Attachment 2:

Example Extract from Application of Model VVUQ S*Pattern and Medical Device S*Pattern

Includes contributions by Marc Horner, from ANSYS and ASME VV40.

Bill Schindel,
ICTT System Sciences
schindel@ictt.com
Oct. 22-23, 2018
V1.3.1
Overview of Initial (exists) and Enhanced (in progress) Model VVUQ Pattern, Medical Device Pattern, related work

1. Initial (2017) version of the Model VVUQ Pattern: Basic configurability of the Pattern to reflect required and resulting VVUQ of the model of interest—model “wrapper” metadata.

2. Integration with generic domain patterns (e.g., General Medical Device Pattern) to pre-capture or suggest potential sources and propagators of uncertainty in specific domains. (Underway, 2018, shown here.)

3. Integration with ASME VV40 standard to include built-in Credibility Factors, other VV40 guidance. (Underway, 2018, shown here.)
General Pattern of Model Uncertainty and Uncertainty Propagation

S*Metamodel

Computational Model of Interest (e.g., insulin infusion system)

Theory and Standards for Model VVUQ

Generic Model VVUQ Pattern

Domain Specific Pattern (e.g., medical device pattern)

Configured Model VVUQ Pattern For Model of Interest

Domain Specific Pattern with VVUQ structures built into it

Model Use Situation

Leveraged generic resources from System 3

What VVUQ process user needs to do: System 2 “Execution” part

Leveraged resources from System 2 “Learning” part.

S*Pattern Configuration Process

S*Pattern Configuration Process

Model VVUQ Analysis

Leveraged resources from System 3
Medical device example being used as basis for illustration

• To provide a concrete example of use, Marc Horner (ANSYS, and AMSE VV40 vice chair) has been collaborating with us by providing an example that he used in public presentations at the 2018 INCOSE Heath Care Conference and the 2018 INCOSE Great Lakes Conference.

• That example involves an insulin infusion pump, with emphasis on computational models of (a) human insulin absorption and metabolism uptake and (b) the pump’s feeder tube flow characteristics.
V&V 40 Analysis of Two Insulin Pump Failure Modes

Marc Horner
Failure Mode 1

• The patient does not receive the expected insulin therapy because there is an occlusion (kink) in the infusion set, potentially resulting in hyperglycemia.
**QOI/COU**

**Question of Interest:** Will the infusion pump properly warn the patient when an occlusion in the flow path is obstructing insulin delivery?

**Context of Use:** A reduced-order model for the relationship between bend angle ($\angle$), flow rate (Q), and pressure rise ($\Delta P$) will be used to predict occlusion by the system control software.
Risk Analysis

• *Model Influence* is MEDIUM since there are other sources of information available for predicting occlusion, e.g. CGM readings predicting occlusion and/or monitoring the flow rate of the insulin delivery over time.

• *Decision Consequence* is MEDIUM since patients can quickly drift away from the target blood glucose concentration, but can administer a correction bolus return to a normal glycemic state if/when the occlusion is detected via other means.
## Credibility Factors

<table>
<thead>
<tr>
<th>Activities (Paragraph)</th>
<th>Credibility Factors (Paragraph)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verification (5.1)</td>
<td></td>
</tr>
<tr>
<td>Code (5.1.1)</td>
<td>Software quality assurance (5.1.1.1)</td>
</tr>
<tr>
<td></td>
<td>Numerical code verification (5.1.1.2)</td>
</tr>
<tr>
<td>Calculation (5.1.2)</td>
<td>Discretization error (5.1.2.1)</td>
</tr>
<tr>
<td></td>
<td>Numerical solver error (5.1.2.2)</td>
</tr>
<tr>
<td></td>
<td>Use error (5.1.2.3)</td>
</tr>
<tr>
<td>Validation (5.2)</td>
<td></td>
</tr>
<tr>
<td>Computational model (5.2.1)</td>
<td>Model form (5.2.1.1)</td>
</tr>
<tr>
<td></td>
<td>Model inputs (5.2.1.2)</td>
</tr>
<tr>
<td>Comparator (5.2.2)</td>
<td>Test samples (5.2.2.1)</td>
</tr>
<tr>
<td></td>
<td>Test conditions (5.2.2.2)</td>
</tr>
<tr>
<td>Assessment (5.2.3)</td>
<td>Equivalency of input parameters (5.2.3.1)</td>
</tr>
<tr>
<td></td>
<td>Output comparison (5.2.3.2)</td>
</tr>
<tr>
<td>Applicability (5.3)</td>
<td>Relevance of the quantities of interest (5.3.1)</td>
</tr>
<tr>
<td></td>
<td>Relevance of the validation activities to the COU (5.3.2)</td>
</tr>
</tbody>
</table>
A heavily used commercial software platform is used for these analyses (Mechanical, Fluent, and DesignXplorerer from ANSYS). The code developer is ISO9001:2015 certified and code verification has been performed internally by the code developer. Mesh refinement studies are performed to ensure a converged solution. Owing to the fact that the physics are relatively straightforward, sensitivity to numerical parameters is only cursorily investigated.

### Code Verification

<table>
<thead>
<tr>
<th>Code Verification</th>
<th>Credibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>SQA</td>
<td>HIGH</td>
</tr>
<tr>
<td>NCV</td>
<td>MEDIUM</td>
</tr>
</tbody>
</table>

### Calculation Verification

<table>
<thead>
<tr>
<th>Calculation Verification</th>
<th>Credibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discretization Error</td>
<td>MEDIUM</td>
</tr>
<tr>
<td>Numerical Solver Error</td>
<td>MEDIUM</td>
</tr>
<tr>
<td>Use Error</td>
<td>MEDIUM</td>
</tr>
</tbody>
</table>
Computational Model Credibility

• The computational model will recreate a series of idealized catheter occlusion scenarios. The resistance to flow will be modeled using a one-way FSI approach, first bending the tube and then modeling the insulin flow over a range of expected flow rates.
  
  • *Mechanical Model:* The geometry of the occlusion will be modeled as a tube under varying degrees of bending. The catheter and cannula materials are readily characterized. Cannula insertion and other skin interactions will not be modeled.
  
  • *Flow Model:* The flow is laminar and the density/viscosity of insulin is readily characterized. The inlet flow rate is well characterized. Peripheral flow resistance due to the presence of skin tissue at the bolus site will not be modeled.

<table>
<thead>
<tr>
<th>Computational Model</th>
<th>Credibility - Model Form</th>
<th>Credibility - Model Inputs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Governing Equations</td>
<td>HIGH</td>
<td>HIGH</td>
</tr>
<tr>
<td>System Configuration</td>
<td>MEDIUM</td>
<td>MEDIUM</td>
</tr>
<tr>
<td>Material Properties</td>
<td>HIGH</td>
<td>HIGH</td>
</tr>
<tr>
<td>Boundary Conditions</td>
<td>MEDIUM</td>
<td>MEDIUM</td>
</tr>
</tbody>
</table>
Comparator Credibility

- An experimental set-up that varies the bend angle of the catheter in a highly controlled manner will be compared to the computational model results. An optical system will be used to measure the bend angle of the catheter. A pressure sensor upstream of the occlusion will measure the total pressure. System response will be investigated for a range of flow rates and catheter bend angles.

<table>
<thead>
<tr>
<th>Comparator</th>
<th>Credibility - Test Samples</th>
<th>Credibility - Test Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantity</td>
<td>MEDIUM</td>
<td>HIGH</td>
</tr>
<tr>
<td>Range</td>
<td>MEDIUM</td>
<td>HIGH</td>
</tr>
<tr>
<td>Measurements</td>
<td>LOW</td>
<td>HIGH</td>
</tr>
<tr>
<td>Uncertainty</td>
<td>LOW</td>
<td>MEDIUM</td>
</tr>
</tbody>
</table>
Failure Mode 2

• The insulin pump embedded software does not predict the correct amount of drug needed to maintain desired glycemic levels after a meal.
QOI/COU

Question of Interest: Can the insulin pump control software maintain each patient’s target blood glucose concentration?

Context of Use: A 5-equation PK/PD model of insulin absorption and glucose metabolism will be developed and tuned using patient historical data.
Risk Analysis

• *Model Influence* is MEDIUM since there are other sources of information available for determining the insulin needs, e.g. blood glucose calculators/apps.

• *Decision Consequence* is MEDIUM since patients can quickly drift away from the target blood glucose concentration, but can administer a correction bolus return to a normal glycemic state if/when the occlusion is detected via other means.
# Credibility Factors

<table>
<thead>
<tr>
<th>Activities (Paragraph)</th>
<th>Credibility Factors (Paragraph)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verification (5.1)</td>
<td></td>
</tr>
<tr>
<td>Code (5.1.1)</td>
<td>Software quality assurance (5.1.1.1)</td>
</tr>
<tr>
<td></td>
<td>Numerical code verification (5.1.1.2)</td>
</tr>
<tr>
<td>Calculation (5.1.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Discretization error (5.1.2.1)</td>
</tr>
<tr>
<td></td>
<td>Numerical solver error (5.1.2.2)</td>
</tr>
<tr>
<td></td>
<td>Use error (5.1.2.3)</td>
</tr>
<tr>
<td>Validation (5.2)</td>
<td></td>
</tr>
<tr>
<td>Computational model (5.2.1)</td>
<td>Model form (5.2.1.1)</td>
</tr>
<tr>
<td></td>
<td>Model inputs (5.2.1.2)</td>
</tr>
<tr>
<td>Comparator (5.2.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test samples (5.2.2.1)</td>
</tr>
<tr>
<td></td>
<td>Test conditions (5.2.2.2)</td>
</tr>
<tr>
<td>Assessment (5.2.3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Equivalency of input parameters (5.2.3.1)</td>
</tr>
<tr>
<td></td>
<td>Output comparison (5.2.3.2)</td>
</tr>
<tr>
<td>Applicability (5.3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Relevance of the quantities of interest (5.3.1)</td>
</tr>
<tr>
<td></td>
<td>Relevance of the validation activities to the COU (5.3.2)</td>
</tr>
</tbody>
</table>
A popular object-oriented modeling language (Modelica) is used for these analyses. Code verification has been performed by the user for this application. Mesh refinement studies are performed to ensure a converged solution. Owing to the fact that the physics are relatively straight-forward, sensitivity to numerical parameters is only cursorily investigated.

<table>
<thead>
<tr>
<th>Code Verification</th>
<th>Credibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>SQA</td>
<td>HIGH</td>
</tr>
<tr>
<td>NCV</td>
<td>HIGH</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Calculation Verification</th>
<th>Credibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discretization Error</td>
<td>MEDIUM</td>
</tr>
<tr>
<td>Numerical Solver Error</td>
<td>MEDIUM</td>
</tr>
<tr>
<td>Use Error</td>
<td>MEDIUM</td>
</tr>
</tbody>
</table>
The 5-equation PK/PD model representing the absorption into the plasma will be modeled. The appearance of glucose and elimination by insulin will also be included. The PK/PD model will be calibrated using the clinical data from all patients over a 48 hour period and then used to predict the glucose concentration in those same patients for an additional 72 hours.

<table>
<thead>
<tr>
<th>Computational Model</th>
<th>Credibility - Model Form</th>
<th>Credibility - Model Inputs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Governing Equations</td>
<td>HIGH</td>
<td>HIGH</td>
</tr>
<tr>
<td>System Configuration</td>
<td>MEDIUM</td>
<td>MEDIUM</td>
</tr>
<tr>
<td>Material Properties</td>
<td>HIGH</td>
<td>HIGH</td>
</tr>
<tr>
<td>Boundary Conditions</td>
<td>HIGH</td>
<td>MEDIUM</td>
</tr>
</tbody>
</table>
Comparator Credibility

• A clinical trial will be used to collect the data required to develop the PK/PD model for multiple patients. The patients will be checked into a hospital and their carbohydrate intake, insulin delivery, and blood glucose concentration will be measured throughout the day. At each time point, only a single sample will be collected from each patient. Multiple meal types and snacks will be given to the patient to test model robustness.

<table>
<thead>
<tr>
<th>Comparator</th>
<th>Credibility - Test Samples</th>
<th>Credibility - Test Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantity</td>
<td>MEDIUM</td>
<td>HIGH</td>
</tr>
<tr>
<td>Range</td>
<td>MEDIUM</td>
<td>HIGH</td>
</tr>
<tr>
<td>Measurements</td>
<td>MEDIUM</td>
<td>MEDIUM</td>
</tr>
<tr>
<td>Uncertainty</td>
<td>LOW</td>
<td>LOW</td>
</tr>
</tbody>
</table>
1. Basic configurability of the initial Model VVUQ Pattern

• To reflect required and resulting VVUQ of the model of interest,
  • As well as many other characteristics of the model of interest

(Using the existing 2017 version of the Model VVUQ Pattern.)
<table>
<thead>
<tr>
<th>Feature Group</th>
<th>Feature Name</th>
<th>Feature Definition</th>
<th>Feature Attribute</th>
<th>Attribute Definition</th>
<th>Multiple Configuration ID(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model Identity and Focus</td>
<td>Modeled System of interest</td>
<td>Identifies the type of system this model describes</td>
<td>Model of interest</td>
<td>Name of system of interest or class of system of interest</td>
<td>Insulin Pump, Infusion Set</td>
</tr>
<tr>
<td></td>
<td>Modeled Environmental Factors</td>
<td>Identifies the type of external environment(s) that the model includes</td>
<td>Domain(s)</td>
<td>Name(s) of domain(s) (manufacturing, distribution, use, etc.)</td>
<td>Patient Environment &amp; Use</td>
</tr>
<tr>
<td></td>
<td>Stakeholder Values</td>
<td>The capability of the model to describe the values or beliefs of the system's interest, by identifying its stakeholders and modeling their role</td>
<td>Stakeholder Values</td>
<td>Classes of current stakeholders (may be multiple)</td>
<td>Patient, Health Care Provider</td>
</tr>
<tr>
<td></td>
<td>Explanatory Decomposition</td>
<td>The capability of the model to represent the decompositions of the external technical behavior as explicit nested (&quot;white-box&quot;) interactions of decomposed roles, further quantified by internal technical performance measures, and varying internal behavioral modes</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Physical Architecture</td>
<td>The capability of the model to represent the physical architecture of the system of interest. This includes identification of major physical components and their architectural relationships</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model Scope of Content</td>
<td>Parametric Graphs—Phases</td>
<td>The capability of the model to represent quantitative (parametric) coupling between stakeholder-value measures of effectiveness and objective external technical performance measures</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Parametric Graphs—Decomposition</td>
<td>The capability of the model to represent quantitative (parametric) coupling between objective external technical performance variables and objective internal behavior boundaries</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Parametric Graphs—Characteristics</td>
<td>The capability of the model to represent numerical (parametric) coupling between objective behavior variables and physical identity (material of construction, part or model number)</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Managed Model Parameters</td>
<td>The capability of the model to include managed datasets for use as inputs, parametric characteristics, or output</td>
<td>Dataset Type</td>
<td>The type(s) of data sets (may be multiple)</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Trusted Customizable Patterns</td>
<td>The capability of the model to serve as a configurable pattern, representing different modeled system configurations across a common domain, enabling the use of establishing trusted model frameworks to serve a community of applications and configurations</td>
<td>Configuration ID</td>
<td>A specific system of interest configuration within the family that the pattern framework can represent</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feature Group</td>
<td>Feature Name</td>
<td>Feature Definition</td>
<td>Feature Attribute</td>
<td>Attribute Definition</td>
<td></td>
</tr>
<tr>
<td>---------------</td>
<td>--------------</td>
<td>--------------------</td>
<td>-------------------</td>
<td>---------------------</td>
<td></td>
</tr>
<tr>
<td>Failure Modes and Effects</td>
<td>The capability of the model to include identification and analysis of system failure modes, their impact, effects, causes, and likelihoods of occurrence.</td>
<td>Model Applications Envelope</td>
<td>The range over which the model is intended for use.</td>
<td>Range of bend angles, flow rates, viscosities</td>
<td></td>
</tr>
<tr>
<td>Describes the credibility of the model</td>
<td>Model Envelope</td>
<td>The capability of the model to meet Model Credibility requirements over a stated range (envelope) of dynamical inputs, outputs, and parameterization.</td>
<td>Quantitative Accuracy Reference</td>
<td>The specification reference describing the quantifiable accuracy of the conceptual model compared to the system of interest.</td>
<td>Tube Crimping Model Study A9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Function Structure Accuracy Reference</td>
<td>The specification reference describing the structural (presence or absence of behaviors) accuracy of the conceptual model compared to the system of interest.</td>
<td>Tube Crimping Model Study A9</td>
</tr>
<tr>
<td></td>
<td>Validated Conceptual Model Credibility</td>
<td>The validated capability of the conceptual portion of the model to represent the System of Interest with acceptable Credibility.</td>
<td>Uncertainty Quantification (UQ) Reference</td>
<td>The specification reference describing the degree of uncertainty of the credibility of the conceptual model to the system of interest.</td>
<td>Tube Crimping Model Study A9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Model Validation Reference</td>
<td>The reference documenting the validation of the conceptual model's credibility to the system of interest.</td>
<td>Tube Crimping Model Study A9</td>
</tr>
<tr>
<td>Model Credibility</td>
<td></td>
<td></td>
<td>Quantitative Accuracy Reference</td>
<td>The specification reference describing the quantifiable accuracy of the executable model to the conceptual model.</td>
<td>Tube Crimping Simulation Study B4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Structural Accuracy Reference</td>
<td>The specification reference describing the structural (presence or absence of elements) accuracy of the executable model to the conceptual model.</td>
<td>Tube Crimping Simulation Study B4</td>
</tr>
<tr>
<td></td>
<td>Verified Executable Model Credibility</td>
<td>The verified capability of the executable portion of the model to represent the System of Interest with acceptable Credibility.</td>
<td>Uncertainty Quantification (UQ) Reference</td>
<td>The specification reference describing the degree of uncertainty of the credibility of the executable model to the conceptual model.</td>
<td>Tube Crimping Simulation Study B4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Speed</td>
<td>The specification reference describing the execution run time (speed) for the executable model.</td>
<td>Tube Crimping Simulation Study B4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Quantification</td>
<td>The specification reference describing the quantification error of the executable model.</td>
<td>Tube Crimping Simulation Study B4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Stability</td>
<td>The specification reference describing the level of stability of the accuracy and uncertainty of the executable model's error characteristics.</td>
<td>Tube Crimping Simulation Study B4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Model Validation Reference</td>
<td>The reference documenting the verification of the executable model's credibility to the conceptual model.</td>
<td>Tube Crimping Simulation Study B4</td>
</tr>
</tbody>
</table>

Identifies the type of representation used by the model.
<table>
<thead>
<tr>
<th>Feature Group</th>
<th>Feature Name</th>
<th>Feature Definition</th>
<th>Feature Attribute</th>
<th>Attribute Definition</th>
<th>Multiple Configuration IDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conceptual Model Representation</td>
<td>Conceptual Model Type</td>
<td>The type of conceptual modeling language or metamodel used.</td>
<td>Neural Net, 4 Layers</td>
<td>Goal 1</td>
<td></td>
</tr>
<tr>
<td>Model Representation</td>
<td>Conceptual Model Interoperability</td>
<td>The degree of interoperability of the conceptual model, for exchange with other environments.</td>
<td>High</td>
<td>Goal 2</td>
<td></td>
</tr>
<tr>
<td>Executable Model Representation</td>
<td>Executable Model Type</td>
<td>The type of executable modeling language or metamodel used.</td>
<td>Matlab NN</td>
<td>Goal 3</td>
<td></td>
</tr>
<tr>
<td>Executable Model Representation</td>
<td>Executable Model Interoperability</td>
<td>The degree of interoperability of the executable model, for exchange with other environments.</td>
<td>Low</td>
<td>Goal 4</td>
<td></td>
</tr>
<tr>
<td>Describes the intended use, utility, and value of the model</td>
<td>Model Intended Use</td>
<td>The intended purpose(s) or use(s) of the model.</td>
<td>Life Cycle Process Supported</td>
<td>Goal 5</td>
<td></td>
</tr>
<tr>
<td>Model Utility</td>
<td>Device Designer, ME Discipline</td>
<td>Device Designer, ME Discipline</td>
<td>Goal 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desired Model Value and Use</td>
<td>User Group Segment</td>
<td>The identity of user group segment (multiple)</td>
<td>Define Design; Verify Design by Simulation</td>
<td>Goal 7</td>
<td></td>
</tr>
<tr>
<td>Model Value and Use</td>
<td>Level of Annual Use</td>
<td>The relative (level of annual use by the segment)</td>
<td>Goal 8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model Value and Use</td>
<td>Value Level</td>
<td>The value (relative) associated with the model by that segment.</td>
<td>Goal 9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model Value and Use</td>
<td>Accepting Authority</td>
<td>The identity (may be multiple) of regulatory agencies, customers, suppliers, etc., that accepts the model.</td>
<td>Moderate</td>
<td>Goal 10</td>
<td></td>
</tr>
<tr>
<td>Model Value and Use</td>
<td>Model State of Use</td>
<td>The perceived ease with which the model can be used, experienced by its intended users.</td>
<td>FDA</td>
<td>Goal 11</td>
<td></td>
</tr>
<tr>
<td>Describes related model lifecycle management capabilities</td>
<td>Model Versioning and Configuration Management</td>
<td>The capability of the model to provide version and configuration management.</td>
<td>CM Capability Type</td>
<td>Goal 12</td>
<td></td>
</tr>
<tr>
<td>Executable Model Environment Compatibility</td>
<td>Executable Model Compatibility</td>
<td>The capability of the model to be computationally supported by specified information technology environment(s); indicating compatibility, portability, and interoperability.</td>
<td>Acme Enterprise IT SOE</td>
<td>Goal 13</td>
<td></td>
</tr>
<tr>
<td>Model Design Life and Retirement</td>
<td>Design Life</td>
<td>The planned retirement date.</td>
<td>31-Dec-28</td>
<td>Goal 14</td>
<td></td>
</tr>
<tr>
<td>Model Sustainability</td>
<td>Maintenance Method</td>
<td>The type of maintenance methodology used to maintain the model's capability and availability for its intended purposes over the intended life cycle.</td>
<td>Review at times of model feedback or design change</td>
<td>Goal 15</td>
<td></td>
</tr>
<tr>
<td>Model Usability</td>
<td>Deployment Method</td>
<td>The type of method used to deploy (possibly in repeating cycles) the model into its intended use environment.</td>
<td>Acme Enterprise PLM</td>
<td>Goal 16</td>
<td></td>
</tr>
<tr>
<td>Feature Group</td>
<td>Feature Name</td>
<td>Feature Definition</td>
<td>Feature Attribute</td>
<td>Attribute Definition</td>
<td>Cost 1</td>
</tr>
<tr>
<td>-----------------------</td>
<td>------------------</td>
<td>------------------------------------------------------------------------------------</td>
<td>------------------------------------</td>
<td>-------------------------------------------------------------------------------------</td>
<td>--------</td>
</tr>
<tr>
<td>Model Life Cycle</td>
<td>Model Cost</td>
<td>The financial cost of the model, including development, operating, and maintenance cost</td>
<td>Development Cost</td>
<td>The cost to develop the model, including testing and documentation, to be first available for service</td>
<td>USD 25,000</td>
</tr>
<tr>
<td>Management</td>
<td></td>
<td></td>
<td>Operational Cost</td>
<td>The cost to execute and otherwise operate the model, in the standardized execution lab tests</td>
<td>USD 1,000/year</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Maintenance Cost</td>
<td>The cost to maintain the model</td>
<td>USD 800/year</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Deployment Cost</td>
<td>The cost to deploy, and redeploy applications, example</td>
<td>USD 500/cycle</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Retirement Cost</td>
<td>The cost to retire the model from service, in a planned fashion</td>
<td>USD 1500</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Life Cycle</td>
<td>Shows how the overall life cycle cost of the model</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Total Availability Date</td>
<td>Shows when version will first be available</td>
<td>01.30.2020</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Total Availability Rate</td>
<td>Shows the scheduled state of first availability</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Total Availability Risk</td>
<td>Shows ongoing availability after production</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>VDDQ Pattern</td>
<td>The ability to accumulate new discoveries about model-based methods for the VDDQ Pattern, and how it is applied over the model life cycle.</td>
<td>VDDQ Pattern Description</td>
<td>A listing of the exceptions noted to the current VDDQ Pattern (may be multiple exceptions)</td>
<td>None yet</td>
</tr>
<tr>
<td>Learning</td>
<td></td>
<td></td>
<td>VDDQ Pattern</td>
<td>The impacted existing, modified, or additional feature of the VDDQ Pattern</td>
<td>None yet</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>VDDQ Pattern Version</td>
<td>The version of the VDDQ Pattern in current use before changes</td>
<td>None yet</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Project</td>
<td>Identifies the project in which the exception was noted</td>
<td>None yet</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Person</td>
<td>Identifies the person describing the exception</td>
<td>None yet</td>
</tr>
</tbody>
</table>
2. Integration with generic domain patterns (e.g., General Medical Device Pattern)

• To pre-capture potential sources and propagators of uncertainty,
  • and build them into the work process.
  • and create some common expectations across community of designers, analysts, regulators

(This is interim material, work on (2) is still in progress.)
More detailed VVUQ Pattern aspects, general systems case first

• Who needs to understand the following?
• A user of the Model VVUQ Pattern need not have studied, understood all of, or even see the following, since that pattern should be placed in the related tooling to simplify application, with most of this “behind the scenes”
• However, a specialist interested in understanding what is being/inside the Model VVUQ Pattern could study these details to analyze, for example, the comprehensiveness of its coverage of model VVUQ issues with respect to principles of V&V 40, V&V 10, etc.
• The General System (generic) case is shown first.
• Then the (general) Controlled Medical Device Pattern case is shown, as a specialization.
• A Configured Model will be created for the illustrative example.
More detailed VVUQ Pattern aspects, general systems case first

General setting, using S*Metamodel elements to describe a System of Interest interacting with its environment.

System models, their use and credibility, and VVUQ of same can be described in this framework.
More detailed VVUQ Pattern aspects, general systems case first

Key portions of S*Metamodel, used in Model VVUQ Pattern
Further specialized to medical device domain
Example Model: Medical device + medication + patient:
From Marc Horner’s INCOSE presentation, April, 2018

Closing the Loop on Medical Device Systems Simulation
Marc Horner, Ph.D.
Technical Lead, Healthcare
ANSYS, Inc.

Drug Delivery Sub-System

Virtual Patient Model

Two-compartment insulin model
\[
\frac{dI_1(t)}{dt} = \frac{-1}{\tau_1} \cdot I_1(t) + \frac{1}{\tau_1} \cdot D(t) + \frac{1}{\tau_1} \cdot I_2(t)
\]

Two-compartment glucose model
\[
\frac{dG(t)}{dt} = -\left(\frac{G(t)}{V_g + \tau_g}\right) - \left(\frac{G(t)}{V_g + \tau_g}\right) + R(t)
\]

Insulin effectiveness
\[
\frac{dI_{eff}(t)}{dt} = -p_1 \cdot I_{eff}(t) + p_2 \cdot S(t) \cdot I_{eff}(t)
\]

*Endeleva 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)*
Mapping to Generic Device Draft Pattern

Drug Delivery Sub-System

Virtual Patient Model

Two-compartment insulin model

\[
\frac{dI_1(t)}{dt} = -\frac{1}{\tau_1} I_1(t) + \frac{1}{\tau_1} I_2(t) \quad (1)
\]

\[
\frac{dI_2(t)}{dt} = -\frac{1}{\tau_2} I_2(t) + \frac{1}{\tau_2} I_3(t) \quad (2)
\]

Insulin effectiveness

\[
\frac{dI_2(t)}{dt} = -p_1 \cdot I_2(t) + p_2 \cdot S_2(t) - I_1(t) \quad (3)
\]

Two-compartment glucose model

\[
\frac{dG(t)}{dt} = \frac{G(t)}{\tau_G} + \frac{E(t) + R(t)}{\tau_G} \quad (4)
\]

\[
R(t) = \frac{C_2(t)}{V_G \cdot \tau_G} + \frac{C_3(t)}{\tau_G} \quad (5)
\]

*Kesic et al., Identification of Intravenous Metabolites Profiles during Closed-Loop Glucose Control in Individuals with Type 1 Diabetes, J Diabetes Sci and Tech, Vol. 9 (2015).*
Mapping to Generic Device Draft Pattern

Model-Based Life Cycle Management Feature
Device Performance Feature
Device Safety Feature
External Health Care Management System
Embedded Control System
Device Life Cycle Management System
Medical Device

Domain Reference Architecture: Managed Medical Device
Mapping to Generic Device Draft Pattern

Virtual Patient Model

Two-compartment insulin model

\[
\frac{dI_1(t)}{dt} = \frac{1}{\tau_1} I_2(t) + \frac{1}{\tau_1} I_1(t) - \frac{1}{\tau_1} I_1(t)
\]

(1)

\[
\frac{dI_2(t)}{dt} = \frac{1}{\tau_2} I_1(t) + \frac{1}{\tau_2} I_2(t) - \frac{1}{\tau_2} I_2(t)
\]

(2)

Insulin effectiveness

\[
\frac{dI_2(t)}{dt} = -p_1 \cdot I_2(t) + p_2 \cdot S \cdot I_2(t)
\]

(3)

Two-compartment glucose model

\[
\frac{dG(t)}{dt} = -(E_{G2} + E_{G2}) \cdot G(t) + E_{G1} + R_{G1}(t)
\]

(4)

\[
R_{G1}(t) = \frac{C_{G1}(t)}{E_{G1} + E_{G1}}
\]

(5)
• We also often model a higher level system that emerges from the interaction of other systems, with global properties resulting from their combination.

• In this case, a good place to represent the emergent:
  • hydraulics of the combined patient anatomy, device hydraulics, and liquid
  • overall therapeutic / metabolic performance.

• Particularly if we want to represent performance model uncertainty at higher combined level.
3. Incorporating ASME VV40 into the Model VVUQ Pattern

- The initial version of the Model VVUQ Pattern was generated in 2017 as a specialization of the INCOSE Model Planning and Assessment Pattern.
- The initial version of that pattern provides ability to record required and resulting information concerning VVUQ of the model of interest.
- Upon reading the draft prose of the ASME VV40 standard, we realized that certain important structures in that standard (e.g., Model Credibility Factors) could be incorporated directly into the VVUQ Pattern, as an improvement
  - thereby building them into the work process
  - and advancing some common expectations across community of designers, analysts, regulators

(This is interim material, work on (3) is still in progress.)
More detailed VVUQ Pattern aspects, general systems case first
More detailed VVUQ Pattern aspects, general systems case first

Application Domain

Subject System

Logical Subsystem

External Actor

Functional Interaction #2

Subject System... Attribute
Envelope

Role-Role Attribute
Coupling, Actor

Confidence Interval
Envelope

System of Access

Functional Role

Input-Output X

Input-Output Y

System Identity

Characterization

Coupling

Confidence Interval
Envelope

Stakeholder

Feature

Feature Role

Functional Interaction #1

State X

Event B

Functional Interaction #3

Functional Interaction #4

Event A

Software Quality Assurance

Verification

Code

Verification Solution

Discretization Error

Use Error

Numerical Solver Error

System Configuration

System Properties

Boundary Conditions

Governing Equations

Sample Characterization

Control Over Test Conditions

Measurement Uncertainty

Equivalency of input and output types

Rigor of Output Comparison

Relevance of the Quantities of Interest

Applicability

Output Applicability

Application Domain Parent System

System Identity

Characterization

Coupling

Confidence Interval
Envelope

Actor Identity

Characterization

Coupling

Confidence Interval
Envelope

Design Component Action

Identity Attribute

Show more
More detailed VVUQ Pattern aspects, general systems case first
More detailed VVUQ Pattern aspects, general systems case first
Back up reference material
The Computational Model Requirements Pattern (from VV50 team)

- The more detailed parts of the Model VVUQ Pattern embeds configurable model-based data structures supporting the capture and representation of guidance as from the VV40 Risk Informed Credibility Framework, including its (configurable) Credibility Factors:
Physics-Based Model

- Predicts the external behavior of the System of Interest, visible externally to the external actors with which it interacts.
- Models internal physical interactions of the System of Interest, and how they combine to cause/explain externally visible behavior.
- Model has both external predictive value and phenomena-based internal-to-external explanatory value.
- Overall model may have high dimensionality.

Data Driven Model

- Predicts the external behavior of the System of Interest, visible to the external actors with which it interacts.
- Model intermediate quantities may not correspond to internal or external physical parameters, but combine to adequately predict external behavior, fitting it to compressed relationships.
- Model has external predictive value, but not internal explanatory value.
- Overall model may have reduced dimensionality.

- Physical scientists and phenomena models from their disciplines can apply here.
- The hard sciences physical laws, and how they can be used to explain the externally visible behavior of the system of interest.

- Data scientists and their math/IT tools can apply here (data mining, pattern extraction, cognitive AI tooling).
- Tools and methods for discovery / extraction of recurring patterns of external behavior.

From: Huang, Zhang, Ding, "An analytical model of residual stress for flank milling of Ti-6Al-4V", 15th CIRP Conference on Modelling of Machining Operations
Physics-Based Model

- Predicts the external behavior of the System of Interest, visible externally to the external actors with which it interacts.
- Models internal physical interactions of the System of Interest, and how they combine to cause/explain externally visible behavior.
- Model has both external predictive value and phenomena-based internal-to-external explanatory value.
- Overall model may have high dimensionality.

Data Driven Model

- Predicts the external behavior of the System of Interest, visible to the external actors with which it interacts.
- Model intermediate quantities may not correspond to internal or external physical parameters, but combine to adequately predict external behavior, fitting it to compressed relationships.
- Model has external predictive value, but not internal explanatory value.
- Overall model may have reduced dimensionality.


- Physical scientists and phenomena models from their disciplines can apply here.
- The hard sciences physical laws, and how they can be used to explain the externally visible behavior of the system of interest.

Data scientists and their math/IT tools can apply here (data mining, pattern extraction, cognitive AI tooling).
- Tools and methods for discovery / extraction of recurring patterns of external behavior.

External "Actors"

System

Optional

predicts, explains

predicts

Residual Stress for Milling Process
Hybrid Model: Both Data Driven and Physics-Based

- Predicts the external behavior of the System of Interest, visible externally to the external actors with which it interacts.
- Models (some aspects of) internal physical interactions of the System of Interest, and how they combine to cause/explain (some aspects of) externally visible behavior.
- Model has both external predictive value and (some) phenomena-based internal-to-external explanatory value.
- (Some) model intermediate quantities may not correspond to internal or external physical parameters, but combine to adequately predict external behavior, fitting it to compressed relationships.
- Model has external predictive value, but (for some aspects) not internal explanatory value.

- Physical scientists and phenomena models from their disciplines can apply here.
- The hard sciences physical laws, and how they can be used to explain the externally visible behavior of the system of interest.
- Data scientists and their math/IT tools can apply here (data mining, pattern extraction, cognitive AI tooling).
- Tools and methods for discovery / extraction of recurring patterns of external behavior.
Hybrid Model: Both Data Driven and Physics-Based

- Predicts the external behavior of the System of Interest, visible externally to the external actors with which it interacts.

- Models (some aspects of) internal physical interactions of the System of Interest, and how they combine to cause/explain (some aspects of) externally visible behavior.

- Model has both external predictive value and (some) phenomena-based internal-to-external explanatory value.

- (Some) model intermediate quantities may not correspond to internal or external physical parameters, but combine to adequately predict external behavior, fitting it to compressed relationships.

- Model has external predictive value, but (for some aspects) not internal explanatory value.

- Physical scientists and phenomena models from their disciplines can apply here.

- The hard sciences physical laws, and how they can be used to explain the externally visible behavior of the system of interest.

- Data scientists and their math/IT tools can apply here (data mining, pattern extraction, cognitive AI tooling).

- Tools and methods for discovery / extraction of recurring patterns of external behavior.
Model VVUQ Pattern: Model Stakeholder Features Overview

Legend:

Model Representation

Model Scope and Content

Model Identity and Focus

Model Utility

Model Credibility

Model Life Cycle Management

- Modeled System of Interest
- Modeled Environmental Domain
- System of Interest
- Domain Type

- Model Intended Use
- Perceived Model Value and Use
- Third Party Acceptance
- Model Ease of Use
- User Group Segments (ISO15288)
- Level of Annual Use
- Value Level

- Model Representation
- Model Scope and Content
- Model Credibility
- Model Identity and Focus
- Model Life Cycle Management

- Modeled Stakeholder Value
- Modeled System External (Black Box) Behavior
- Explanatory Decomposition
- Failure Modes and Effects

- Parametric Couplings--Fitness
- Parametric Couplings--Decomposition
- Physical Architecture
- Managed Model Datasets

- Trusted Configurable Pattern
- Configuration ID
- Dataset Type

- Model Versioning and Configuration Management
- Model Maintainability
- Model Deployability
- Model Cost
- Model Availability
- VVUQ Pattern Learning

- First Availability Date
- First Availability Risk
- Lifecycle Availability Risk
- Development Cost
- Operational Cost
- Maintenance Cost
- Deployment Cost
- Retirement Cost
- Lifecycle Financial Risk

- Executable Model Environmental Compatibility
- Design Life Cycle and Retirement
- VVUQ Pattern Exception

- Conceptual Model Implementation Type
- Conceptual Model Interoperability
- Conceptual Model Representation
- Executable Model Implementation Type
- Executable Model Interoperability
- Executable Model Representation

- Project
- Person
- Failure Modes and Effects
- Impacted VVUQ Feature
- VVUQ Pattern Version

- Conceptual Model Accuracy Reference
- Function Structure Accuracy Reference
- Quantitative Accuracy Reference
- Function Structure Annotation (OQ) Reference
- Quantitative Validation (OQ) Reference
- Model Validation Reference
- Speed
- Quantization
- Weakly
- Model Validation Reference

- Stakeholder Feature Model for Computational Models

- Version: 1.5.4
- Date: 31 Aug 2017
- Drawn By: B Schindel
2.6.1 Failure Mode: The model shall include identification of component failure modes, as to underlying state leading to predicted failure.
The Computational Model Requirements Pattern (from VV50 team)
The Computational Model Requirements Pattern (from VV50 team)
• Med device generic features
• Med device generic interactions
• Med device generic states