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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

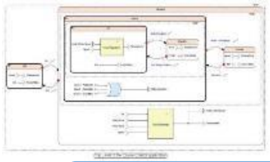
Electric		Smarter		Connected
IVD devices	Physiological Monitors	Mobile Medical Apps	Wearables	Capital Intensive Devices
Blood Analyzers Immuno-assays Breast Biopsy Equipment HIV Detection Systems	Weighing scales Pulse Oximeter BP Meter ECG Ventilators Blood Glucose Meters Heart Rate Monitors	Medication 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

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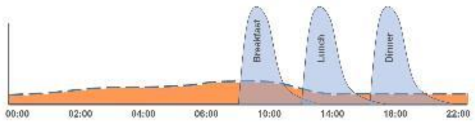
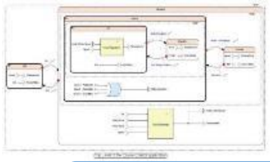
…are ultimately part of a system

Electronic Control

Actuators



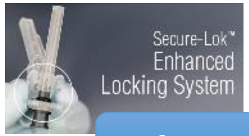
Operational Profiles



Embedded Software

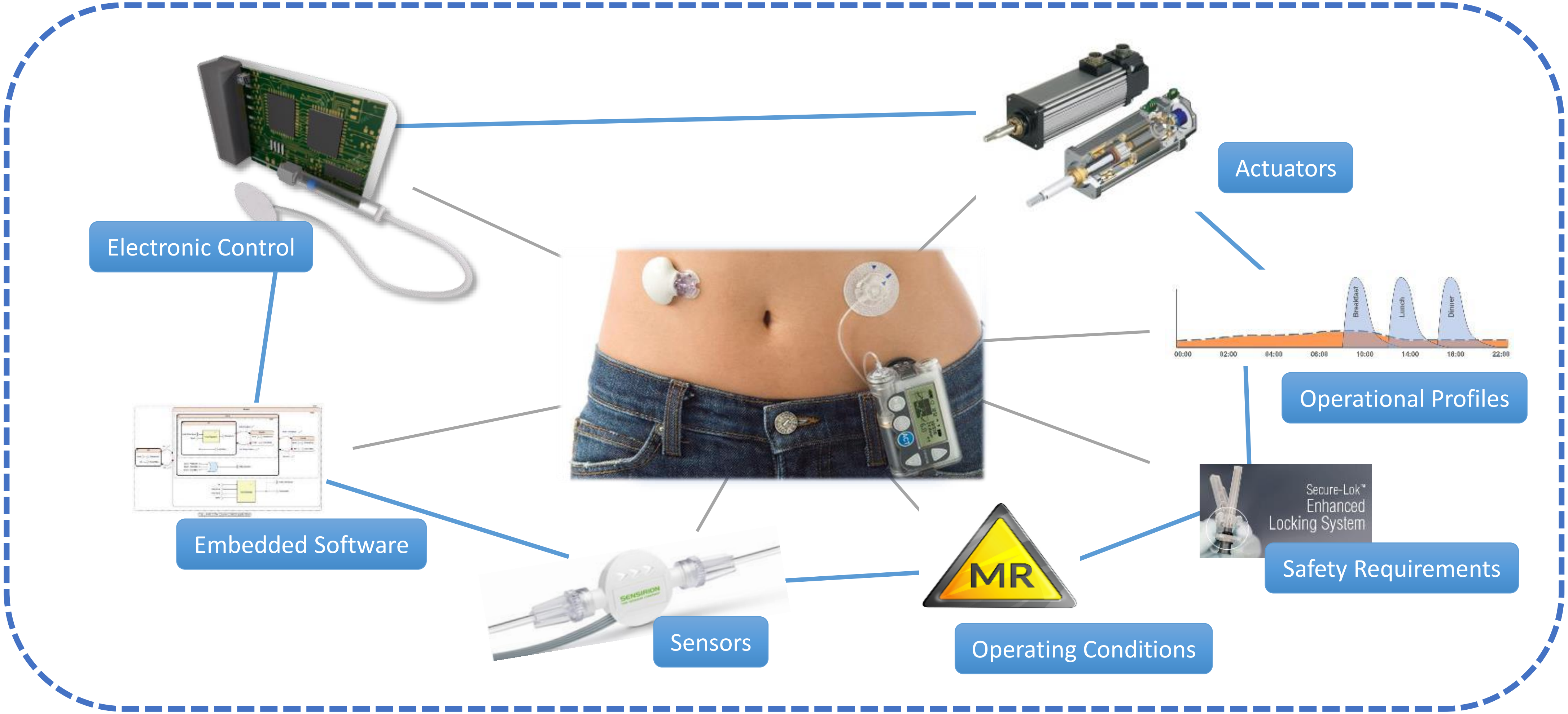
Sensors

Operating Conditions



Safety Requirements

…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.

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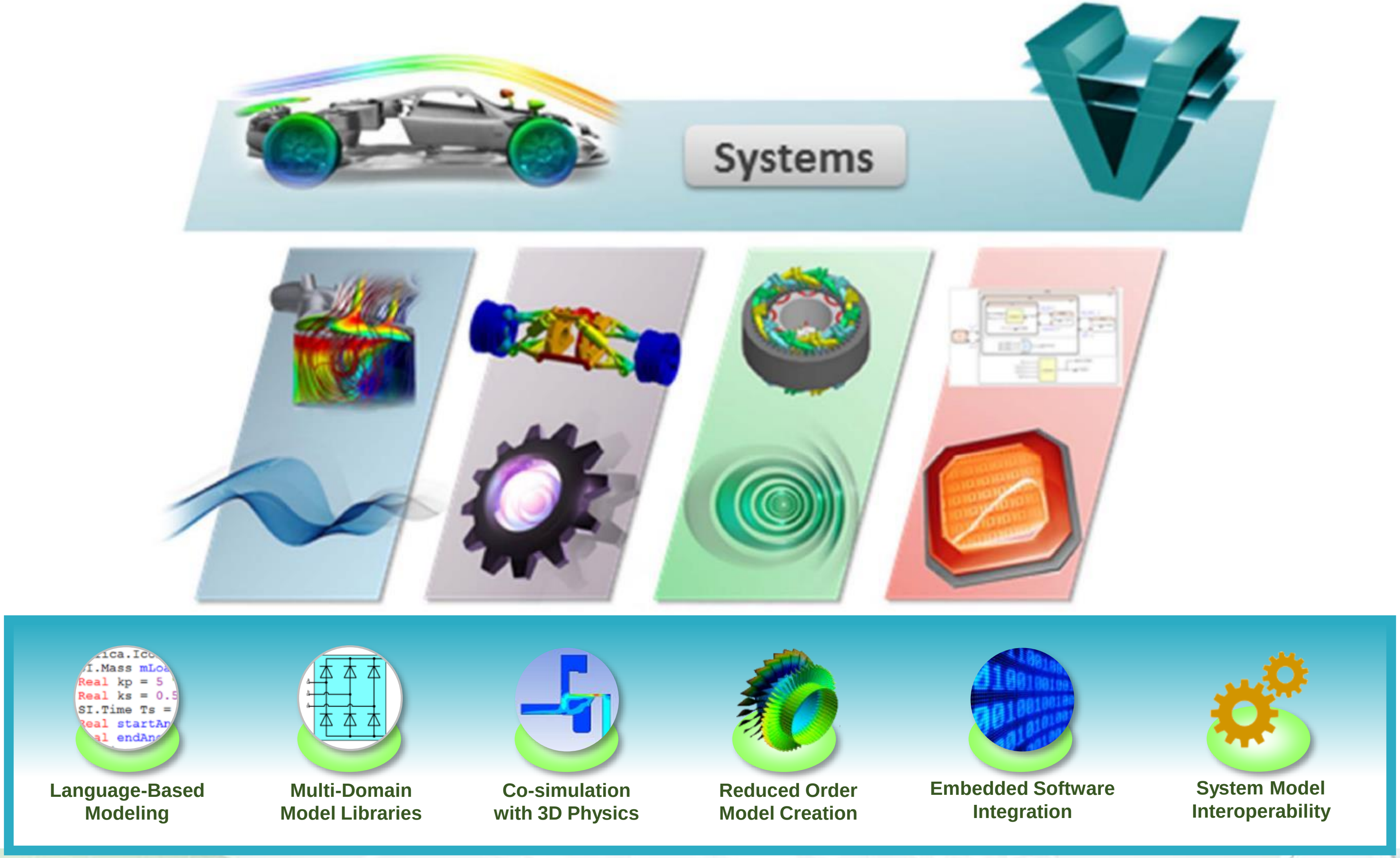
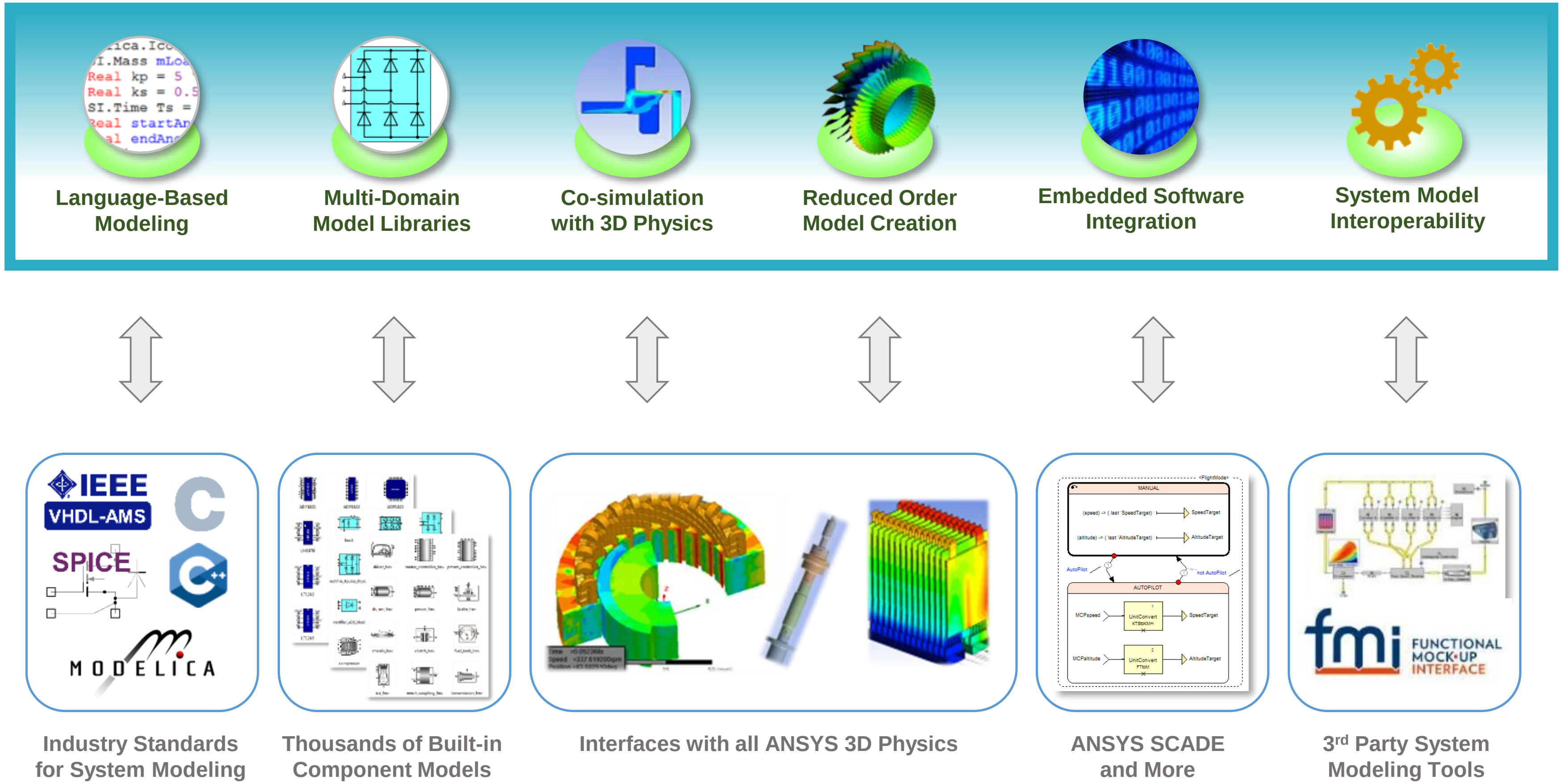
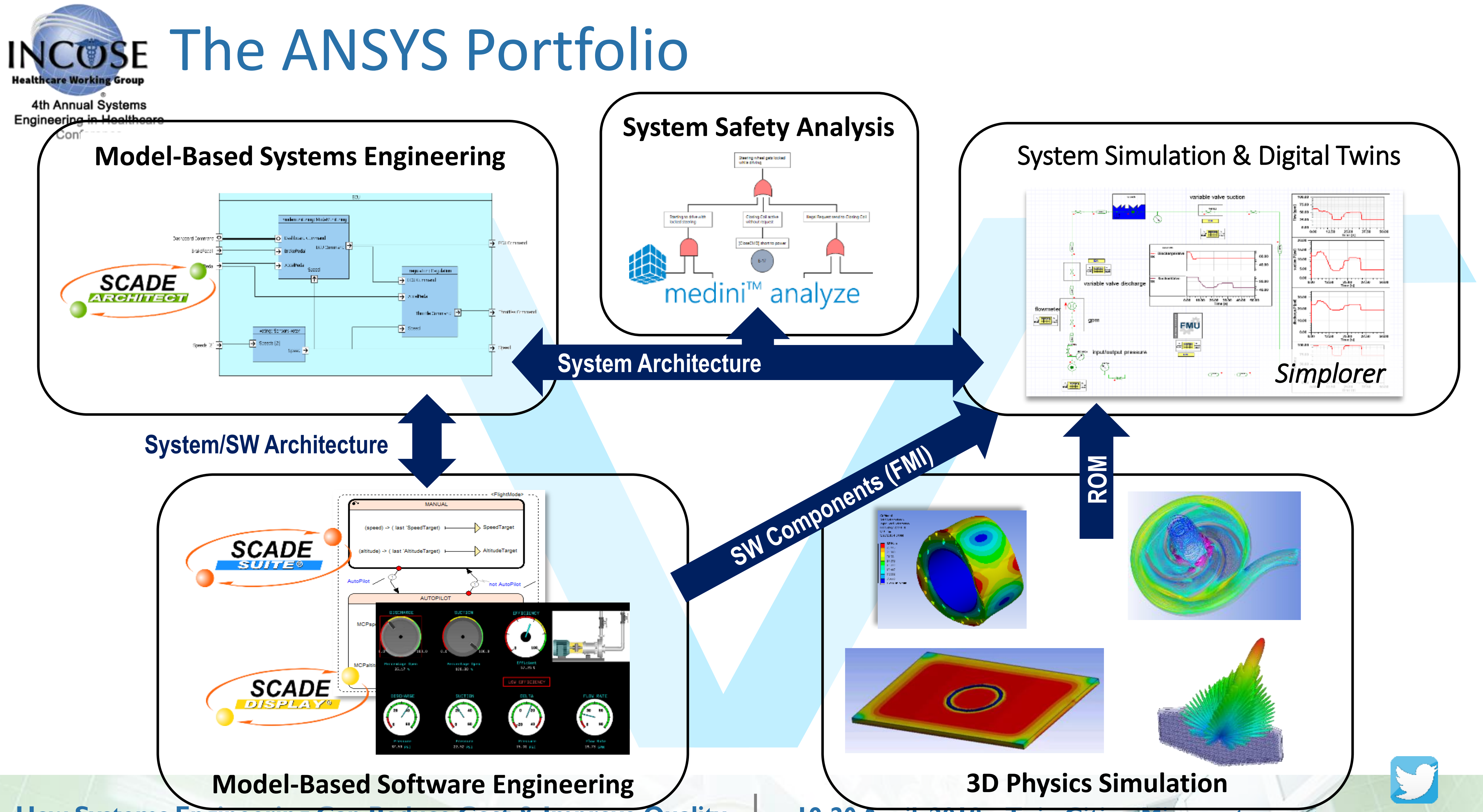
Systems Engineering: A Unifying Approach



Systems Modeling
– Model Flexibility, Reusability, and Interoperability



The ANSYS Portfolio



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FDA Analyses of Product Recalls

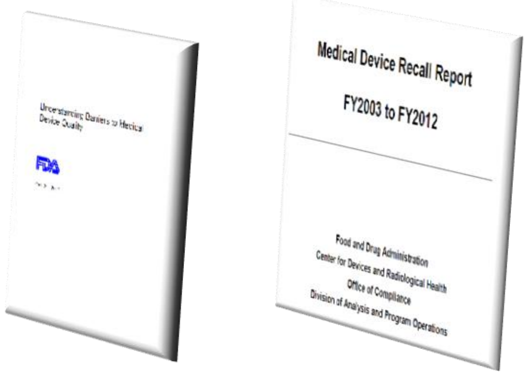


Exhibit 11: Recall case codes by root cause

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

Legend: >=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."

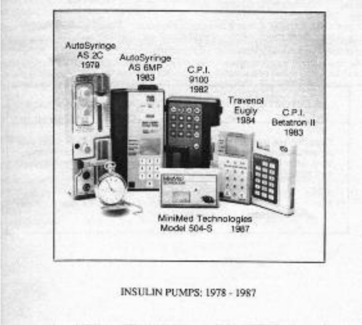
1. *from FDA Report "Understanding Barriers to Medical Device Quality" (2011)*

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

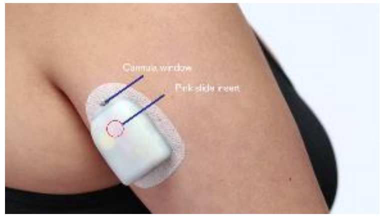
FDA Launches Initiative to Reduce Infusion Pump Risks
Agency calls for improvements in device design



…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.



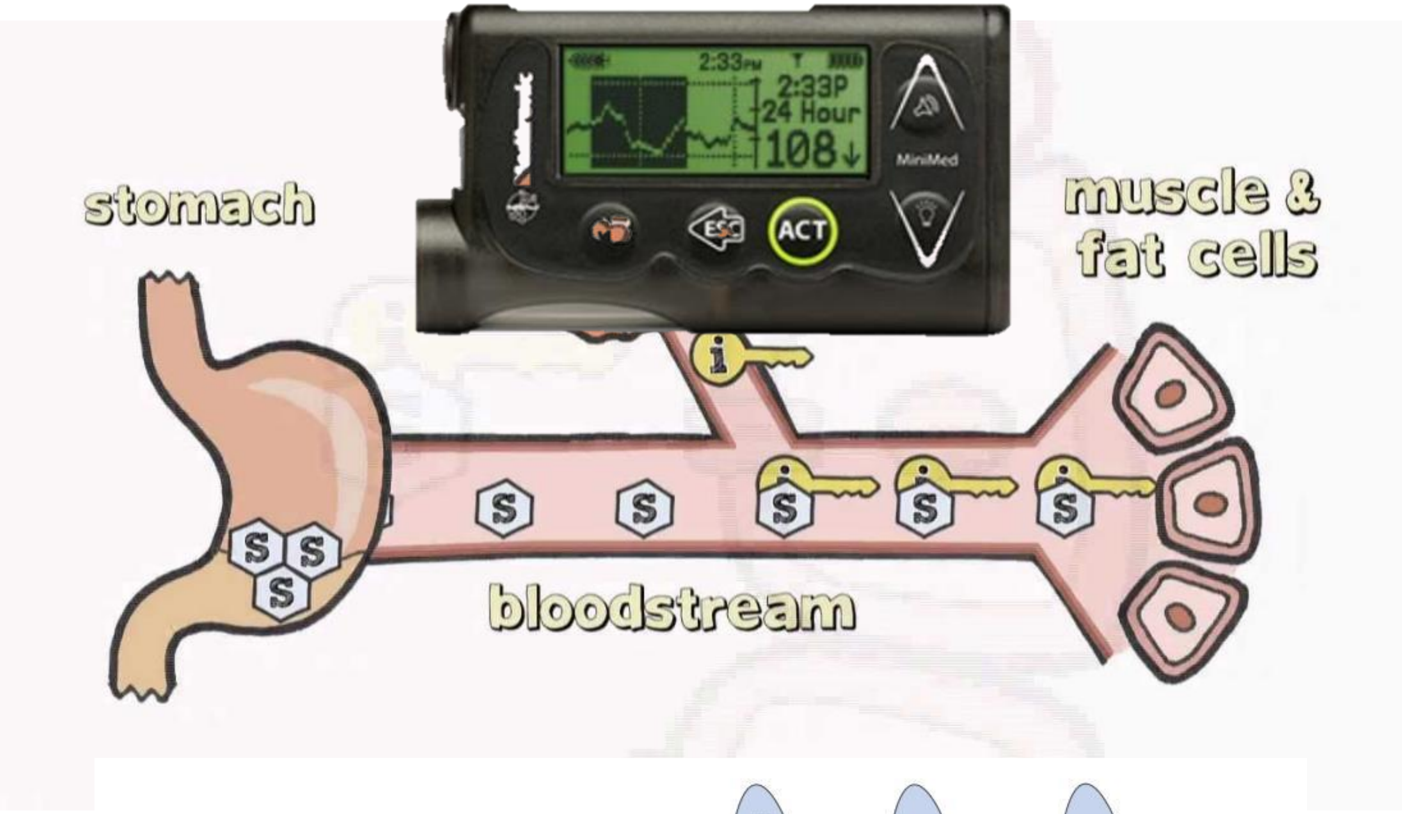
"many of the reported problems appear to be related to deficiencies in device design and engineering"

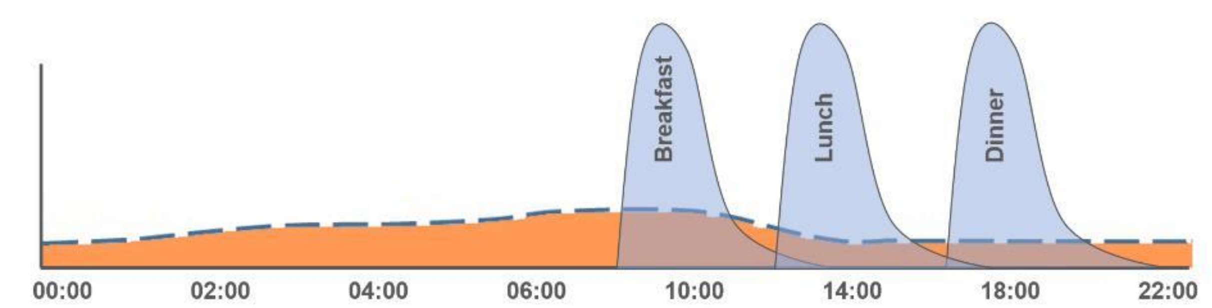
http://diyabetimben.com/diyabet-muzesi/

Insulin Pump Model

What is Diabetes?

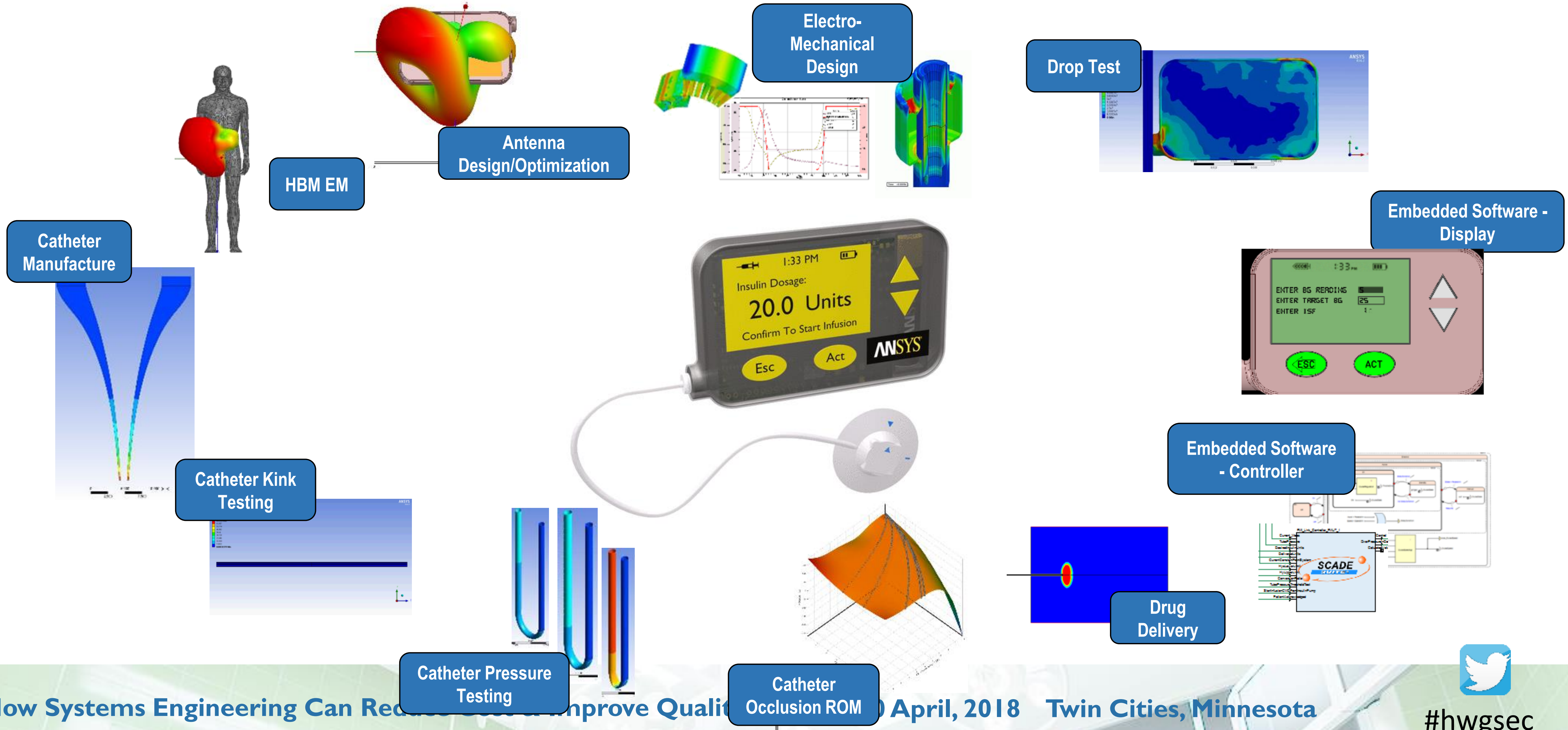
- Insulin is a hormone created by the pancreas. It is required for sugar molecules (from the food you eat) to move inside cells. Patients with diabetes either do not produce insulin (Type 1) or do not use insulin the right way (Type 2).
- Insulin pumps replace the function of the pancreas by injecting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



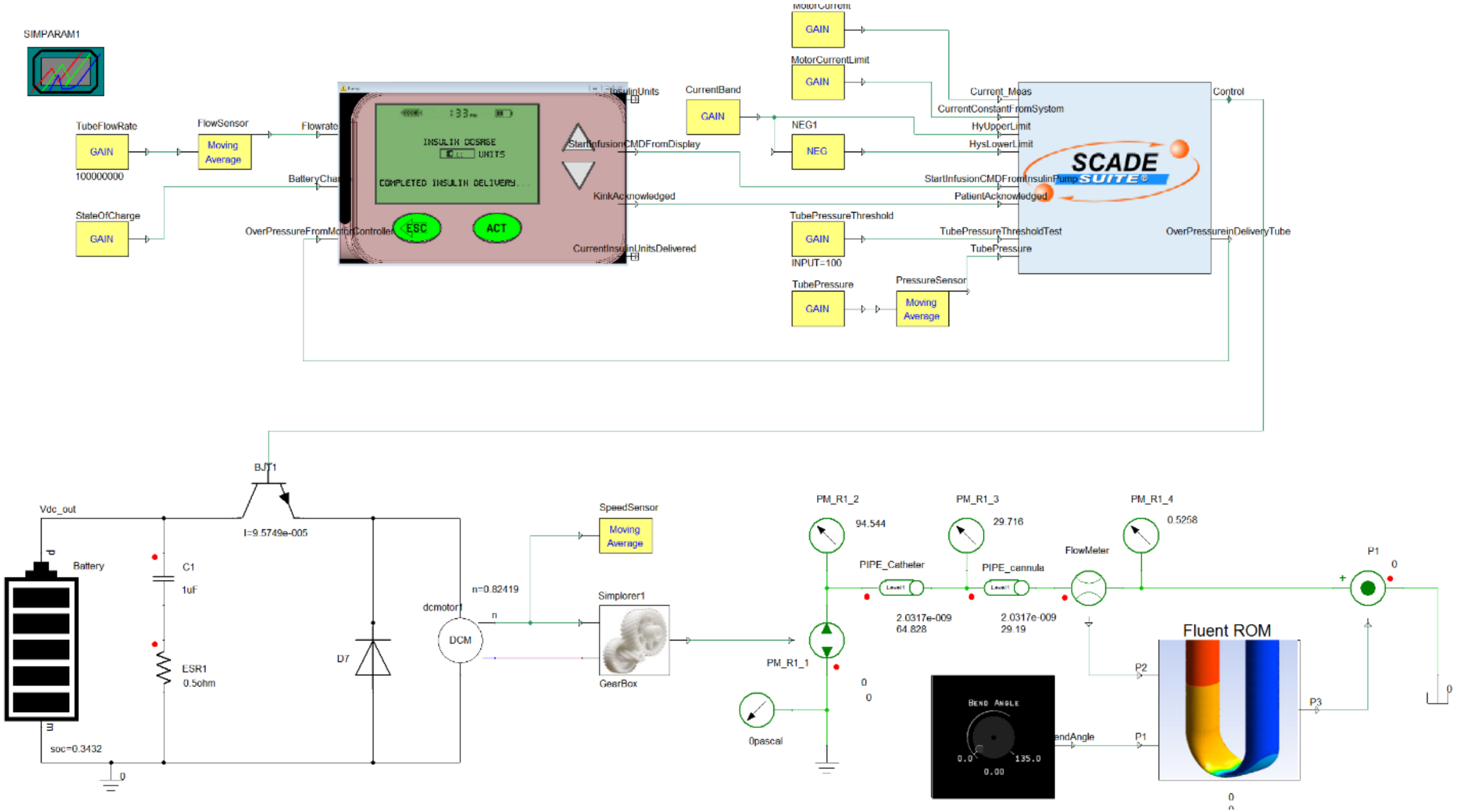


diabetes image from https://i.ytimg.com/vi/SCCb5GqhnrI/maxresdefault.jpg
Pump image from http://www.medtronicdiabetes.com/products/minimed-530g-diabetes-system-with-enlite

Components, Components, Components



Drug Delivery Sub-System



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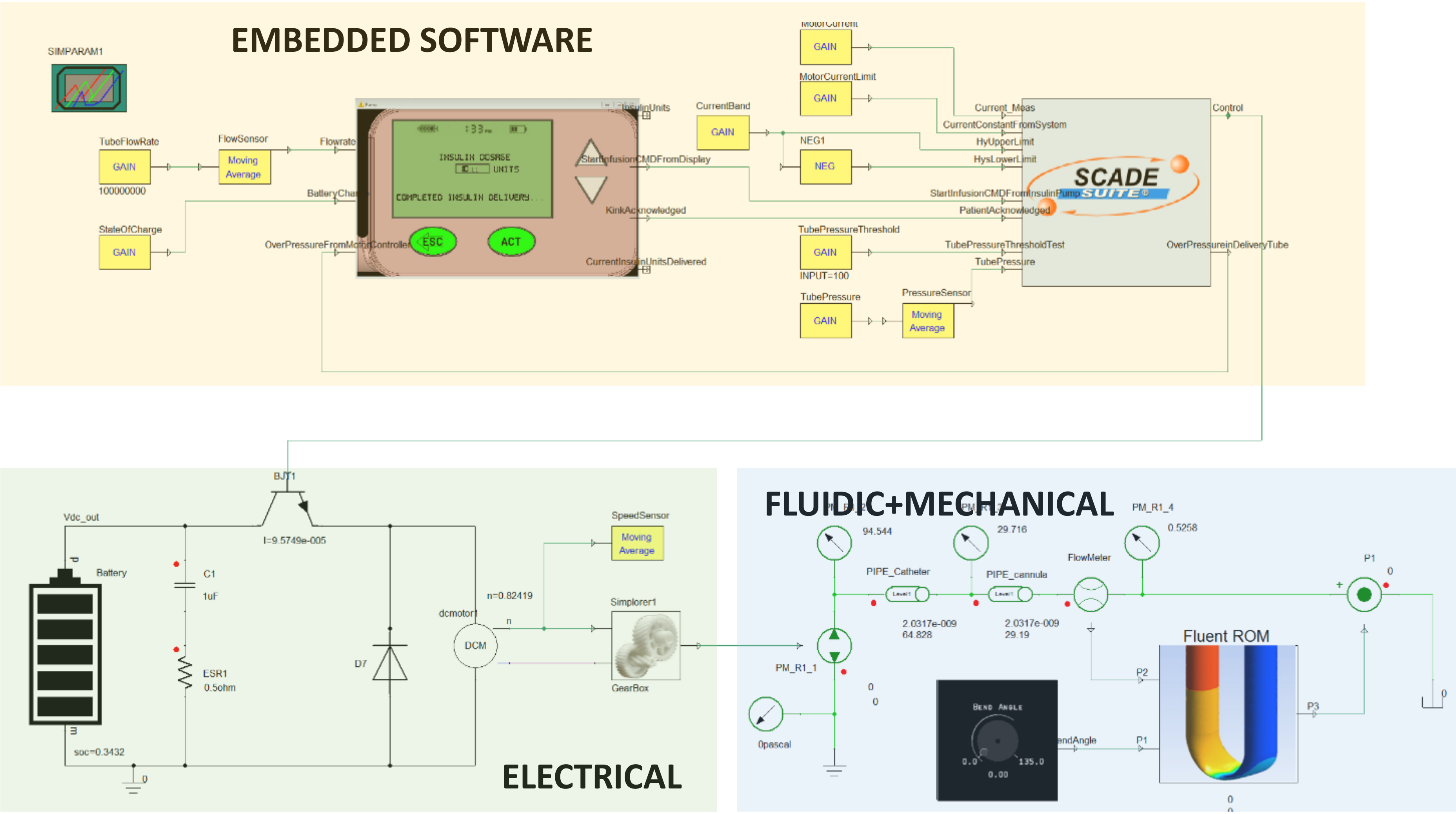
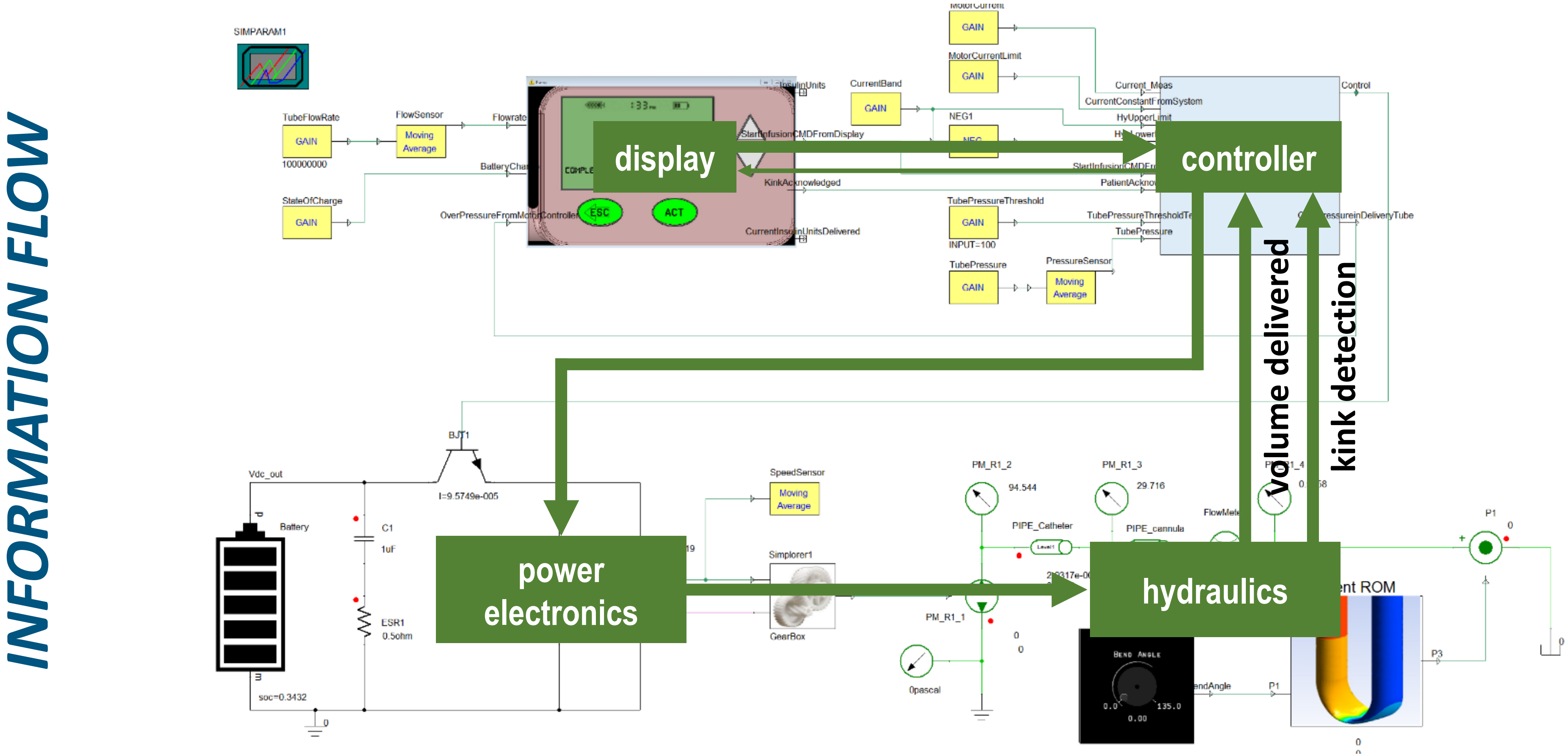
Drug Delivery Sub-System

MODEL DOMAINS

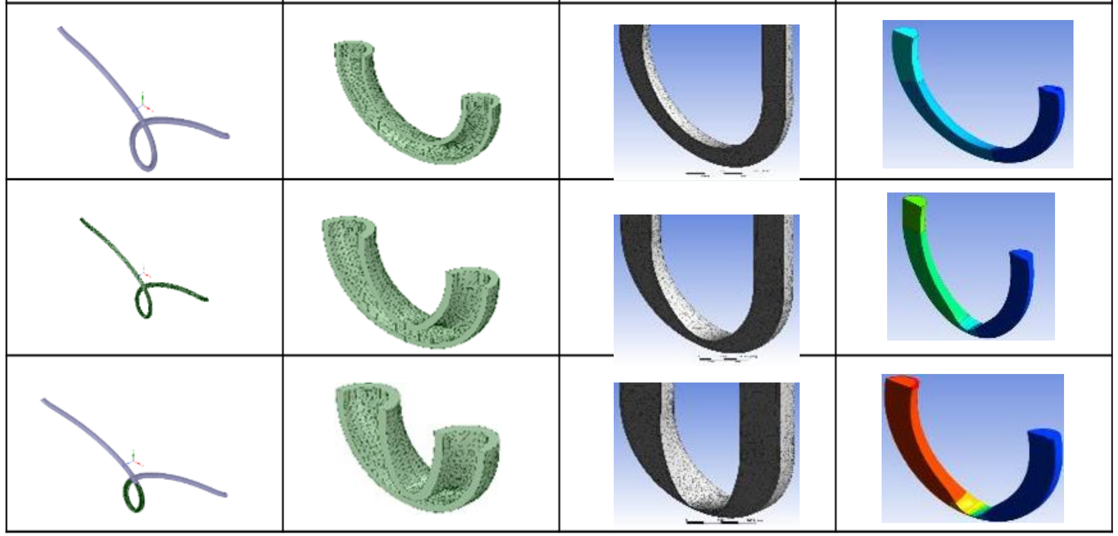


Drug Delivery Sub-System

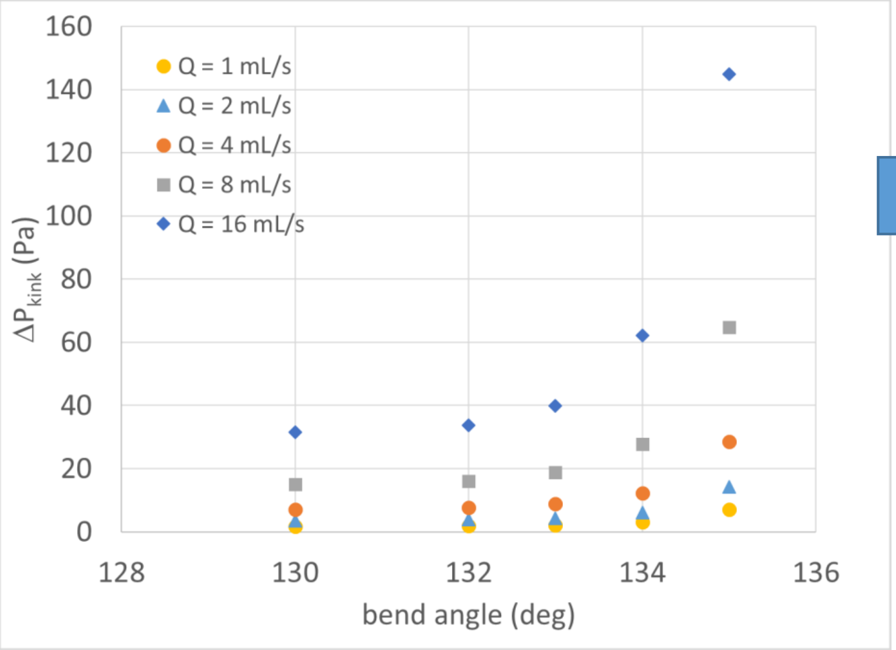


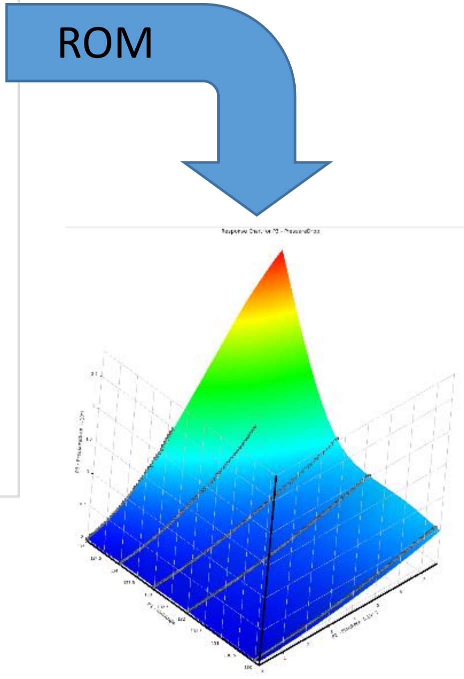
Pressure-Flow Analysis of Tube Bending

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



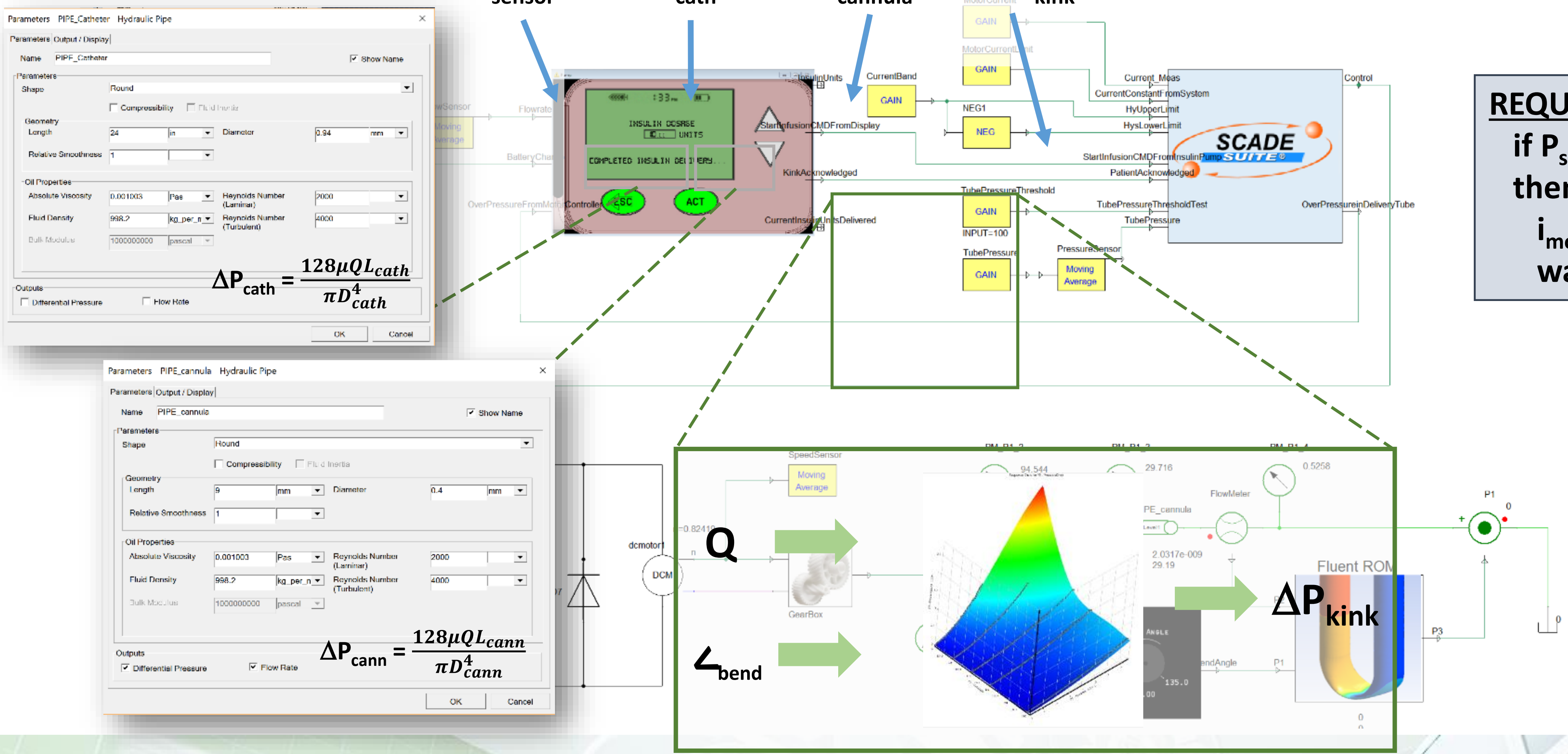
Family of Structural Fluid Simulations





Insulin Pump – ROM Behavior

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



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

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

ΔP_{kink}

REQUIREMENT:

if $P_{sensor} > P_{threshold}$
then (
$i_{motor} = 0$;
warn patient;)

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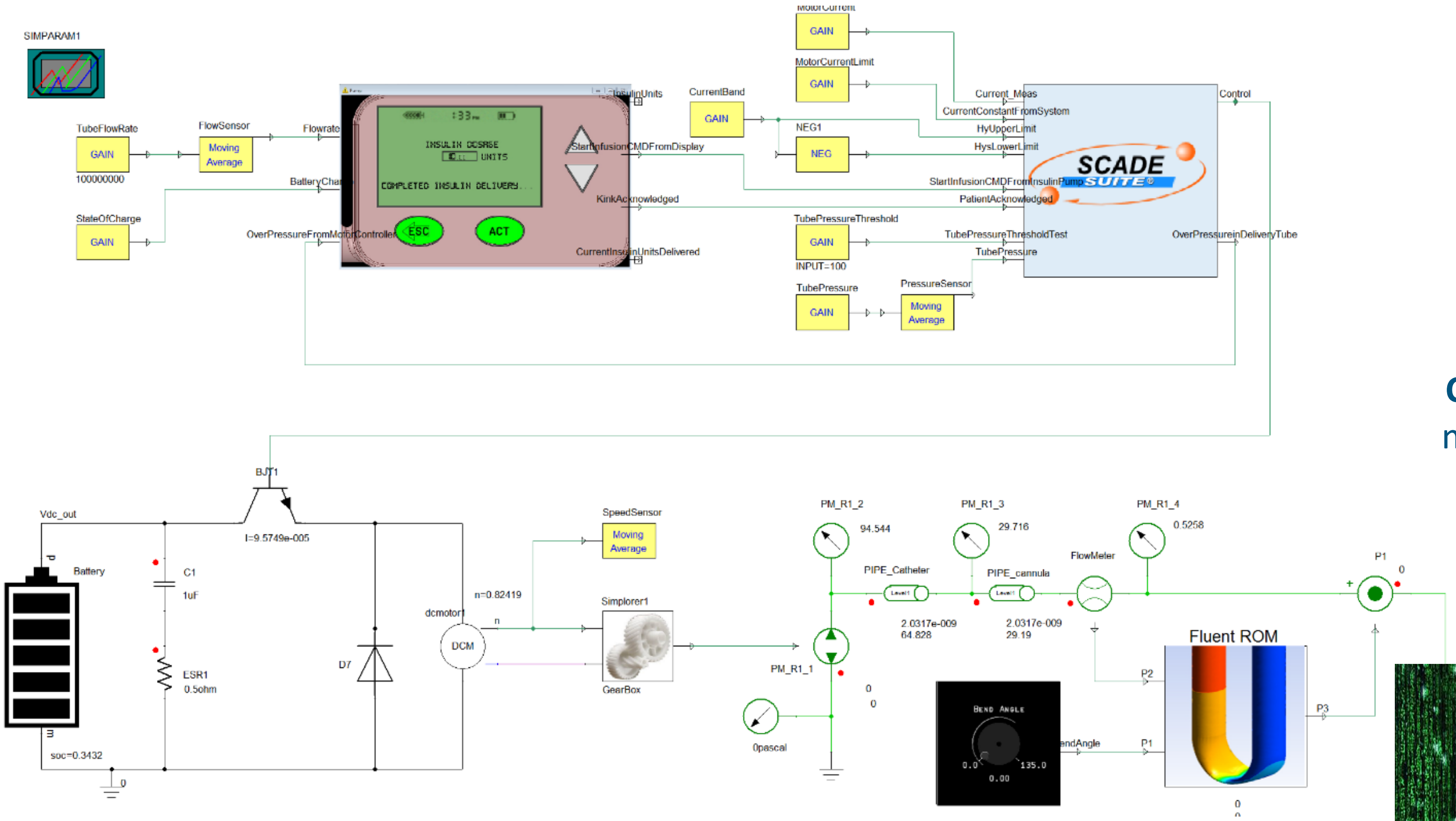
Drug Delivery Sub-System

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

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

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

- 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).

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Virtual Patient Model

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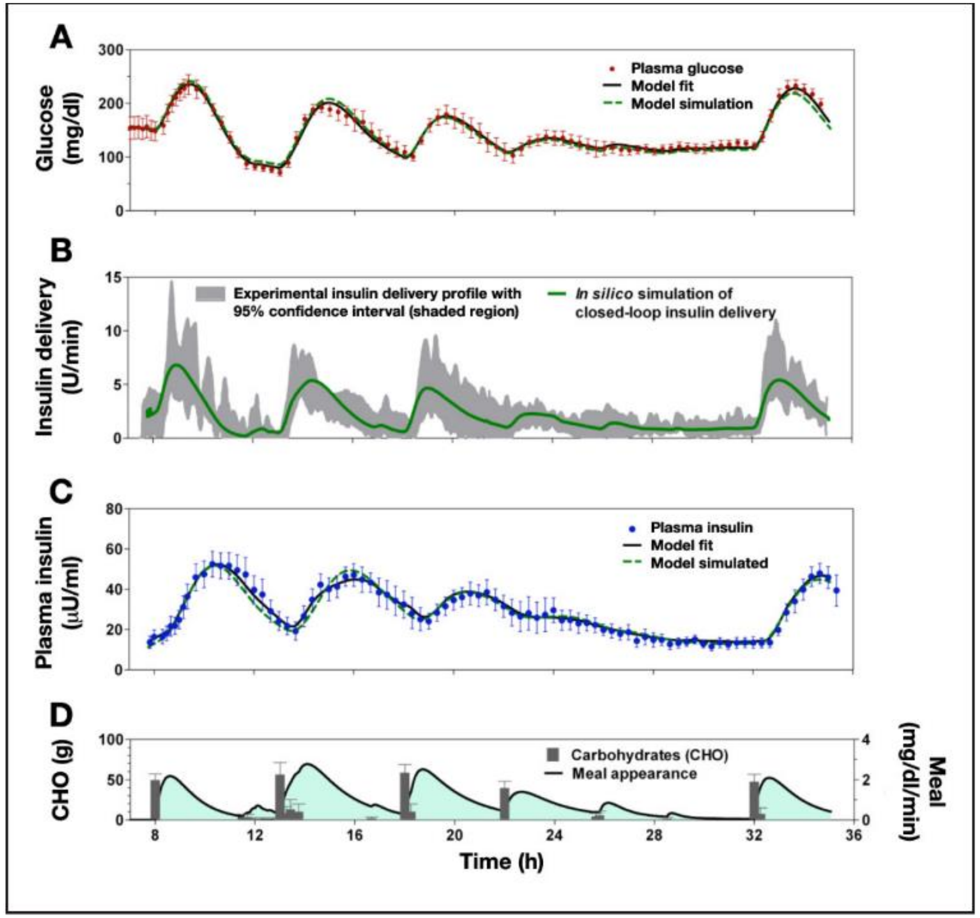
CLINICAL DATA



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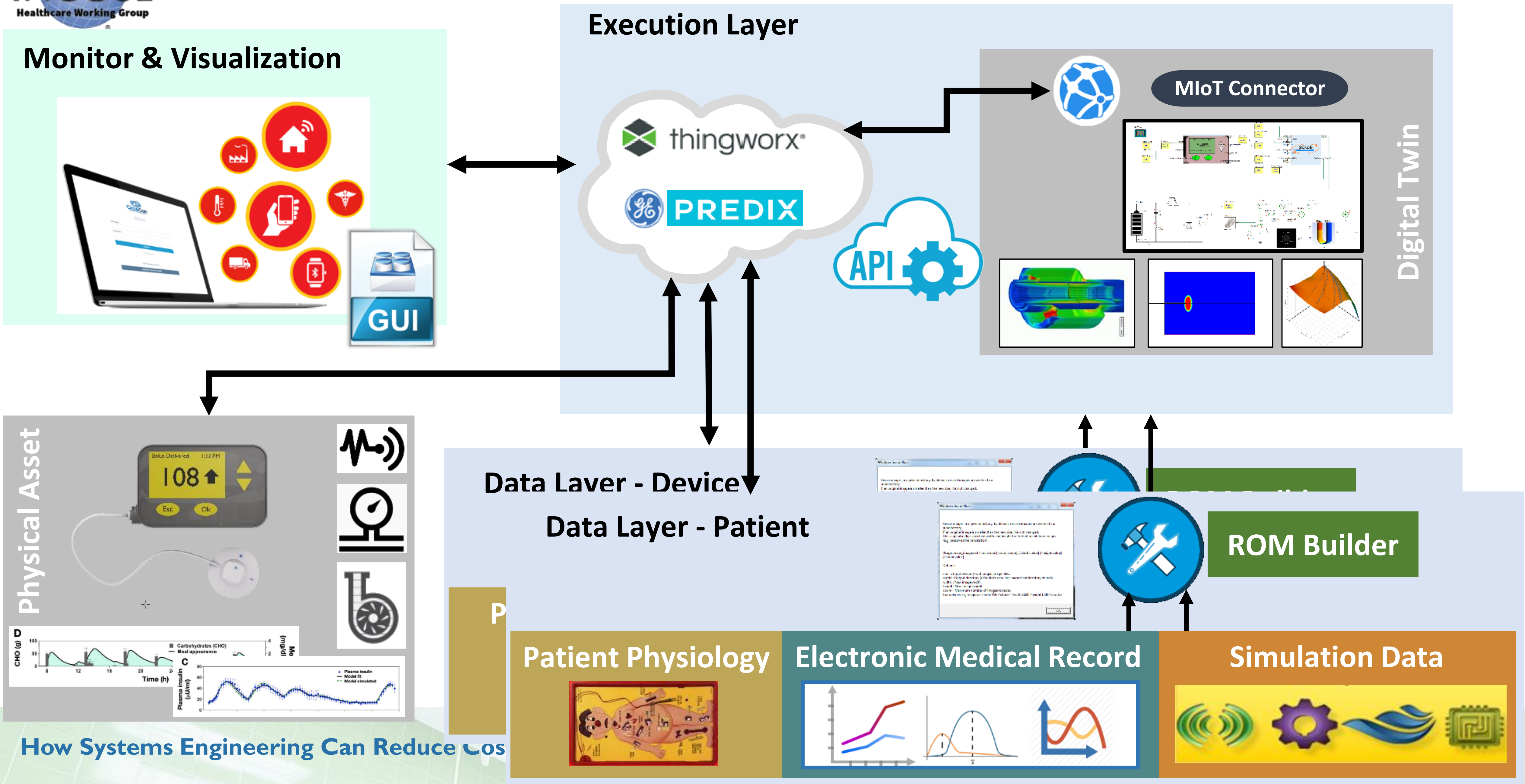
Digital Twin Predictive Platform



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.

Thank you for attending!
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