Shaping the Future of Biomedical Device Design and Diagnostics

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Overview

Biomedical Device Design: Benchtop and Clinical Trial Support

- Simulation and the regulatory system
  - ASME V&V 40, MDDT, MDIC, Avicenna
- Case Studies: the path forward
  - VEXTEC Corp and CD-adapco: drug delivery in the cardiovascular system
  - Simulia Living Heart Project
  - System Integration: Lumped Parameter Model Optimization with Optimate+

Biomedical Diagnostics

- inFluids LLC
### Biomedical Device Design: The Possibilities

**Directions and Trends**
- Regulatory and Industry converging on solutions through consortia work
- “Diagnostics Simulations” put new business concepts to the test
- A shared vision of Computational Clinical Trials is evolving

**Challenges**
- New to Simulation: Understand the benefits, needs and pain? → Evangelism
- Already using Simulation: Transition from Benchtop to Clinical Trials

**Goal: Accelerate Industry Acceptance**
- Work with Consortia, Academics, Marketing
- Collaborate with Diagnostic Tool Makers
- Demonstrate Clinical Trial Project Success / Go Beyond Simulation
Relevance of Simulation and Modeling to Support Clinical Trials

- Device development and modeling under consideration of:
  - Variation of patient specific data
  - Product variations
  - Variation of patient/environment conditions: Rest, Exercise, Blood Pressure, Drug Effects etc.
- CD-adapco member of ASME V&V-40, MDIC
**MDIC**

Computational Modeling & Simulation

**Increasing Confidence in Safety and Efficacy through Regulatory Grade Computer Models & Simulations**

- Increase Evaluation Confidence
- Faster Market Clearance
- Decrease Cost

**Project Goals**

- Advancing medical device innovation, and evaluating new and emerging technologies
- Developing state of the art preclinical methods for assessing device safety and performance
- Developing novel ways to use clinical data in evaluating medical devices – Big Data
ASME V&V 40, MDDT, MDIC, Avicenna

**TPLC Use of CM&S Evidence**

Total Product Life Cycle
**Roadmap:** Increasing the Use of CM&S Evidence

- **Nonclinical**
  - Replace existing bench with simulation
  - Leap-frog technology safety evidence by simulation
  - Mock Submissions
  - Benchmarks
  - Pilot
  - 1-2 years

- **Clinical**
  - Research to describe disease states
  - Autonomous control embedded systems
  - Accredited models libraries
  - 5 years
  - 10+ years

- **Methods, Tools, Approaches, and Process**
  - Model Credibility
  - Data Archival
  - Interoperability
  - ??

Who: Academia informed by Industry and OSEL

Who: Industry and OSEL informed by ODE

Future

Computer Modeling and Simulation Roadmap

MDIC, ASME & FDA
Avicenna: A Strategy for *in silico* Clinical Trials

Tasked by the European Commission (EC) to produce a Roadmap for the introduction of *in silico* clinical trials, the Avicenna project began in October 2013 and runs until September 2015.

The project will develop and promote this Roadmap, and work to overcome the legal, financial, organizational and technical barriers that could slow the adoption of computer simulation in this domain.

http://avicenna-isct.org/
The FDA’s MDDT - Medical Device Development Tools

- The FDA’s Medical Device Development Tools (MDDT) program is a way for the FDA to qualify tools that medical device sponsors can use in the development and evaluation of medical devices.
- Qualification means that the FDA has evaluated the tool and concurs with available supporting evidence that the tool produces scientifically-plausible measurements and works as intended within the specified context of use …

Medical Device Development Tools

Draft Guidance for Industry, Tool Developers, and Food and Drug Administration Staff

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Document issued on: November 14, 2013
Objective: Simulate the motion of a large number of interacting particles through the human vasculature
  – Example: loaded drug-eluting beads being delivered to a target site as treatment

Key features
  – Tracking the particles in a numerically efficient manner
  – Modeling contact forces and interactions
  – Considering stochastic effects associated with random distributions of particle size and number
  – Goal: Determine the impact of above factors and variability of inlet flow conditions on the effectiveness of the therapy → the coverage fraction by the particles with the target vasculature.

Case Studies: VEXTEC Corp
Case Studies: VEXTEC Corp

- STAR-CCM+ used to model flow of particles within the vessels along with the interactions.

- VEXTEC's VLM Uncertainty Management platform handles random statistical nature of the problem to generate the uncertainty scenarios.
The Living Heart Project

Mission

Through simulation, connect the individual efforts of leading cardiovascular researchers, therapeutic device developers, and cardiac practitioners with the goal of advancing computational science to revolutionize bio-sciences and cardiovascular medicine.

FSI Use Cases

- Transcatheter Aorta Valve Replacements
- Devices to treat aortic aneurysms
- Devices used to treat holes in the heart
- Occluders
- Any other device that alters flow within and around the heart
Workflow: Biomedical Device Design using Patient Specific Data → Simulating Systems

STAR-CCM+ Workflow Capabilities:
STL Cleanup – Java (Windkessel) – Simulation Assistant - Optimization
The gold standard for haemodynamic simulations is the use of lumped parameter models to described the downstream impedance of the vasculature.

- The most commonly used lumped parameter model is the three element Windkessel which is constructed from two resistors in series and a capacitor in parallel.

A key challenge to using a Windkessel model (or any other lumped model) is the appropriate choice of parameter values.

- Common approaches are:
  - Simplified analytical calculations – often good to get realistic initial values but generally not suitable for “matched” or production cases.
  - Manual trial and error – time consuming and generally only gets you so far.
  - Optimisation procedure – automated process which should obtain the “best” fit.
When running an optimisation study we have to define parameters which can be modified by the algorithm and an objective(s) which is to be minimised or maximised.

**Parameters**

- These are simply the Windkessel parameters, Z, R and C.
- Since these parameters are defined in a java macro, which can’t be “seen” by Optimate+, we have to modify our approach to allow Optimate+ access.
  - This can be done by creating a field function for each of the Windkessel parameters and modifying the java to read the value of these field functions rather than setting them explicitly in the java macro.

```java
// Get Windkessel Variables from FF
UserFieldFunction uFF_R = ((UserFieldFunction) simu.getFieldFunctionManager().getFunction("R1"));
UserFieldFunction uFF_C = ((UserFieldFunction) simu.getFieldFunctionManager().getFunction("C1"));
UserFieldFunction uFF_Z = ((UserFieldFunction) simu.getFieldFunctionManager().getFunction("Z1"));
```
Parameter definition

- $Z$ is allowed to vary between $9\times 10^6$ to $1.3\times 10^7$ with a resolution of 51
  - Baseline value of $1.1\times 10^7$
- $R$ is allowed to vary between $1.15\times 10^8$ to $1.75\times 10^8$ with a resolution of 51
  - Baseline value of $1.45\times 10^8$
- $C$ is allowed to vary between $1.1\times 10^{-8}$ to $2.1\times 10^{-8}$ with a resolution of 201
  - Baseline value of $1.45\times 10^{-8}$

The baseline values had already been manually tuned to match the clinical waveform in previous work.

- Comparison of baseline values
  - Green = Clinical Pressure
  - Red = Windkessel Pressure
Variation in Windkessel pressures
Comparison of the clinical, baseline, and “best” fit pressure waveforms

Outlet Pressure Comparison

- Best Fit Windkessel Pressure Monitor
- Clinical Pressure Monitor
- Baseline Windkessel Pressure Monitor
Lean Startups

Reimbursement Strategy: Heartflow

The “Uberization” of Healthcare (Stuart Karten - founder of Karten Design)

– Just as Uber changed transportation ...., healthcare will be infiltrated by startups wanting to change the healthcare model from hospital-centric to patient-centric. Medical device companies and other healthcare providers that don’t realize that a major shift is taking place will become the equivalent of today’s taxi industry......

– We are also seeing a transformation of the man-machine relationship—we are starting to wear computers, and soon, we will be implanting them into our bodies to connect with our communication systems, cars, and homes. As artificial intelligence improves, it will help us interact with increasingly smart environments. In healthcare, highly evolved sensors and powerful algorithms will give us proactive, personalized care. By 2035, the majority of our treatments will occur at home. Our home will be watching us and helping us track our health .....

– We are already seeing more empowered patients. People want information. They want to make their own diagnosis. They want to research their doctors. They want their own health data.....

– It all starts now. Healthcare must shift its focus toward the patient. Successful medical products will put the patient’s needs first and foremost. ....

Impact on Simulation Market?
“Saving lives, one simulation at a time”™

At InFluidS, we bring clarity and insight to pulmonary physician’s most complex diagnostic challenges.
Through the development of non-invasive diagnostic tool, InFluidS is dedicated to assist physicians with a superior diagnostic tool for a wide variety of pulmonary diseases such as Pulmonary Embolism which affects more than One Million people in the United States, with 20% of these cases being fatal.

A CFD-based diagnostic system provides physicians with the possibility of obtaining both functional and anatomical data, having only utilized one diagnostic resource.

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Accelerating Industry Acceptance

Examples:

- MS Ramaiah: Clinical Trial for MedTech
- Exponent: Troubleshooting for FDA Approvals
Thank you

Solution Time 0.7108 (s)