID(t)}{C_I} \quad (1)$$

$$\frac{dI_P(t)}{dt} = -\frac{1}{\tau_2}\cdot I_P(t) + \frac{1}{\tau_2}\cdot I_{SC}(t) \quad (2)$$

Insulin effectiveness

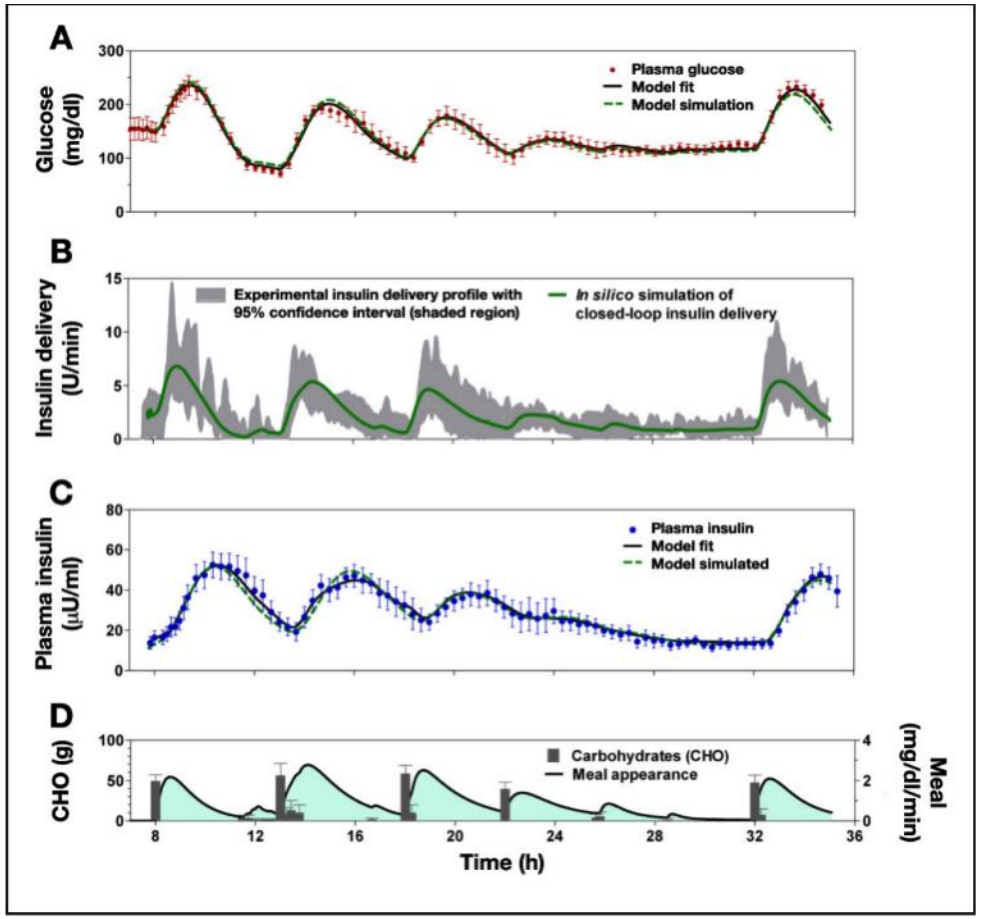
$$\frac{dI_{EFF}(t)}{dt} = -p_2\cdot I_{EFF}(t) + p_2\cdot S_I\cdot I_P(t) \quad (3)$$

CLINICAL DATA

Two-compartment glucose model

$$\frac{dG(t)}{dt} = -\left(GEZI + I_{EFF}\right)\cdot G(t) + EGP + R_A(t) \quad (4)$$

$$R_A(t) = \frac{C_H(t)}{V_G\cdot\tau_m{}^2}\cdot t\cdot e^{-\frac{t}{\tau_m}} \quad (5)$$



*Kanderian et al., Identification of Intraday Metabolic Profiles during Closed-Loop Glucose Control in Individuals with Type 1 Diabetes, J Diabetes Sci and Tech , Vol. 3 (2009).

Digital Twin Predictive Platform

INCOSE Healthcare Working Group

Monitor & Visualization

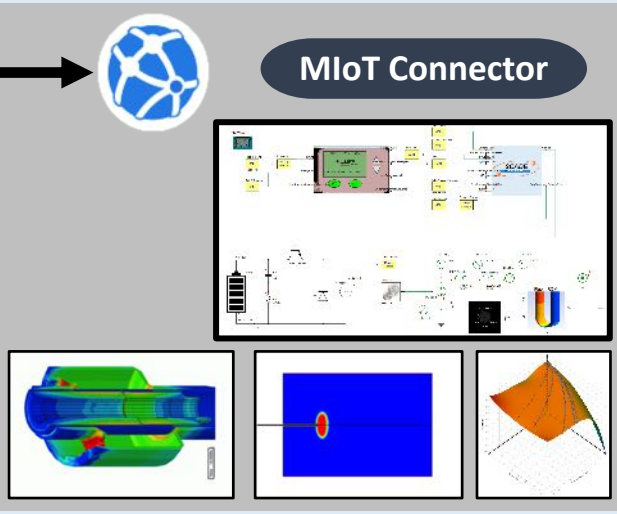
Execution Layer

thingworx

PREDIX

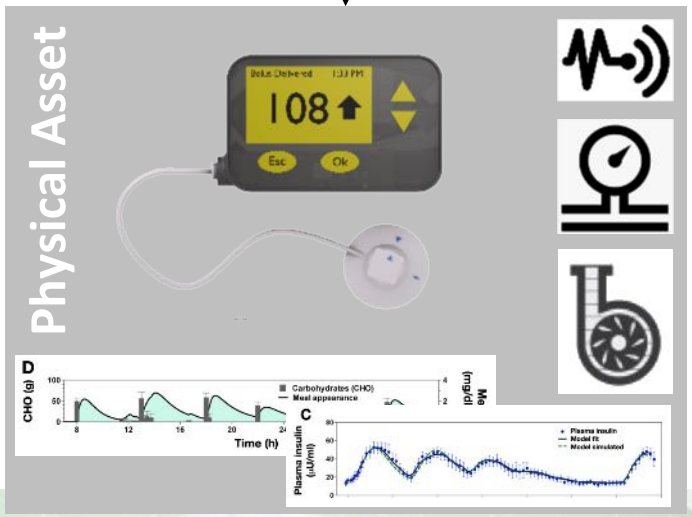
API

MIoT Connector



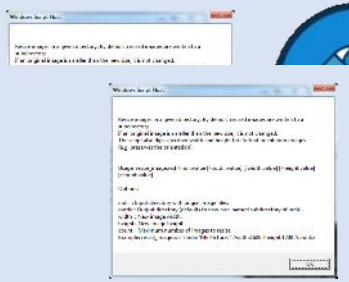
Digital Twin

Physical Asset



Data Layer - Device

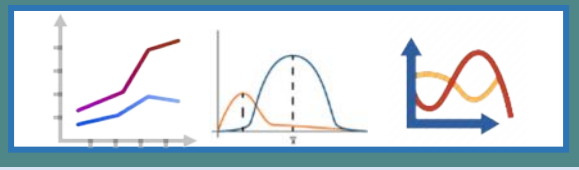
Data Layer - Patient



ROM Builder

Patient Physiology

Electronic Medical Record



Simulation Data

Conclusions

- Chronic diseases and the aging population are placing significant strain on healthcare systems, motivating the need for more effective medical technologies.
- The risk (and failure) of medical devices has increased since incorporating new technologies and functionality, much of which is related to embedded software.
- Systems modeling can improve the robustness and safety of today's medical devices.
- Digital twins for implanted devices that include models of human physiology (enabled by computer modeling) can improve treatment outcomes.

INCOSE
Healthcare Working Group
4th Annual Systems Engineering in Healthcare Conference

Thank you for attending!
Share your experiences at #HWGSEC