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

<table>
<thead>
<tr>
<th>Electric</th>
<th>Smarter</th>
<th>Connected</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVD devices</td>
<td>Physiological Monitors</td>
<td>Mobile Medical Apps</td>
</tr>
<tr>
<td>Blood Analyzers</td>
<td>Weighing scales</td>
<td>Medication Adherence Systems</td>
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<tr>
<td>Immuno-assays</td>
<td>Pulse Oximeter</td>
<td>Dosage Calculation Systems</td>
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<tr>
<td>Breast Biopsy Equipment</td>
<td>BP Meter</td>
<td>Sleep Apnea Detector</td>
</tr>
<tr>
<td>HIV Detection Systems</td>
<td>ECG</td>
<td>Heart Rate Monitors</td>
</tr>
</tbody>
</table>

*Cogizant, How the IOT is Transforming Medical Devices, May 2016*
Components

Electronic Control
Embedded Software
Sensors
Actuators

Domain-specific
Component-centric
...are ultimately part of a system
...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

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How Systems Engineering Can Reduce Cost & Improve Quality

19-20 April, 2018 Twin Cities, Minnesota

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The ANSYS Portfolio

Model-Based Systems Engineering

- System Safety Analysis
  - medini™ analyze

System Simulation & Digital Twins

- Simploter

System Architecture

System/Software Architecture

Model-Based Software Engineering

- SW Components (FMI)

3D Physics Simulation

The ANSYS Portfolio

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FDA Analyses of Product Recalls

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

1. from FDA Report “Understanding Barriers to Medical Device Quality” (2011)
Infusion Pump Safety

...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/SCCb5Gqhnrl/maxresdefault.jpg
Components, Components, Components

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HBM EM
Antenna Design/Optimization
Electro-Mechanical Design
Drop Test
Embedded Software - Display

Catheter Manufacture
Catheter Kink Testing
Catheter Pressure Testing
Catheter Occlusion ROM

Components, Components, Components
Drug Delivery Sub-System
Drug Delivery Sub-System

MODEL DOMAINS

EMBEDDED SOFTWARE

FLUIDIC+MECHANICAL

ELECTRICAL

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Drug Delivery Sub-System

INFORMATION FLOW

- Task 1: Display
- Task 2: Controller
- Task 3: Volume Delivered
- Task 4: KinkDetection

INFORMATION FLOW:

- Power Electronics
- Hydraulics

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### Pressure-Flow Analysis of Tube Bending

#### Family of Structural Fluid Simulations

<table>
<thead>
<tr>
<th>Non Linear Kink Prediction</th>
<th>Deformed Geometry Export</th>
<th>Fluid volume extraction of kinked model</th>
<th>Detailed Flow Simulation (kink angles &amp; flow rates → pressure drop)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3D FEA</td>
<td>3D FEA → CAD</td>
<td>CAD → 3D CFD</td>
<td>3D CFD</td>
</tr>
</tbody>
</table>

![Diagram showing flow analysis and parameters](image)

**Figure:** Graph showing pressure drop ($\Delta P_{\text{sink}}$) vs. bend angle (deg) for different flow rates ($Q$). The legend indicates different flow rates: $Q = 1 \text{ mL/s}$, $Q = 2 \text{ mL/s}$, $Q = 4 \text{ mL/s}$, $Q = 8 \text{ mL/s}$, and $Q = 16 \text{ mL/s}$. The graph displays data points for each flow rate, showing the relationship between pressure drop and bend angle.
Insulin Pump – ROM Behavior

\[ P_{\text{sensor}} = \Delta P_{\text{cath}} + \Delta P_{\text{cannula}} + \Delta P_{\text{kink}} \]

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

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

**REQUIREMENT:**

if \( P_{\text{sensor}} > P_{\text{threshold}} \) then

\( i_{\text{motor}} = 0; \)

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

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

\[
\frac{dI_{P}(t)}{dt} = -\frac{1}{\tau_2} \cdot I_{P}(t) + \frac{1}{\tau_2} \cdot I_{SC}(t) \quad (2)
\]

Insulin effectiveness

\[
\frac{dI_{EFF}(t)}{dt} = -p_2 \cdot I_{EFF}(t) + p_2 \cdot S_1 \cdot I_{P}(t) \quad (3)
\]

Two-compartment glucose model

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

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

- 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

**Two-compartment insulin model**

\[
\frac{dI_{SC}(t)}{dt} = -\frac{1}{\tau_1} \cdot I_{SC}(t) + \frac{1}{\tau_1} \cdot \frac{ID(t)}{C_l}
\]  

\[
\frac{dI_P(t)}{dt} = -\frac{1}{\tau_2} \cdot I_P(t) + \frac{1}{\tau_2} \cdot I_{SC}(t)
\]

**Insulin effectiveness**

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**Two-compartment glucose model**

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Digital Twin Predictive Platform

Monitor & Visualization

Execution Layer

- thingworx
- PREDIX

Digital Twin

MloT Connector

ROM Builder

Data Layer - Device

Data Layer - Patient

Physical Asset

Visualization

GUI

Physical Asset

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ROM Builder

Patient Physiology

Electronic Medical Record

Simulation Data

How Systems Engineering Can Reduce Cost & Improve Quality
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.
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