Case Study: Enhancing Credibility and Reliability in Medical Device Evaluation through Computational Fluid Dynamics for Risk-Informed Decision-Making

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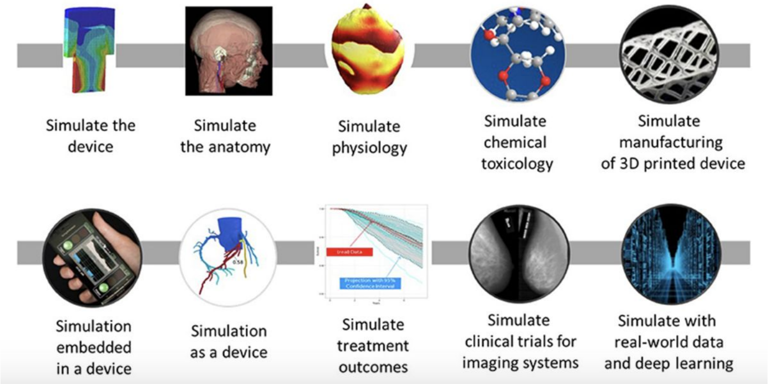
DOE CSGF

Dissertation Proposal Presentation: 05/03/2024

Dissertation Proposal

Case Study: Enhancing Credibility and Reliability in Medical Device Evaluation through Computational Fluid Dynamics for Risk-Informed Decision-Making

Motivation



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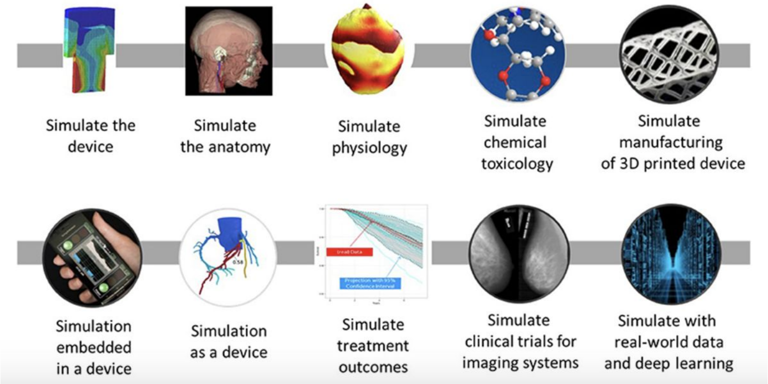
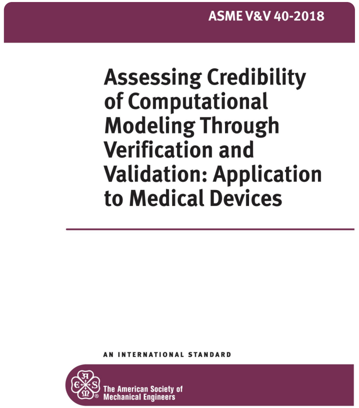
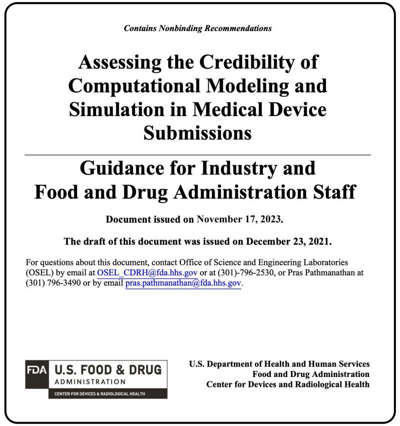



ASME V&V 40-2018

Assessing Credibility of Computational Modeling Through Verification and Validation: Application to Medical Devices

AN INTERNATIONAL STANDARD

The American Society of Mechanical Engineers


Contains Nonbinding Recommendations

Assessing the Credibility of Computational Modeling and Simulation in Medical Device Submissions

Guidance for Industry and Food and Drug Administration Staff

Document issued on November 17, 2023.

The draft of this document was issued on December 23, 2021.

For questions about this document, contact Office of Science and Engineering Laboratories (OSEL) by email at OSEL_CDRH@fda.hhs.gov or at (301)-796-2530, or Pras Pathmanathan at (301) 796-3490 or by email pras.pathmanathan@fda.hhs.gov.

FDA U.S. FOOD & DRUG ADMINISTRATION CENTER FOR DEVICES & RADIOLOGICAL HEALTH

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

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State of the Field

Credibility Challenges

- Scarcity of Comprehensive Examples
- Novelty of the ASME V&V 40 Standard

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Growing Recognition of Reproducibility

- Funding Agency Requirements (NIH & NSF)
- Publication Journal Reproducibility Badges (SIAM & SC)

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Promise of High-Performance Computing (HPC) for credibility building

State of the Field: Lack of clear roadmap for generating *computational evidence** that can be used to establish trust in computational modeling and simulation for use in risk informed regulatory decision making.

***Computational Evidence:** data and analyses obtained from computational modeling and simulations, including the assessment of accuracy and reliability of the models.

Research Question

How can computational modeling and simulation (CM&S) be effectively harnessed to inform regulatory decisions in the medical device domain while addressing credibility, transparency, and reliability concerns?

Aims

Aim 1 : Computational Case Study

Construct a comprehensive case study illustrating the complete process of developing and simulating a computational model for a medical device system. This includes **establishing a credibility plan**, **developing the computational model**, **establishing a reproducibility workflow**, and utilizing high performance computing to improve the rigor of the study.

Aim 2: Credibility Evidence

Build credibility evidence using **Verification, Validation, and Uncertainty Quantification (VVUQ)** methods established by the credibility goals in Aim 1.

Aim 3: Assessment

Evaluate the **applicability of the medical device Computational Model and Simulation (CM&S)**, leveraging credibility evidence and the reproducibility infrastructure.

Background

How can computational modeling and simulation (CM&S) be effectively harnessed to inform regulatory decisions in the medical device domain while addressing credibility, transparency, and reliability concerns?

Medical Device System

Conservation Equations

Simulation Software

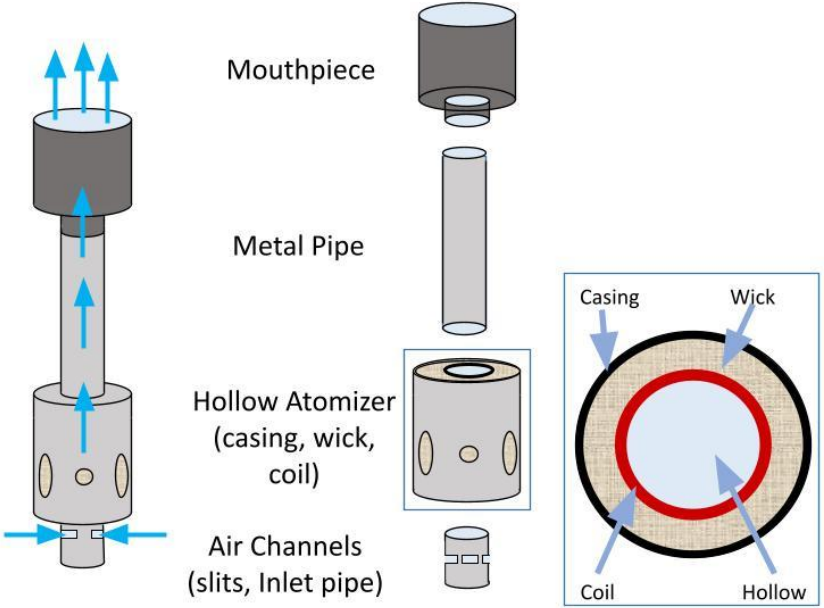
CM&S System

Credibility

Medical Device System

Medical Device System

Electronic Drug Delivery System (EDDS)



Medical Device System

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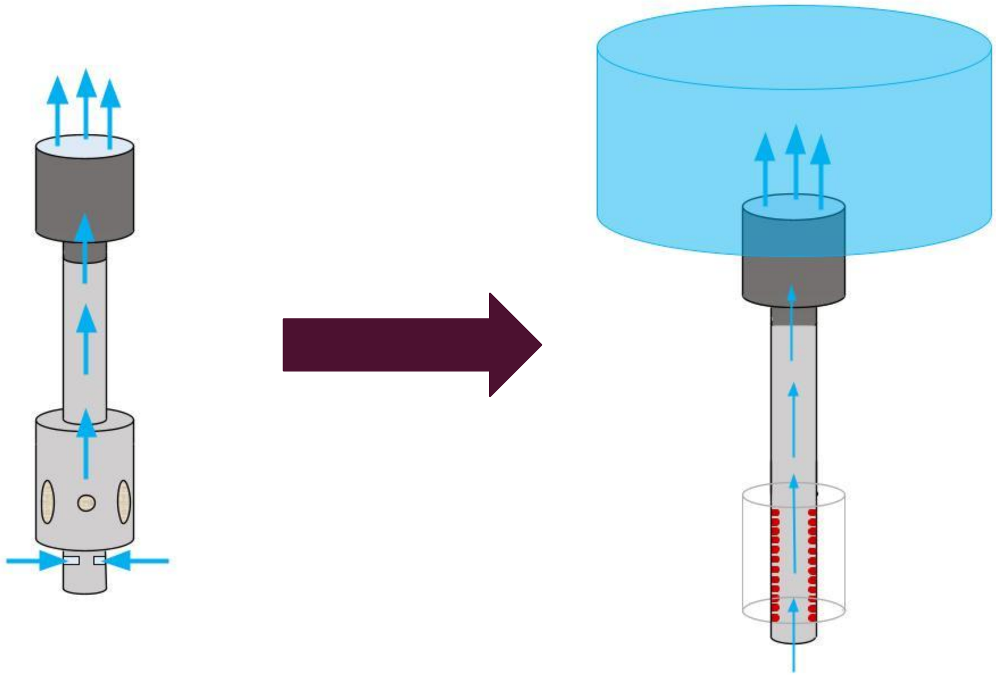
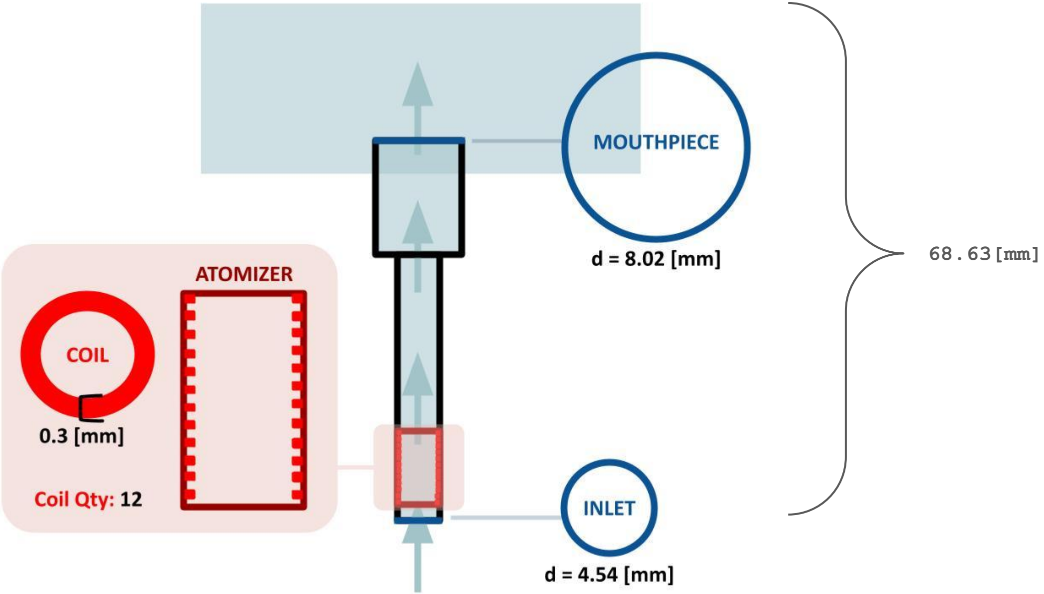


Medical Device System

Electronic Drug Delivery System (EDDS)

System:

- Inlet Pipe
- Atomizer
    - 12 heating coils
- Connecting Pipe
- Mouthpiece
- Open Air



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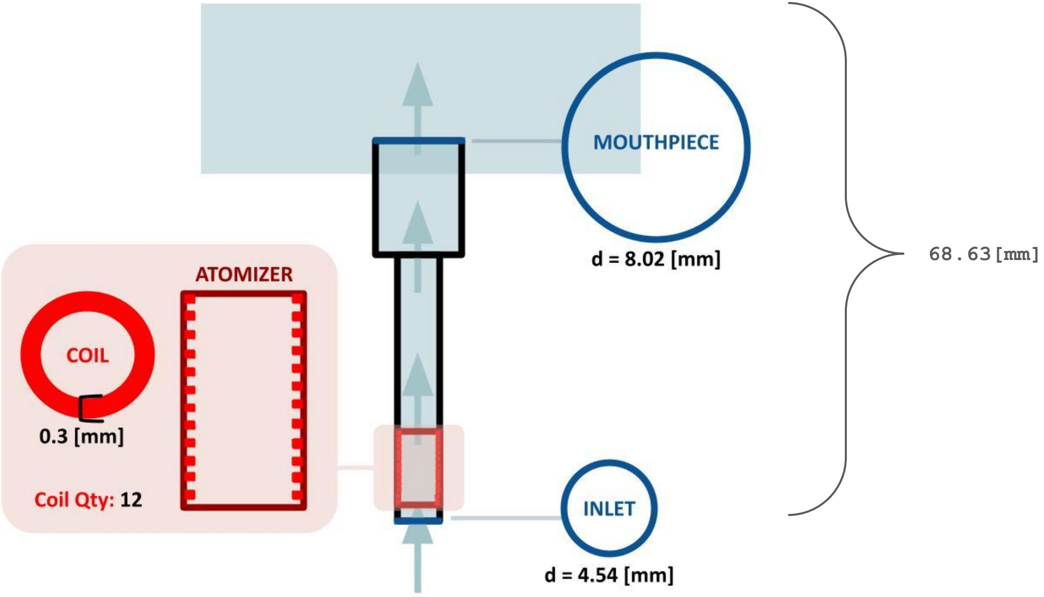
Physics:

- Fluid Dynamics
- Conjugate Heat Transfer



Conservation Equations

Fluid Dynamics & Heat Transfer

Conservation of momentum (Fluid)

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \mathbf{U}) = 0$$

Conservation of Mass (Fluid)

$$\frac{\partial (\rho \mathbf{U})}{\partial t} + \nabla \cdot (\rho \mathbf{U}\mathbf{U}) = -\nabla p + \nabla \cdot \tau + \rho g$$

Fluid Dynamics

Thermal Energy Equation (Fluid)

$$\frac{\partial (\rho c_p T)}{\partial t} + \nabla \cdot (\rho c_p \mathbf{U} T) = \nabla \cdot (\kappa \nabla T) + S_E$$

Conduction Equation (Solid)

$$\frac{\partial (\rho c_p T)}{\partial t} = \nabla \cdot (\kappa \nabla T) + S_E$$

Heat Transfer

$\mathbf{U}$: Fluid Velocity, T : Temperature, t : Time, ρ : Density, p : Pressure, ρg : Gravity, τ :Shear Stress,
c_p : Specific Heat Capacity, κ : Thermal Conductivity, S_E : Heat source

Simulation Software

Multiphysics Simulation Software

Ansys

- Commercial Software
- Integrated solver architecture
- C++ for core functionalities
- **Requires licenses for access**
- Graphical User Interface (GUI): Workbench
- GUI Post-Processing: CFX-Post
- Solver: **`CFX`**
    - Node-based Finite Volume Method
    - Coupled Solver
    - Mesh Overlay

OpenFOAM

- Open Source Software
- Modular solver architecture
- C++ with OOP principles
- **Free software, no licensing fees**
- Command-line driven interface
- ParaView: GUI Post-Processing*
- Solver: **`chtMultiRegionFoam.C`**
    - Cell-centered Finite Volume Method
    - Segregated Solver
    - PIMPLE Algorithm Solver

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  - PIMPLE Algorithm Solver
- Mesh Decomposition & Reconstruction
  - **`simpleGeomDecomp`**
  - **`multiLevelDecomp`**
  - **`reconstructPar`**

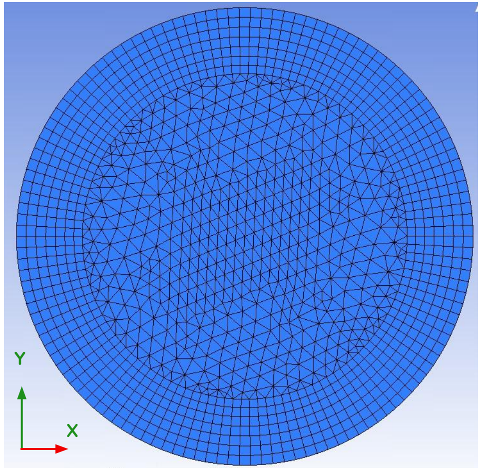
CM&S System

Mesh

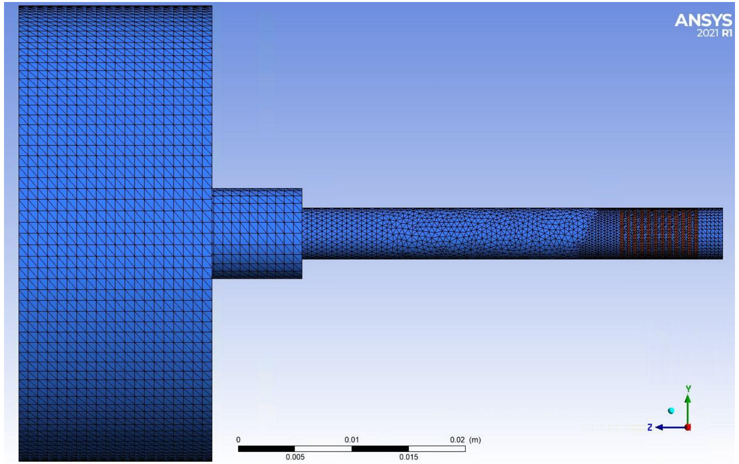
Tetrahedral and hexahedral elements

Unstructured Mesh

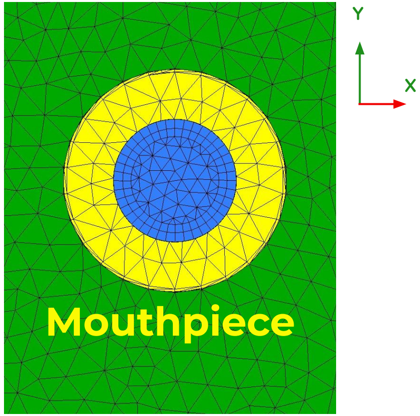
Open Air



EDDS Device



Inlet



Open Air

Boundary & Initial Conditions

Boundary Conditions

Inlet

- Volumetric Flow Rate = 0.5 L/min
- Temperature = 20 ℃

Outlet

- Static Pressure = 101.325 kPa
- Temperature = 20 ℃

Walls

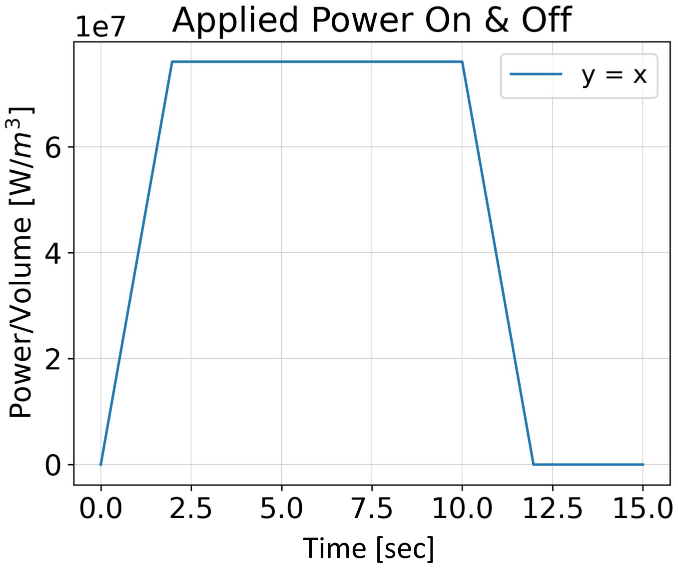
- No-Slip Conditions
- Temperature of Walls = Adiabatic

Initial Conditions

Heat Source (Coil Volume) = 0 Watts

Operating Conditions

Heat Source = 1 Watt for 10 sec



System Response Quantity (SRQ)

Velocity and Temperature

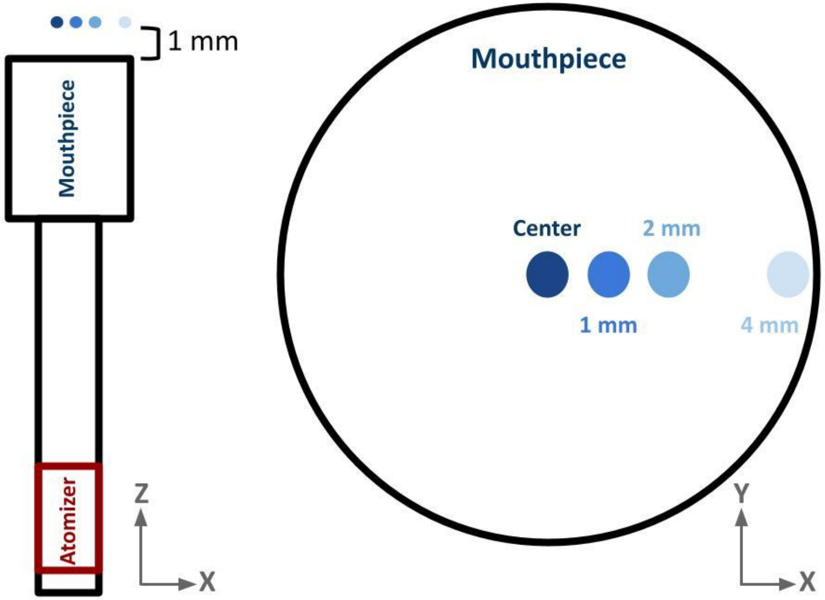
- Quantity, Maximum, Average

Spatial

- 1 mm above the mouthpiece.
- Center (r = 0)
- r = 1 mm
- r = 2 mm
- r = 4 mm

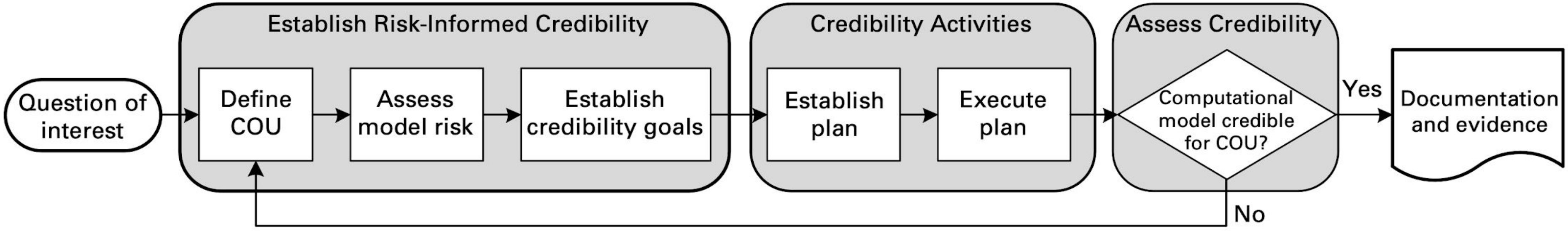
Temporal

- 2 seconds
- 5 seconds
- 10 seconds
- 11 seconds
- 12 seconds



Credibility

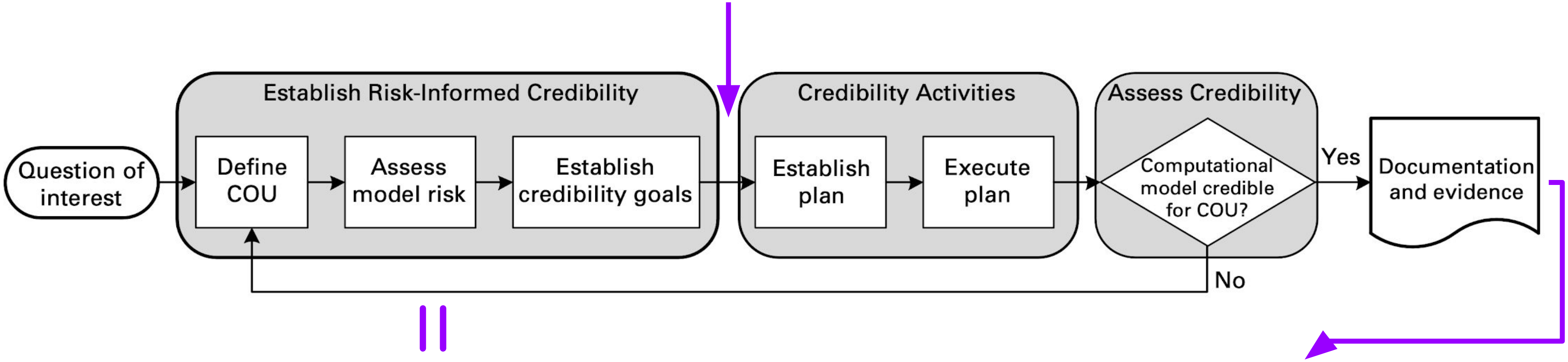
Credibility Framework



ASME V&V 40-2018: Assessing Credibility of Computational Modeling Through Verification and Validation: Application to Medical Devices, (2019).

Credibility Framework & Reproducibility

Implement
Reproducibility
Infrastructure



Establish
Reproducibility Plan

Assess
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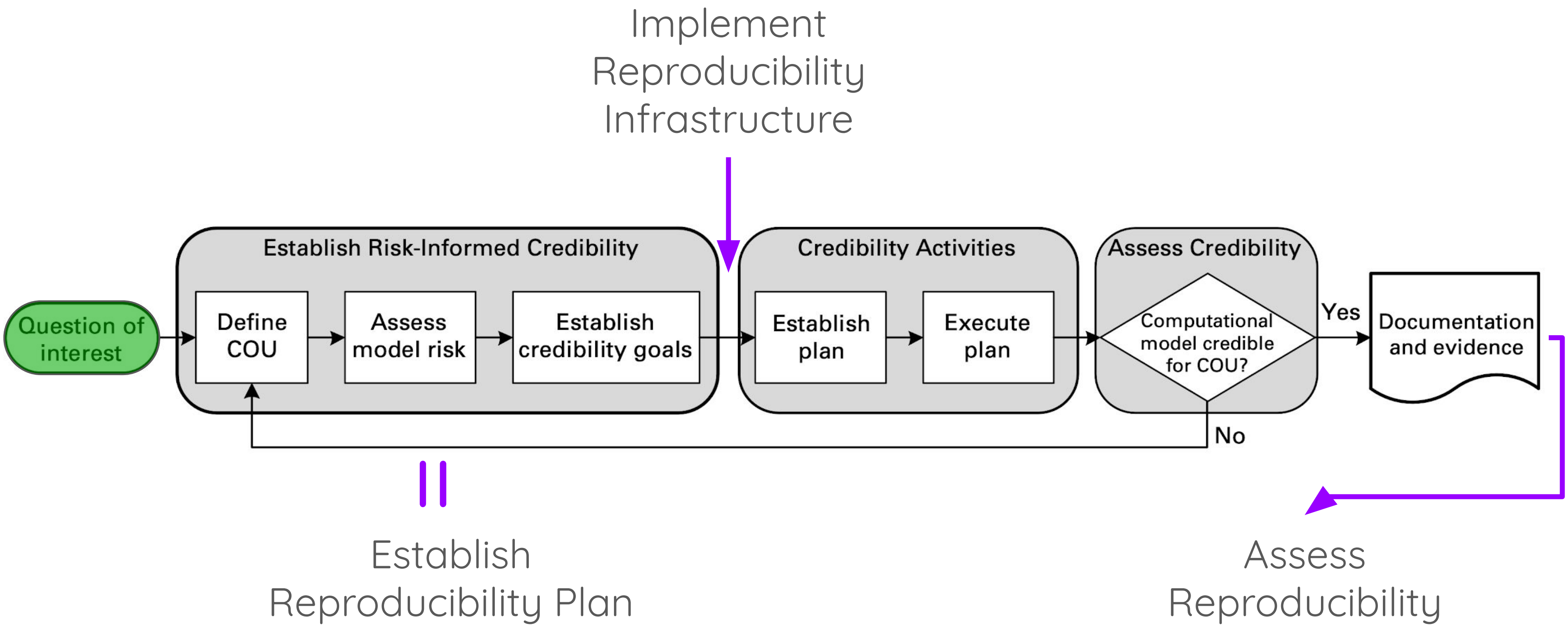

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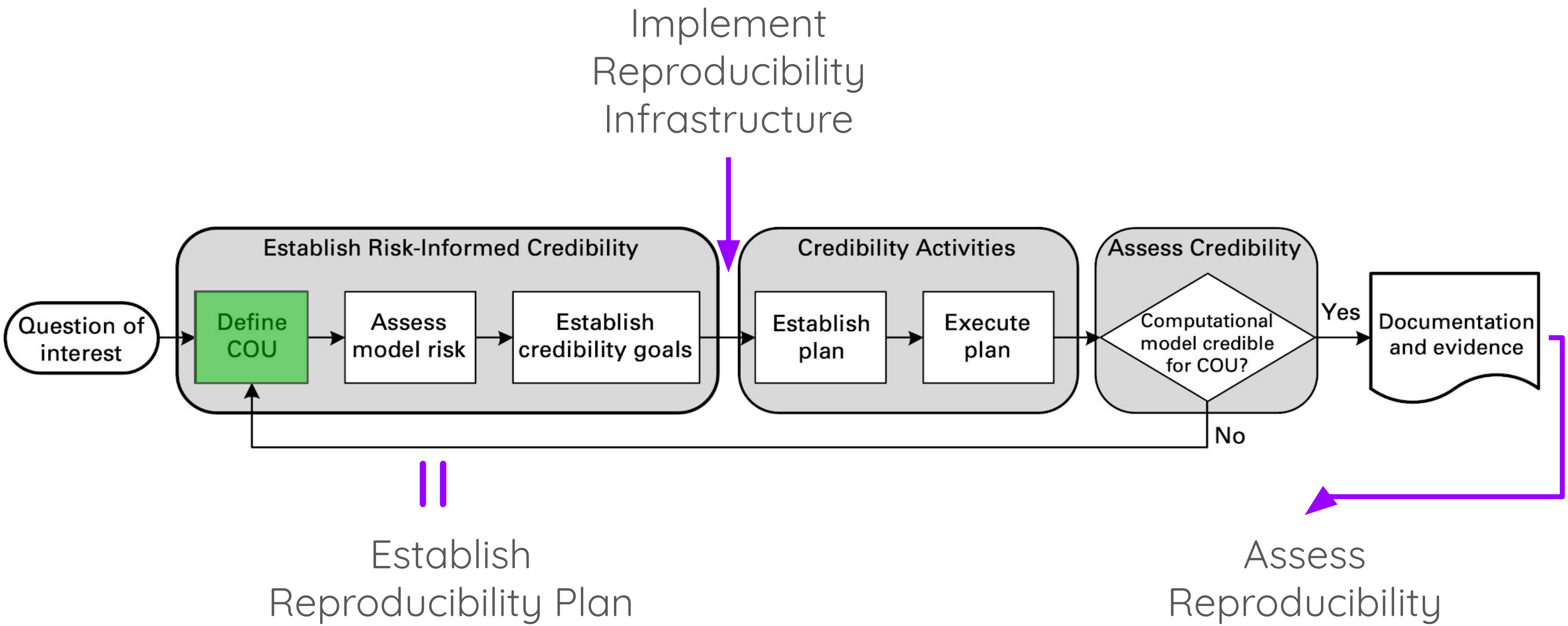

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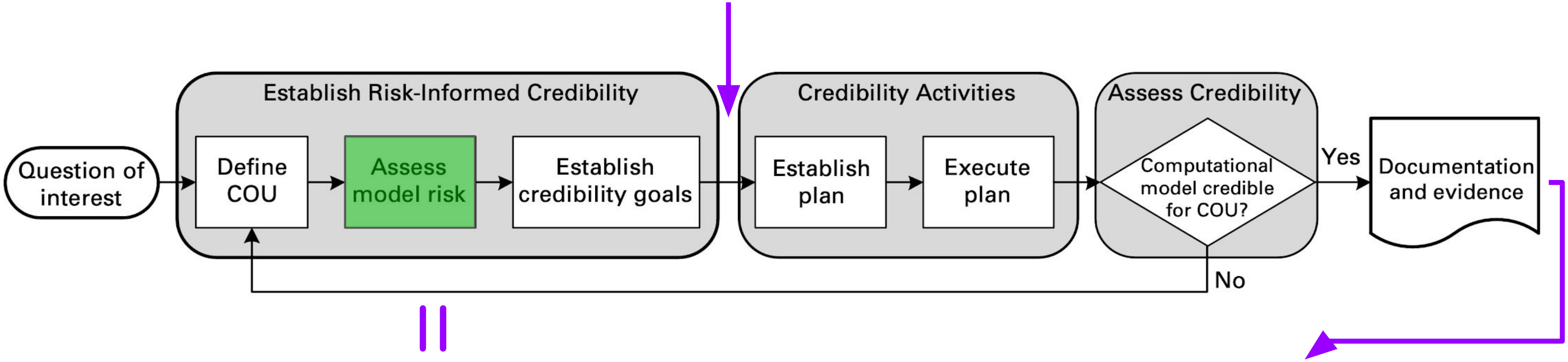

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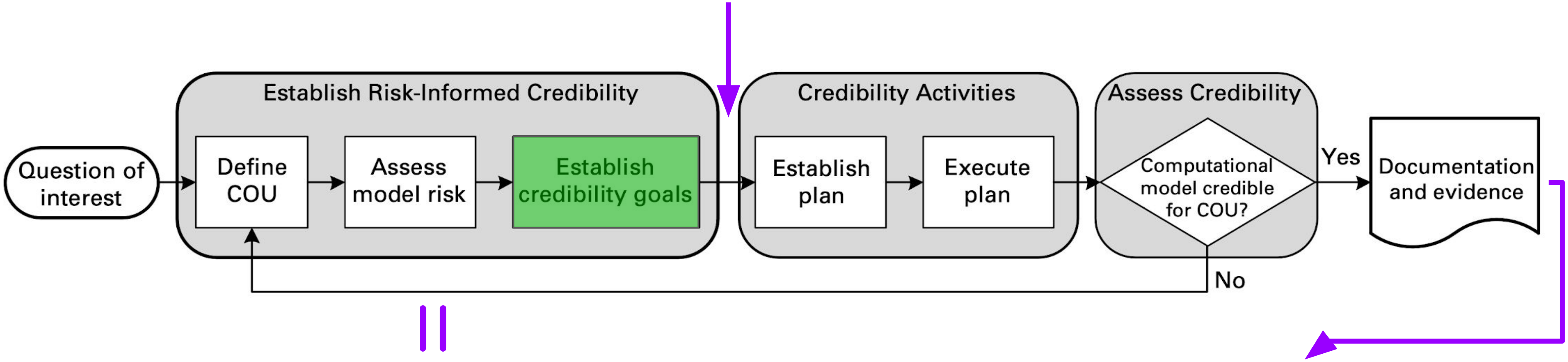

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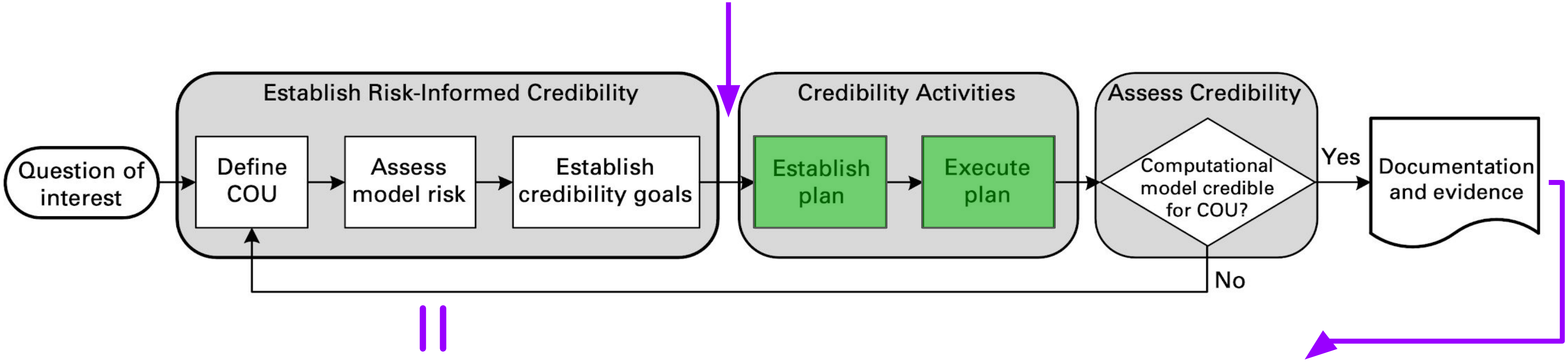

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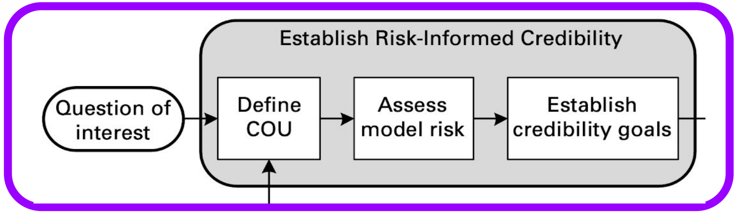

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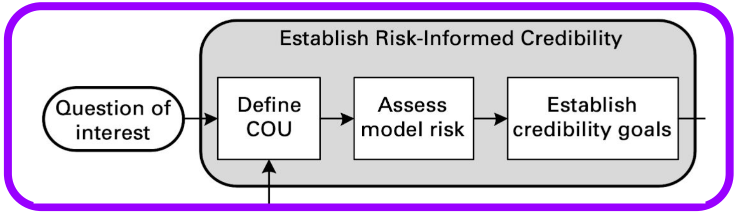
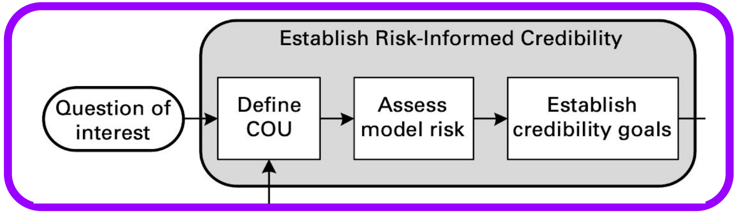


Question of Interest (QOI): What are the bioeffects arising from deposition of potential chemicals generated by EDDS onto the oral mucosa?

Credibility Plan



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Context of Use (COU): A fluid and heat transfer model is required to characterization the flow field and temperature distribution of the flow in representative mouth cavities of an EDDS user.

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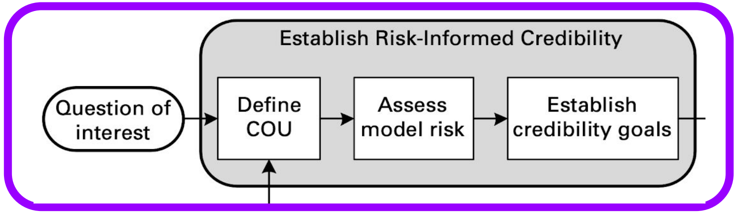

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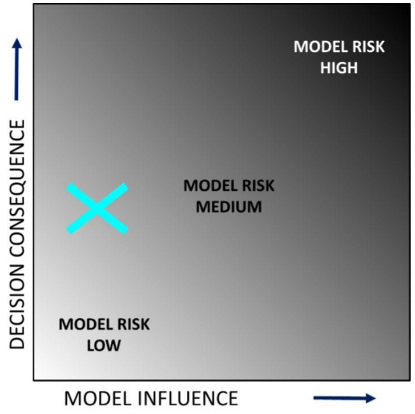
Context of Use (COU): A fluid and heat transfer model is required to characterization the flow field and temperature distribution of the flow in representative mouth cavities of an EDDS user.

Risk Assessment: Less than moderate but more than low

- Model Influence = Low
- Decision Consequence = Moderate



Credibility Goals

Verification	Code	Software Quality Assurance
		Numerical Code Verification
	Calculation	Discretization Error
		Numerical Solver Error
		Use Error
Validation	Computational Model	Model Form
		Model Inputs
	Comparator	Test Samples
		Test Conditions
	Assessment	Equivalency of Input Parameters
		Output Comparison
Applicability		Relevance of SRQ's
		Relevance of the Validation Activities

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Credibility Goals

Mathematical model is correctly implemented and solved.

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Credibility Goals

How well the CM&S represents the physical world.

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Credibility Goals

Validation activities support the use of the CM&S for a specific COU.

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Credibility Goals

Perform with a medium to low level of rigor…

Verification		
Code	Software Quality Assurance	SQA procedures were specified and documented.
	Numerical Code Verification	NCV was not performed.
Calculation	Discretization	Applicable grid or time-step convergence analyses were performed and their respective convergence behaviors were observed to be stable, but the discretization error was not estimated.
	Numerical Solver Error	No solver parameter sensitivity was performed.
	Use Error	Key inputs and outputs were verified by internal peer review.
Validation		
CM&S Model Form		Influence of expected key model form assumptions was explored.
CM&S Model Input	Quantification of Sensitivities	Sensitivity analysis on expected key parameters was performed.
	Quantification of Uncertainties	Uncertainties on expected key inputs were identified and quantified, but were not propagated to quantitatively assess the effect on the simulation results.
Comparator	Test Samples	Quantity
		Multiple samples were used, but not enough to be statistically relevant.
		Measurement
		All key characteristics of the test samples were measured.
		Range of Characteristics
		Sample(s) with a single set of characteristics was included.
		Uncertainties of Test Sample Measurements
		Uncertainty analysis incorporated instrument accuracy and repeatability (i.e., statistical treatment of repeated measurements).
	Test Condition	Quantity
		Multiple (2-4) test conditions were examined.
		Measurement
		All key characteristics of the test conditions were measured.
		Range of Characteristics
		Test conditions representing the entire range of conditions were examined.
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Assessment		
Equivalency of Input Parameters		The types and ranges of all inputs were equivalent.
Output Comparison	Quantity	Multiple outputs were compared.
	Equivalency of Output Parameters	Types of outputs were equivalent.
	Rigor of Output Comparisons	Comparison performed by determining the difference between computational results and experimental results.

Credibility Goals

Except for these!

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Code	Software Quality Assurance	SQA procedures were specified and documented.	
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Credibility Goals

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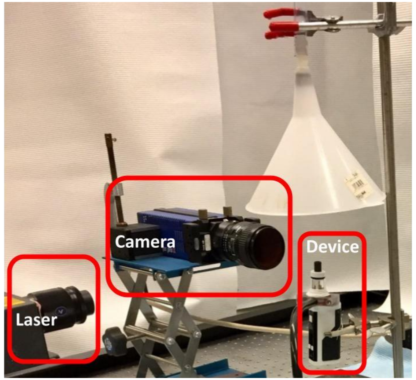
Credibility Plan > Applicability Analysis Plan

Reality of
Interest
R - COU

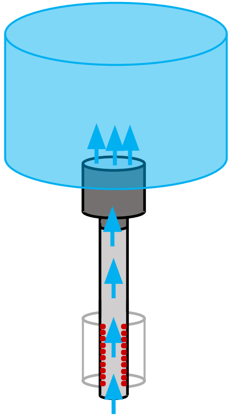
Reality of
Interest CM&S
M-COU

Context of Use



Validation
Comparator
R-VAL

Validation
CM&S
M-VAL



Primary Validation Evidence

https://www.gettyimages.ca/detail/illustration/woman-using-a-vaporizer-royalty-free-illustration/614740308?adppopup=true
https://www.cnn.com/2019/07/22/health/ecigarette-vaping-fda-real-cost-tv-ads-bn/index.html

Credibility Plan > Applicability Analysis Plan

Reality of
Interest
R - COU

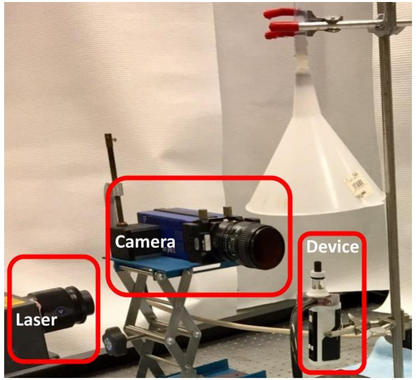
?

Reality of
Interest CM&S
M-COU

Context of Use

ΔR

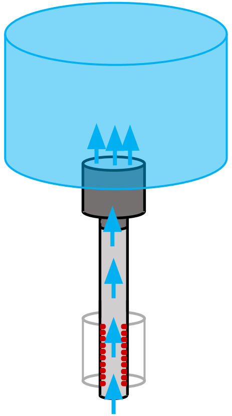
ΔM



Validation
Comparator
R-VAL

Comparable

Validation
CM&S
M-VAL



Primary Validation Evidence

https://www.gettyimages.ca/detail/illustration/woman-using-a-vaporizer-royalty-free-illustration/614740308?adppopup=true
https://www.cnn.com/2019/07/22/health/ecigarette-vaping-fda-real-cost-tv-ads-bn/index.html

Results

Air Flow (AF)

Heated Air Flow (HAF)

Air Flow (AF)

Credibility > Verification

Code

- Software Quality Assurance (SQA)
- Numerical Code Verification (NCV)

Calculation

- Discretization Error
- Numerical Solver Error
- Use Error

Credibility > Verification > Code

Code

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https://www.ansys.com/company-information/quality-assurance , https://openfoam.org/support/

Credibility > Verification > Code

Code

- **Software Quality Assurance (SQA)**
- Numerical Code Verification (NCV)

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SQA

ANSYS Software

- Meets the ISO 9001 quality management standard
- Follows the United States Nuclear Regulatory Commission's Quality Assurance Requirements for Computer Software

OpenFOAM

- Creates and maintains verification tests for critical functionality
- Conducts code Review to assess community code and to find bugs
- Builds and runs unit tests to test for integration, performance, interoperability and installation.

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NCV

Calculate Error by comparing CM&S with an analytic solution.

https://www.ansys.com/company-information/quality-assurance , https://openfoam.org/support/

Credibility > Verification > Code > NCV

Hagen-Poiseuille Pipe Flow*

Radius = 2.227 mm

Fluid = Air

Length = 0.12 m

Entry Length = 0.0493 m

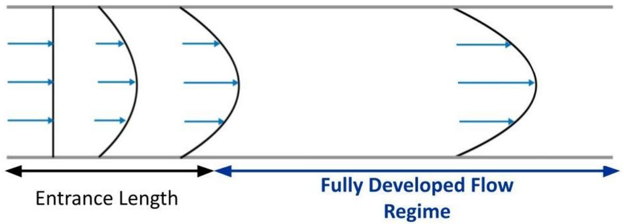
Uniform Inlet Velocity = 0.5216 m/s

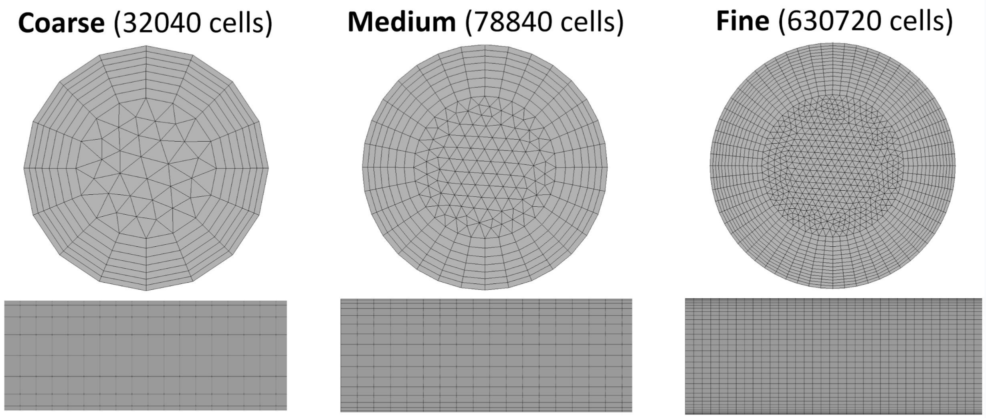
Reynolds Number = 158

Steady State

Analytic Solution:

$$U_{max} = 2U_{avg} = 1.0432 m/s$$

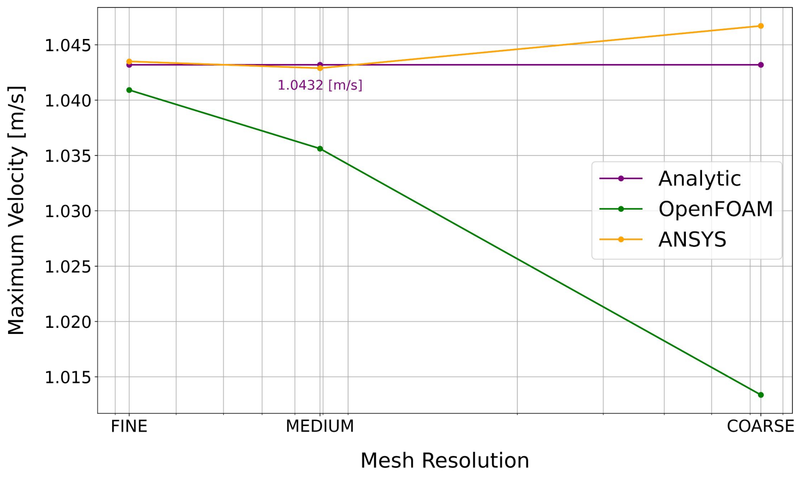


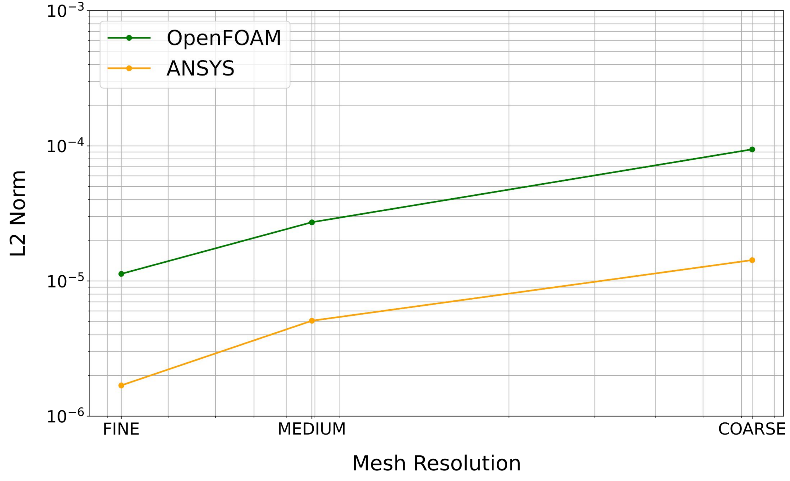


* These efforts were conducted under the NSF/FDA SIR grant in collaboration with fellow graduate student Anastasia Sarmakeeva.

Credibility > Verification > Code > NCV

Numerical Code Verification



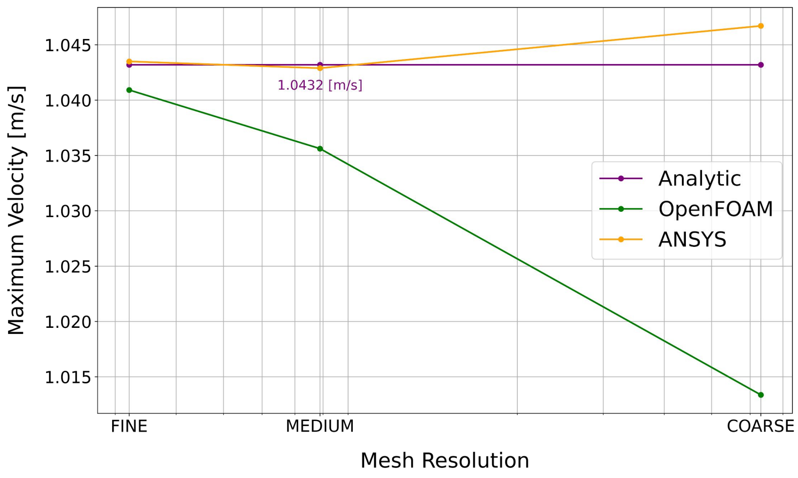


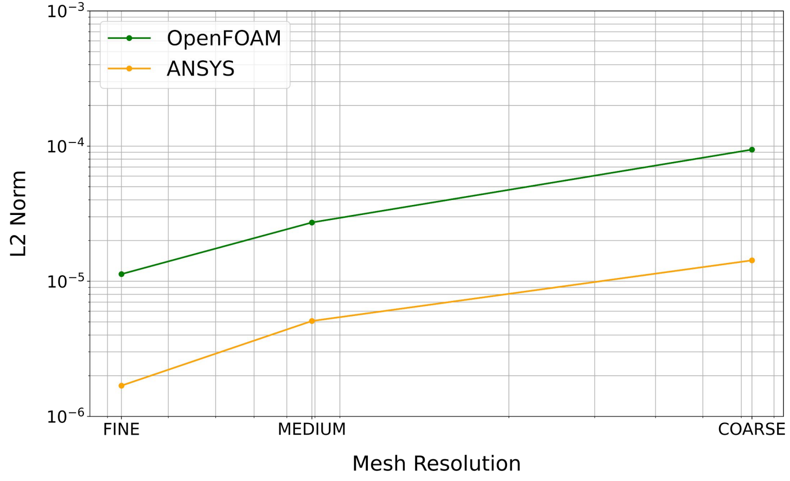
	Coarse Mesh	Medium Mesh	Fine Mesh
ANSYS	1.427e-05	5.079e-06	1.688e-06
OpenFOAM	9.421e-05	2.721e-05	1.129e-05

Credibility > Verification > Code > NCV

OpenFOAM requires a finer mesh for comparable accuracy to ANSYS.

Numerical Code Verification





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Credibility > Verification > Calculation

Code

- Software Quality Assurance (SQA)
- Numerical Code Verification (NCV)

Calculation

- Discretization Error
- Numerical Solver Error
- Use Error

Credibility > Verification > Calculation

Code

- Software Quality Assurance (SQA)
- Numerical Code Verification (NCV)

Calculation

- **Discretization Error**
- Numerical Solver Error
- Use Error

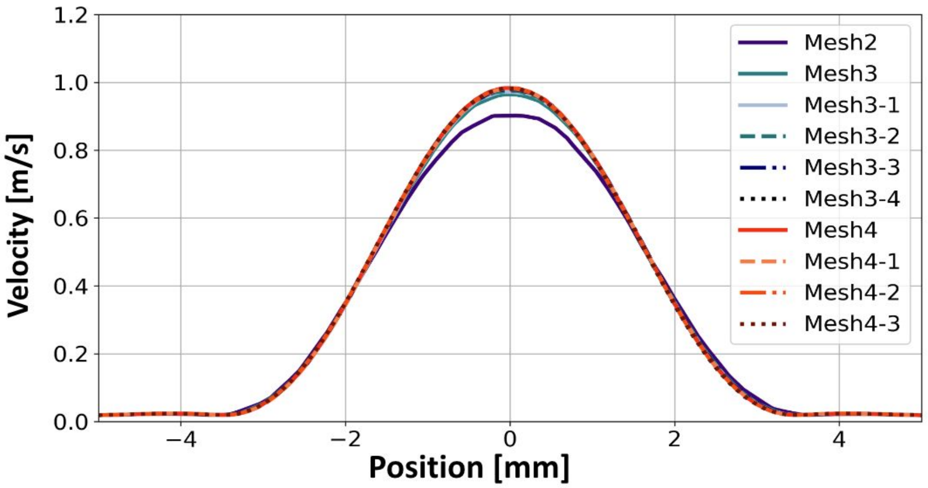
Discretization Error

- Mesh Convergence Study
- Uncertainty Estimation
  - Finest Mesh SRQ
  - Richardson Extrapolation

Credibility > Verification > Calculation > Discretization

Mesh Convergence Study

- Meshes: 10 Resolutions
- Solver Tolerance: 1 × 10−6



Label	Element Size	Number of Elements
M2	0.0004	1,723,087
M3	0.0003	3,993,266
M3-1	0.00028	4,897,382
M3-2	0.00026	6,096,385
M3-3	0.00024	7,735,148
M3-4	0.00022	10,022,241
M4	0.0002	13,328,905
M4-1	0.00018	18,250,030
M4-2	0.00016	25,940,033
M4-3	0.00014	38,678,387

Credibility > Verification > Calculation > Discretization

Mesh Convergence Study

- Meshes: 10 Resolutions
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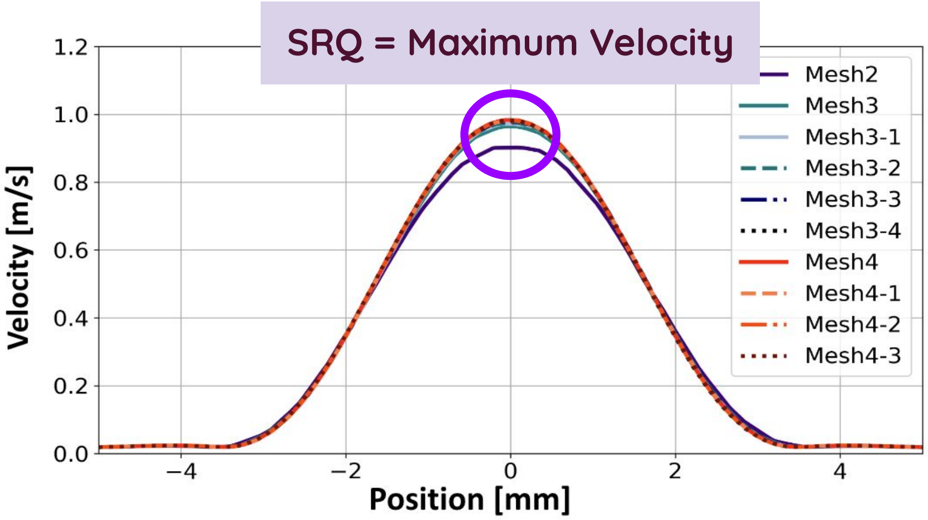

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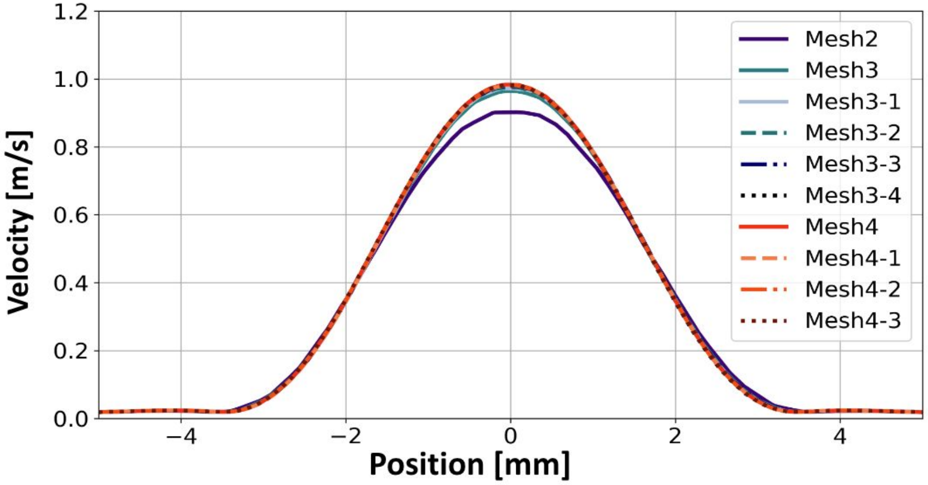
Credibility > Verification > Calculation > Discretization

Mesh Convergence Study

- Meshes: 10 Resolutions
- Solver Tolerance: 1 × 10−6
- Meshes 2, 3, and 4 (& finest mesh too!)
  - Refinement Factor: 2



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Credibility > Verification > Calculation > Discretization

Mesh Convergence Study

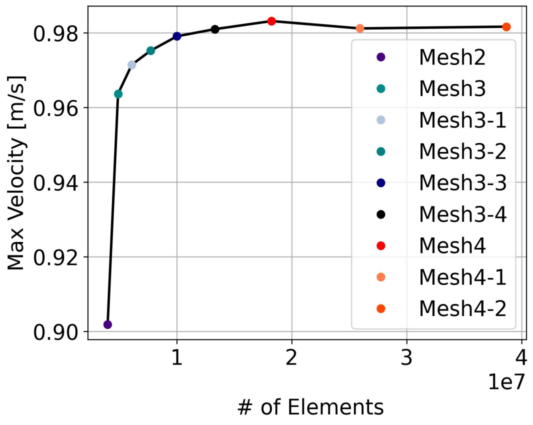


Figure 1: Maximum Velocity

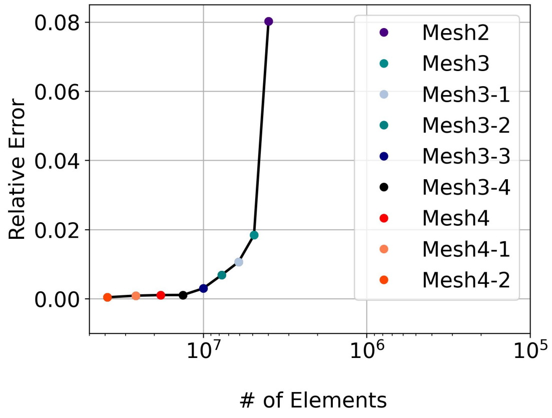


Figure 2: Relative Error with Finest Mesh (4-2)

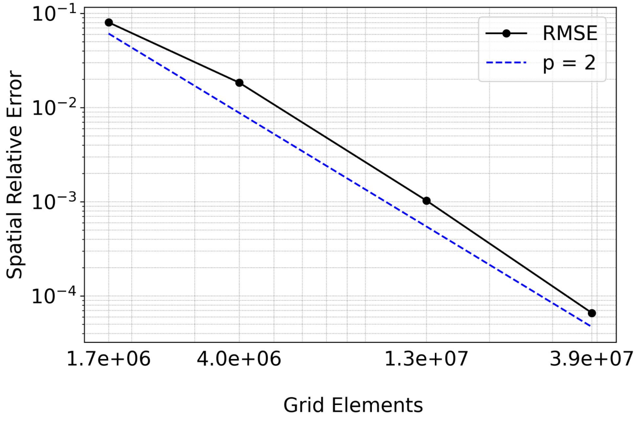


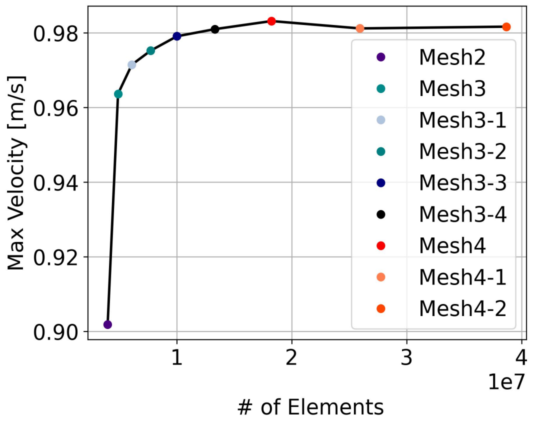
Figure 3: RMSE with Richardson Extrapolation

*ASME V&V 20-2009 (R2021): Standard for Verification and Validation in Computational Fluid Dynamics and Heat Transfer, (2022).

Credibility > Verification > Calculation > Discretization

Mesh Convergence Study

- Observed order of convergence: p = 1.7 (~2)
- Discretization Error: $u_{num} = GCI/2 = 5.60 \times 10^{-05}$



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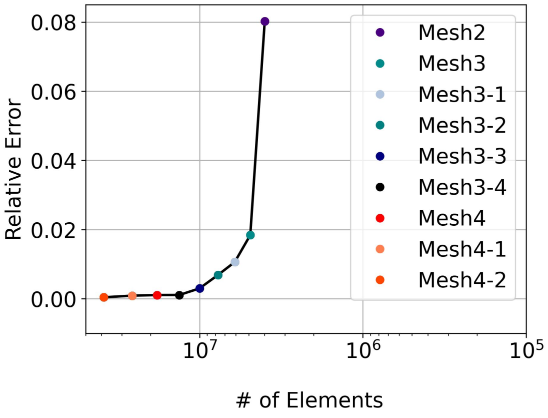

Figure 2: Relative Error with Finest Mesh (4-2)

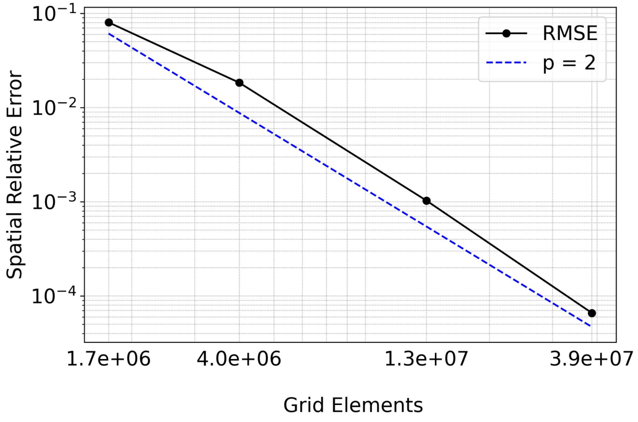

Figure 3: RMSE with Richardson Extrapolation

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Credibility > Verification > Calculation > Discretization

Maximum Velocity reaches mesh independence.

Mesh Convergence Study

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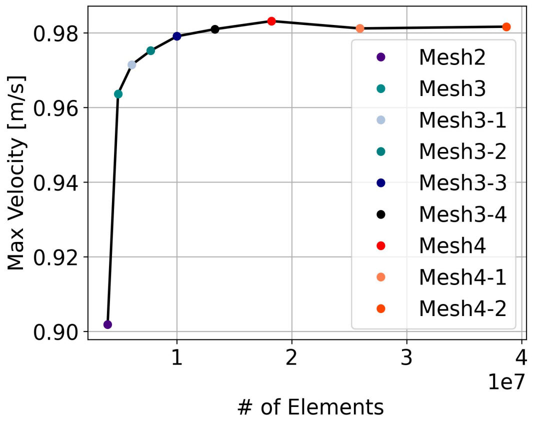

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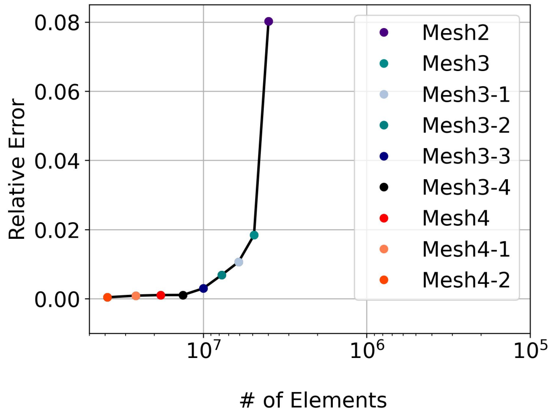
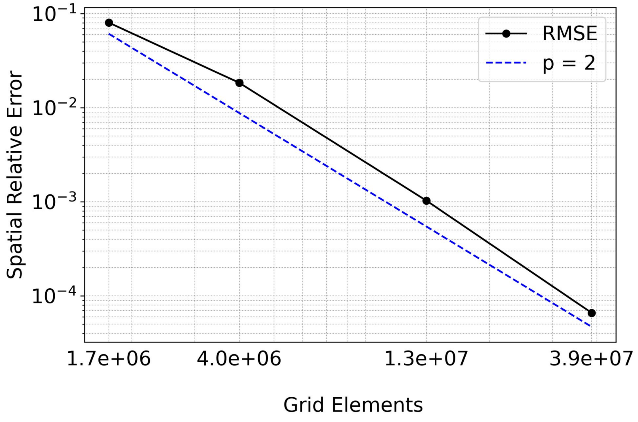


Figure 2: Relative Error with Finest Mesh (4-2)



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Credibility > Verification > Calculation > Discretization

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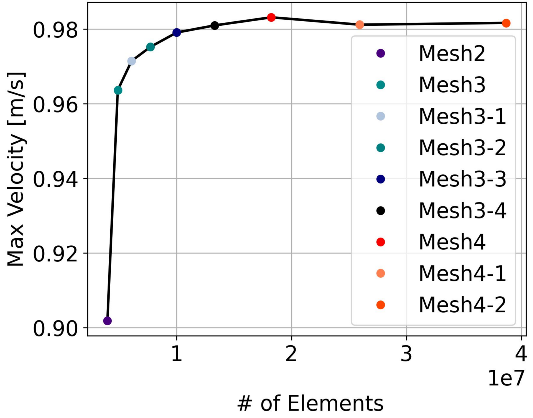

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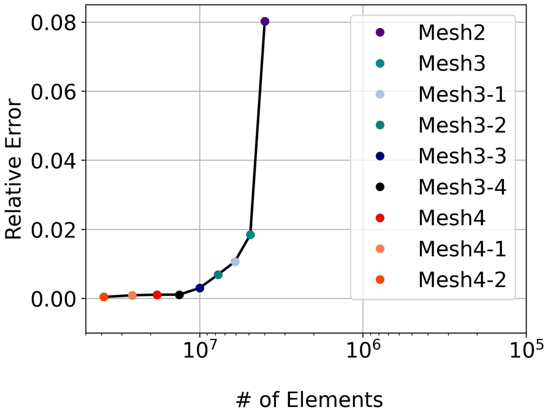

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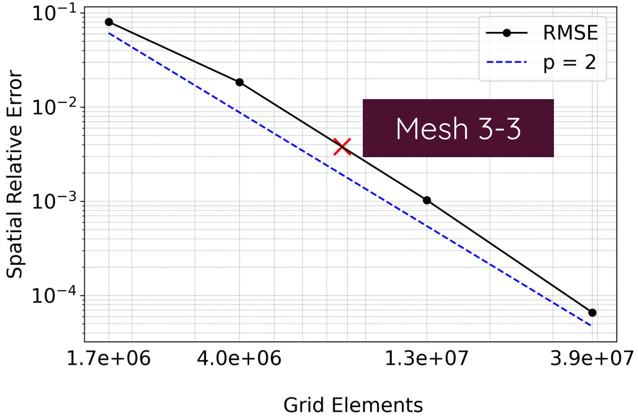

Figure 3: RMSE with Richardson Extrapolation

*ASME V&V 20-2009 (R2021): Standard for Verification and Validation in Computational Fluid Dynamics and Heat Transfer, (2022).

Credibility > Verification > Calculation

Code

- Software Quality Assurance (SQA)
- Numerical Code Verification (NCV)

Calculation

- Discretization Error
- Numerical Solver Error
- Use Error

Credibility > Verification > Calculation

Code

- Software Quality Assurance (SQA)
- Numerical Code Verification (NCV)

Calculation

- Discretization Error
- **Numerical Solver Error**
- Use Error

Numerical Solve Error

Asses impacts of solver parameter

- Solver Tolerance

Credibility > Verification > Calculation

Code

- Software Quality Assurance (SQA)
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Calculation

- Discretization Error
- Numerical Solver Error
- **Use Error**

Numerical Solve Error

Asses impacts of solver parameter

- Solver Tolerance

Use Error (Experimentalists)

Peer reviewed the correctness of all inputs and conditions.

Credibility > Verification > Calculation > NSE

Numerical Solver Error (NSE)

Mesh 3-3

- Element Size = 0.0003
- Number of Elements = 3,993,266

Inlet Volumetric Flow Rate: 0.5 L/min

SRQ_{NSE}: Outlet Average Velocity

1e-5	1e-6	1e-7	1e-8
0.576579 [m/s]	0.576586 [m/s]	0.576587[m/s]	0.576587 [m/s]

Credibility > Verification > Calculation > NSE

Numerical Solver Error (NSE)

Mesh 3-3

- Element Size = 0.0003
- Number of Elements = 3,993,266

Inlet Volumetric Flow Rate: 0.5 L/min

SRQ_{NSE}: Outlet Average Velocity

Numerical Solver Error (1e-6):

$$1.0295 \times 10^{-6} [m/s]$$

1e-5	1e-6	1e-7	1e-8
0.576579 [m/s]	**0.576586 [m/s]**	0.576587[m/s]	0.576587 [m/s]

Verification Study Summary

Code Verification

- Numerical Code Verification Error:
  - ANSYS: $1.69 \times 10^{-06} [m/s]$
  - OpenFOAM: $1.13 \times 10^{-05} [m/s]$

Calculation Verification (ANSYS)

- Discretization Uncertainty*:

$$CGI/2 = 5.60 \times 10^{-05} \ [m/s]$$

- Numerical Solver Error: $1.0295 \times 10^{-6} [m/s]$

Total Uncertainties (ANSYS):

$$5.8719 \times 10^{-5} \ [m/s]$$

Relevant Notes

- OpenFOAM requires a finer mesh for comparable accuracy to ANSYS.
- SRQ of Maximum Velocity reaches mesh independence for meshes: M3-3, M3-4, M4, M4-1, M4-2, M4-3
- Viable solver tolerance: 1e-6
- Verification Study order of magnitude 10^-5

Credibility Activities Performed

	ANSYS	OpenFOAM
Verification - Pipe Flow	X	X
Verification - EDDS	X	

*ASME V&V 20-2009 (R2021): Standard for Verification and Validation in Computational Fluid Dynamics and Heat Transfer, (2022).

Credibility > Validation

Comparator

- Quantification of test samples
- Quantification of test conditions

Computational Model & Simulation (CM&S)

- Model Form
- Mode Input
  - Quantification of Sensitivities
  - Quantification of Uncertainties

Assessment

- Equivalency of input parameters
- Output comparison

Credibility > Validation

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- Quantification of test samples
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Credibility > Validation > Comparator

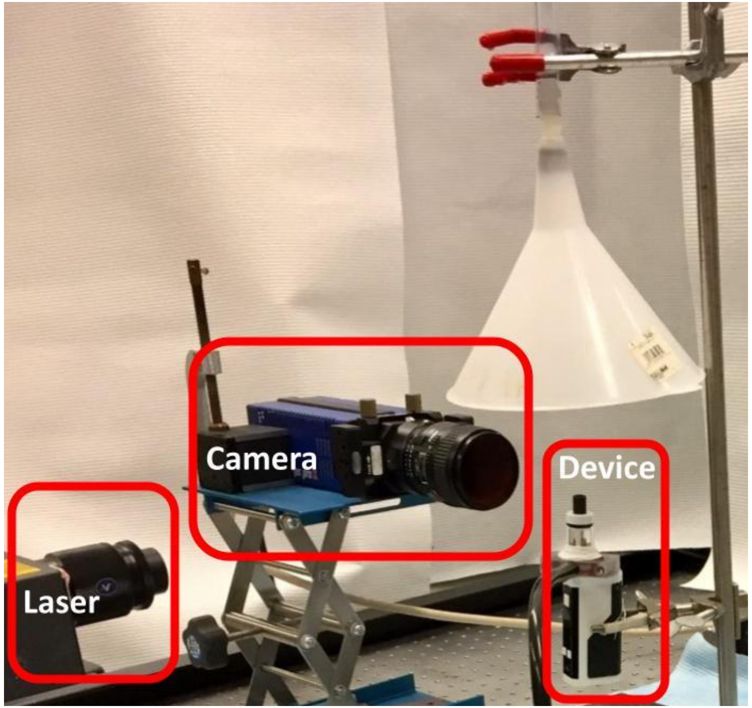
Vapor generation

- Produced by the active device
- Passed through a connecting tube
- Vapor enters and passes through passive device

Liquid composition (active)

- Vegetable Glycerin: 35%
- Propylene Glycol: 65%
- Nicotine: 3 mg

Vapor exhaustion: Funnel placed on passive device



Credibility > Validation > Comparator

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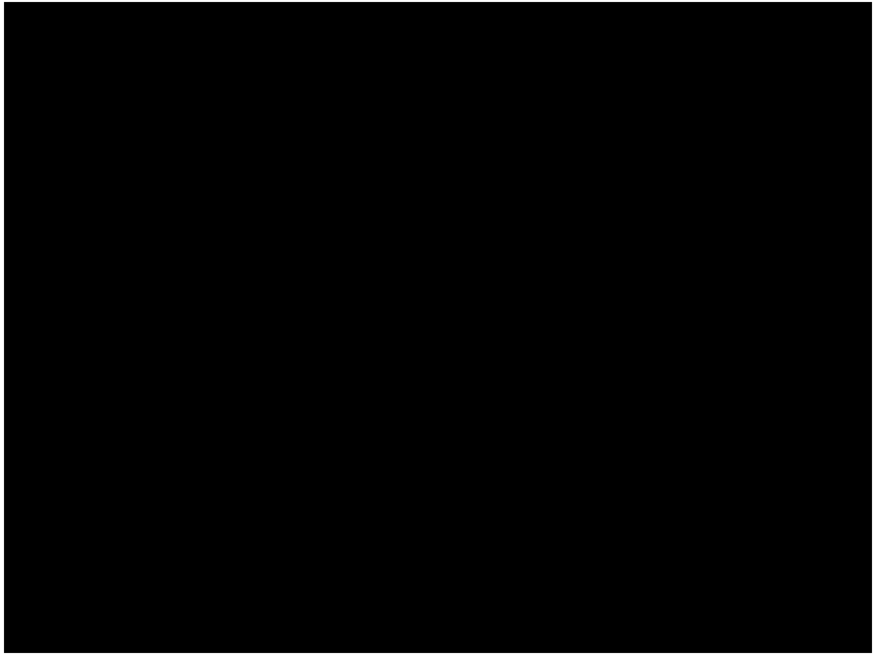
Vapor exhaustion: Funnel placed on passive device

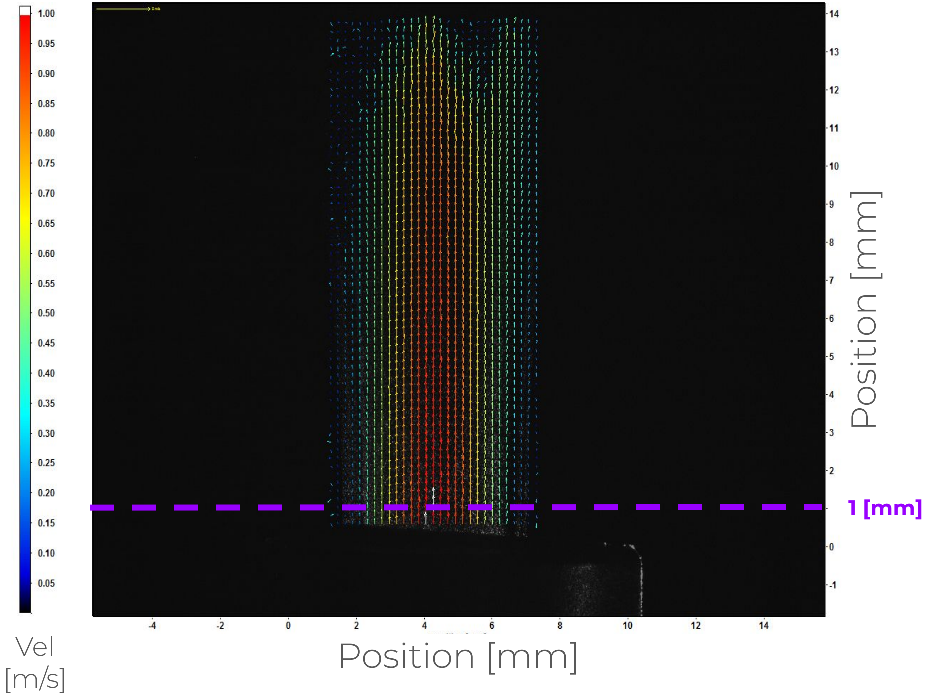
Particle Image Velocimetry (PIV) Measurements

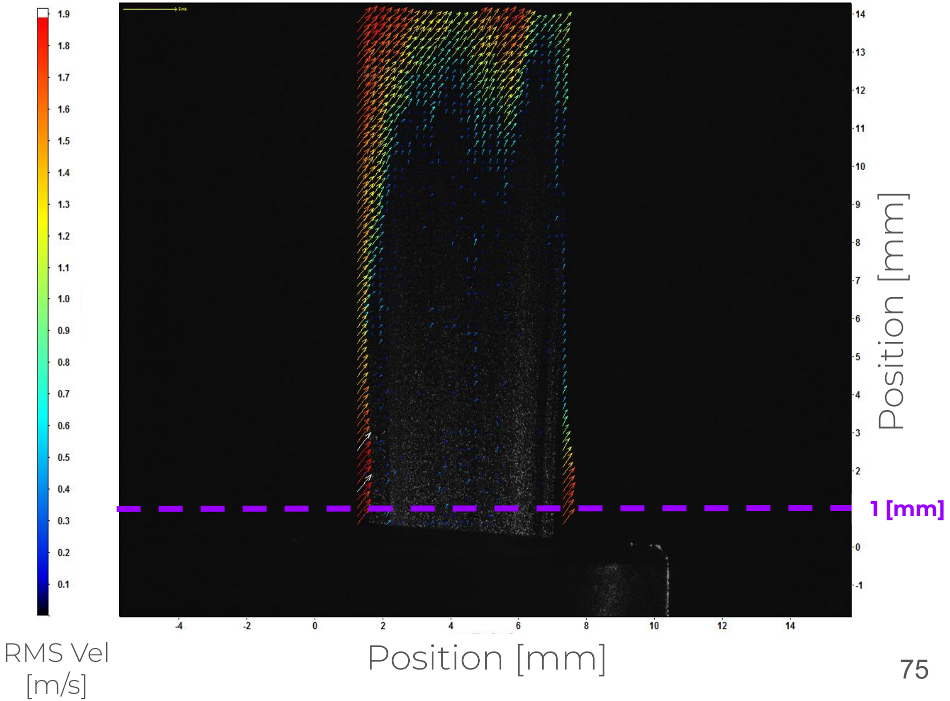
- Camera: LaVision Imager Pro X 2MP
- Laser: New Wave Solo I, New Wave Corp



Credibility > Validation > Comparator

PIV Measurements

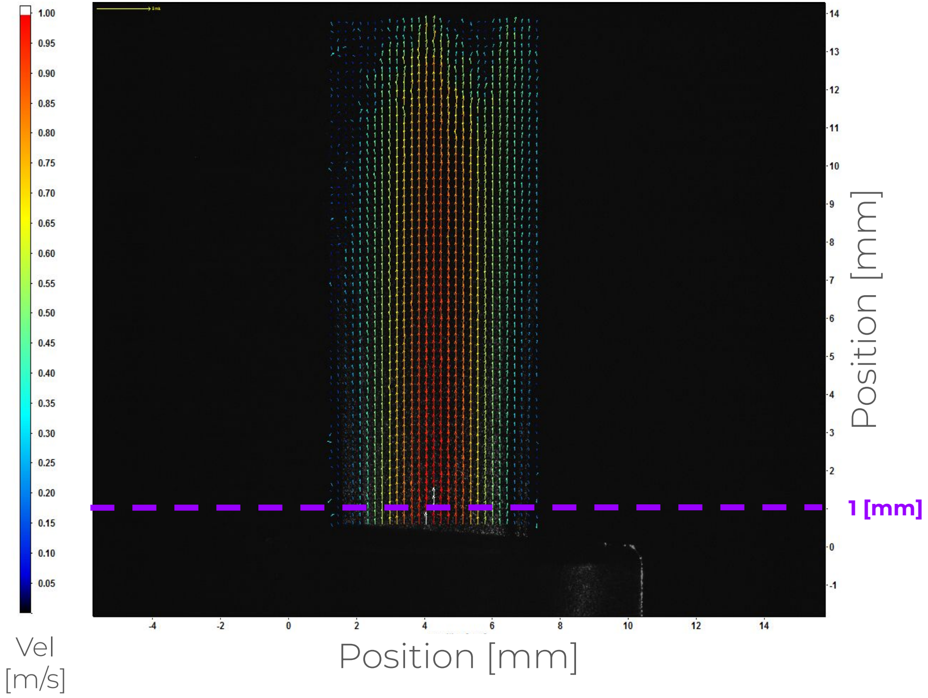


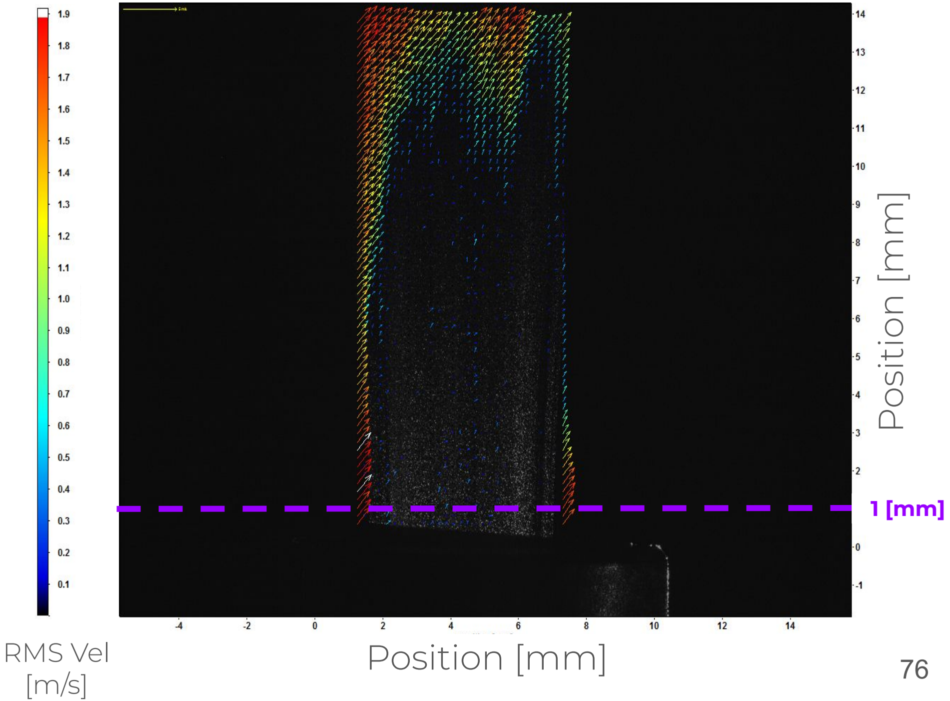


Credibility > Validation > Comparator

Larger errors near low density regions

PIV Measurements





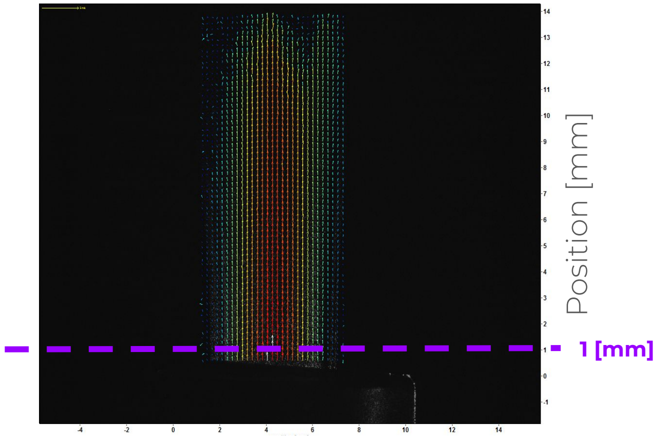
Credibility > Validation > Comparator

Operating Conditions

- Inlet Volumetric Flow Rate = 0.5 L/min
- Steady State

Measurements at 1 mm above mouthpiece

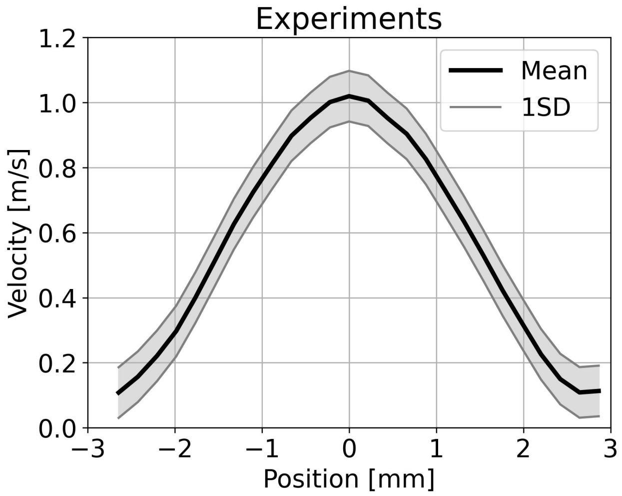
3 Replicate Samples (n= 3)



Sources of Uncertainty:

b_1 : PIV Measurement Uncertainty
b_2 : Replicates (3)

Experiment Uncertainty: $u_D = \sqrt{b_1^2 + b_2^2} = 0.1348$



*ASME V&V 20-2009 (R2021): Standard for Verification and Validation in Computational Fluid Dynamics and Heat Transfer, (2022).

Credibility > Validation > CM&S

Comparator

- Quantification of test samples
- Quantification of test conditions

Computational Model & Simulation (CM&S)

- Model Form
- Mode Input
  - Quantification of Sensitivities
  - Quantification of Uncertainties

Assessment

- Equivalency of input parameters
- Output comparison

Credibility > Validation > CM&S > Model Form

Comparator

- Quantification of test samples
- Quantification of test conditions

Computational Model & Simulation (CM&S)

- **Model Form**
- Mode Input
    - Quantification of Sensitivities
    - Quantification of Uncertainties

Assessment

- Equivalency of input parameters
- Output comparison

Model Form

Ensure the CM&S is a good representation of the physics, including the governing equations, system configuration, properties, and conditions.

- Use a Phenomena Identification and Ranking Table (PIRT)

PIRT

Importance Scale: 1(most) to 3(least)
System: EDDS & mouthcavity

Type of Phenomena	Phenomena	Knowledge we have about what we're simulating	Our ability/knowledge to actually simulate it	Importance	Confidence in Importance	Confidence in Knowledge	How to Improve Confidence in Knowledge	VAL Domain	COU Domain	Notes

Credibility > Validation > CM&S > Model Input

Comparator

- Quantification of test samples
- Quantification of test conditions

Computational Model & Simulation (CM&S)

- Model Form
- **Model Input**
  - **Quantification of Sensitivities**
  - Quantification of Uncertainties

Assessment

- Equivalency of input parameters
- Output comparison

Quantification of Sensitivities

Local Sensitivity Analysis

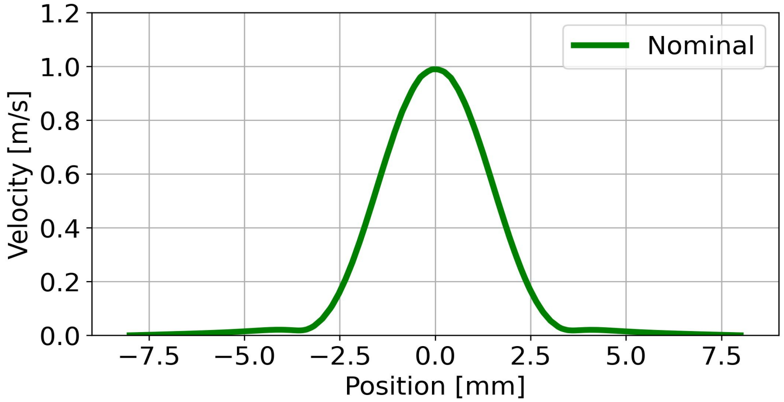
- Local finite differences by investigating nominal parameter quantities and exploring variability in the parameter.

Credibility > Validation > CM&S > Model Input

Steady State

Boundary Conditions

- Inlet Volumetric Flow Rate = 0.5 L/min
- Outlet Pressure = 101.325 kPa



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Credibility > Validation > CM&S > Model Input

Steady State

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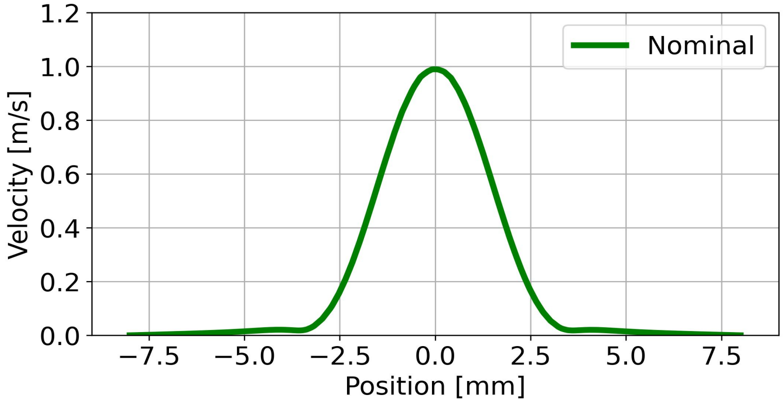
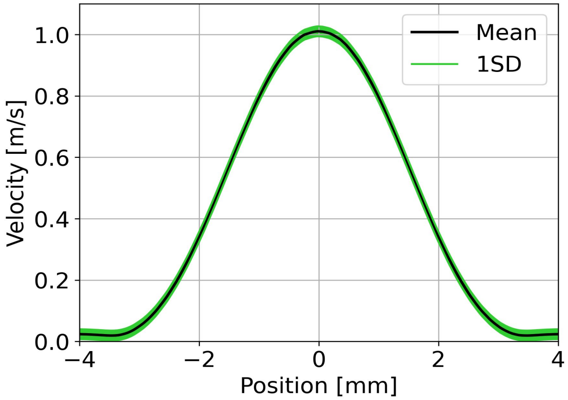


Samples

- Geometry Representative Samples
- n = 3

Uncertainty

- $u_{input} = 0.0140[m/s]$



*ASME V&V 20-2009 (R2021): Standard for Verification and Validation in Computational Fluid Dynamics and Heat Transfer, (2022).

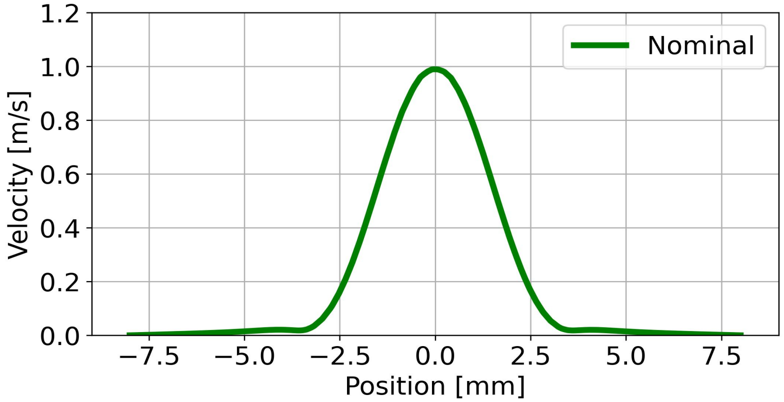
Credibility > Validation > CM&S > Model Input

Device to device variability is not a concern.

Steady State

Boundary Conditions

- Inlet Volumetric Flow Rate = 0.5 L/min
- Outlet Pressure = 101.325 kPa



Samples

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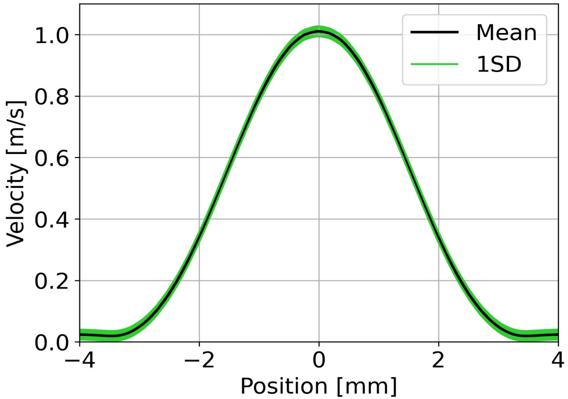
Uncertainty

- $u_{input} = 0.0140[m/s]$



*ASME V&V 20-2009 (R2021): Standard for Verification and Validation in Computational Fluid Dynamics and Heat Transfer, (2022).

Credibility > Validation > Assessment

Comparator

- Quantification of test samples
- Quantification of test conditions

Computational Model & Simulation (CM&S)

- Model Form
- Mode Input
  - Quantification of Sensitivities
  - Quantification of Uncertainties

Assessment

- Equivalency of input parameters
- Output comparison > Validation Metrics

K. A. Maupin and L. P. Swiler. Validation Metrics for Deterministic and Probabilistic Data. Sandia technical report (2017).

Credibility > Validation > Assessment > Comparison

Comparator

- Quantification of test samples
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Computational Model & Simulation (CM&S)

- Model Form
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  - Quantification of Sensitivities
  - Quantification of Uncertainties

Assessment

- Equivalency of input parameters
- **Output comparison > Validation Metrics**

Validation Metric

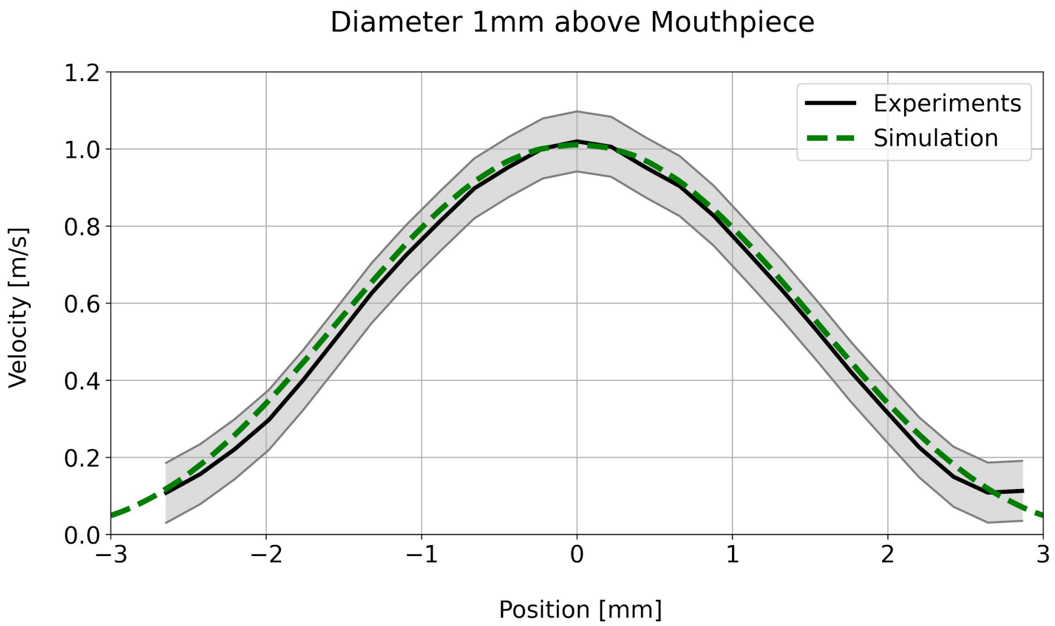
Deterministic:

- Root Mean Square Error (RMSE)

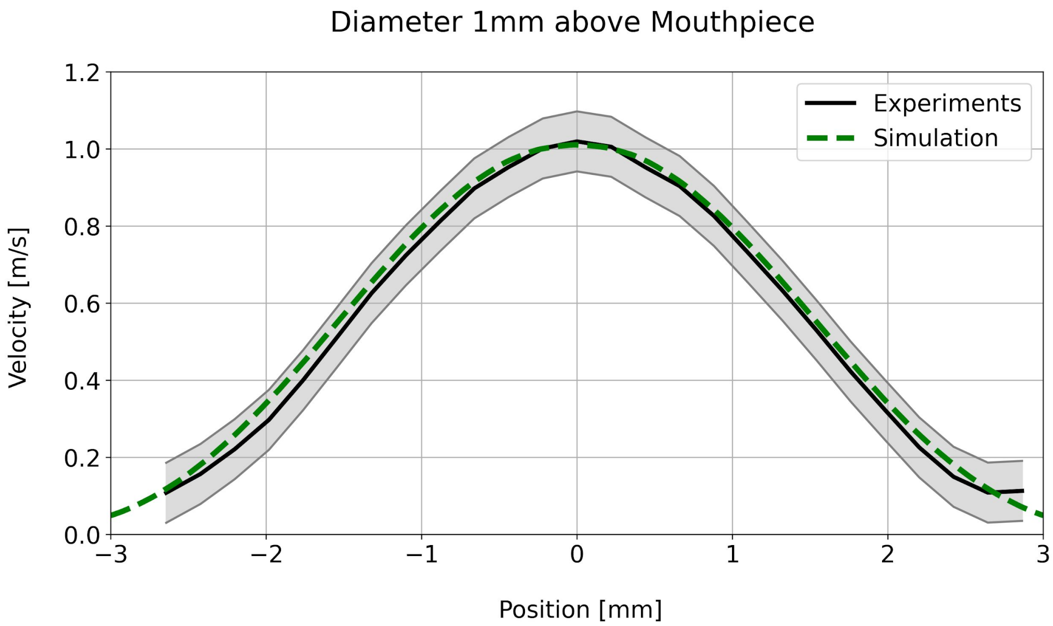
$$d_{rmse} = \sqrt{\frac{1}{N}\sum(P_i - D_i)^2}$$

K. A. Maupin and L. P. Swiler. Validation Metrics for Deterministic and Probabilistic Data. Sandia technical report (2017).

Credibility > Validation > Comparison

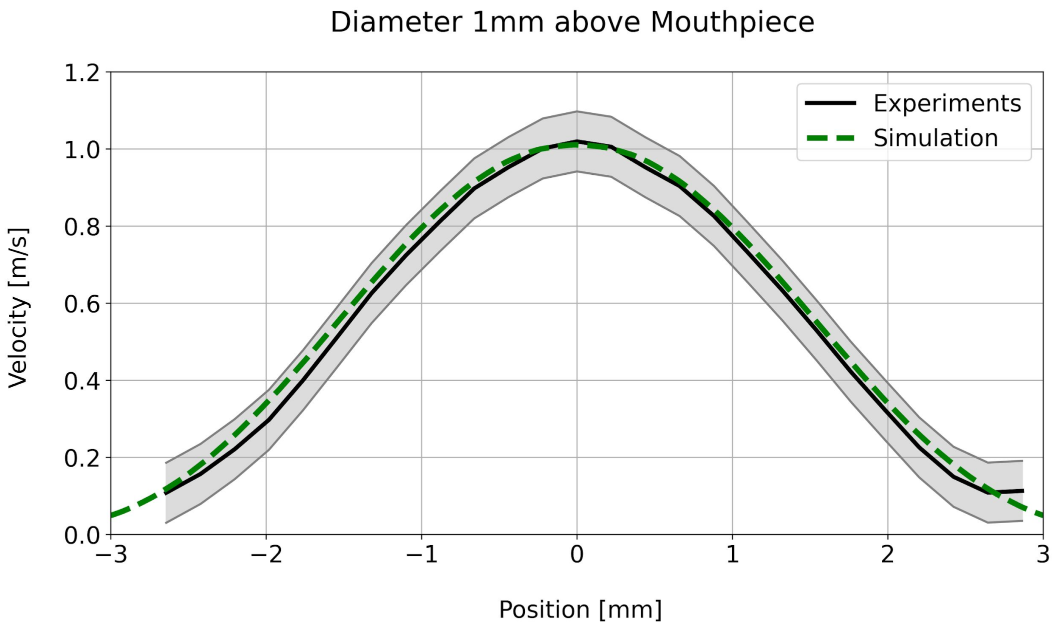


Credibility > Validation > Comparison



	Difference	RMSE
Max Velocity	-0.00893 m/s	0.00631 m/s
Mean Velocity	0.04649 m/s	0.03288 m/s

Credibility > Validation > Comparison



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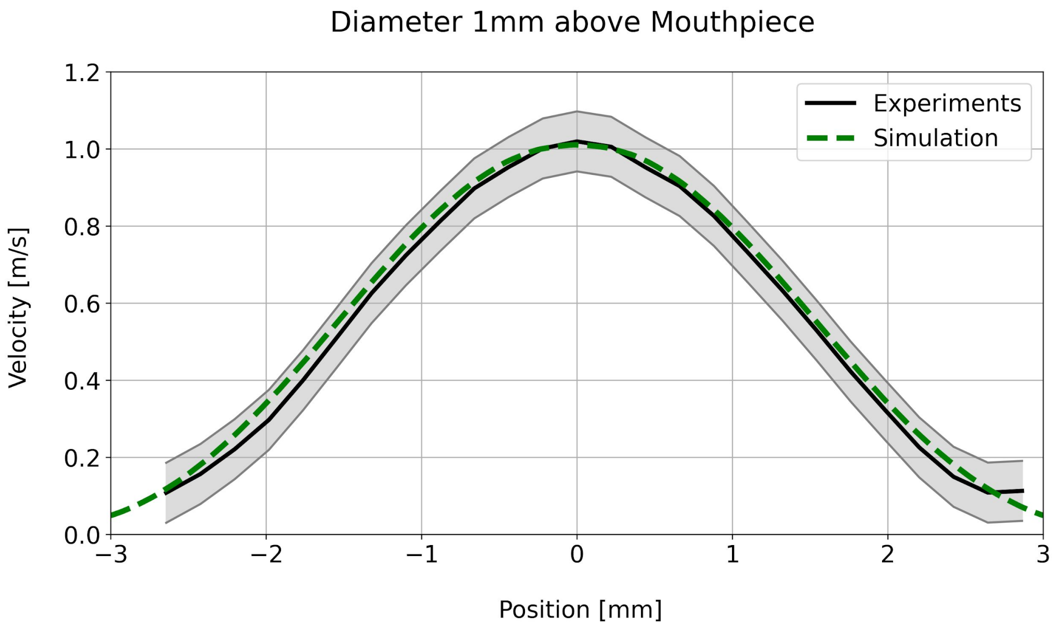


	Difference	RMSE
Max Velocity	-0.00893 m/s	0.00631 m/s
Mean Velocity	0.04649 m/s	**0.03288 m/s**

Validation Study Summary

Qualitative agreement is adequate

Deterministic validation concurs

$$Error_{vel} = Error_{sim} - Error_{exp}$$

- $Error_{max} = 0.00631 m/s$
- $Error_{mean} = 0.03288 m/s$

Uncertainties:

$$u_{input} = 0.0140 [m/s]$$

$$u_{num} = 5.8719 \times 10^{-5} [m/s]$$

$$u_D = 0.1348 [m/s]$$

Relevant Notes

- Device to device variability is not critical in the CM&S

$$u_{exp} = 0.1348 [m/s] \qquad u_{sim} = 0.0140 [m/s]$$

- CM&S underestimates the Max velocity
- PIV low density measurements impact Mean Velocity RMSE

Credibility Activities Performed

	ANSYS	**OpenFOAM**
Validation - EDDS	**X**	

Heated Air Flow (HAF)

Credibility > Validation > Comparator

Comparator

- Quantification of test samples
- Quantification of test conditions

Computational Model & Simulation (CM&S)

- Model Form
- Mode Input
    - Quantification of Sensitivities
    - Quantification of Uncertainties

Assessment

- Equivalency of input parameters
- Output comparison

Credibility > Validation > Comparator

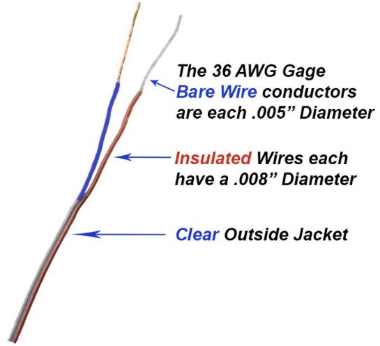
No Vapor Generation

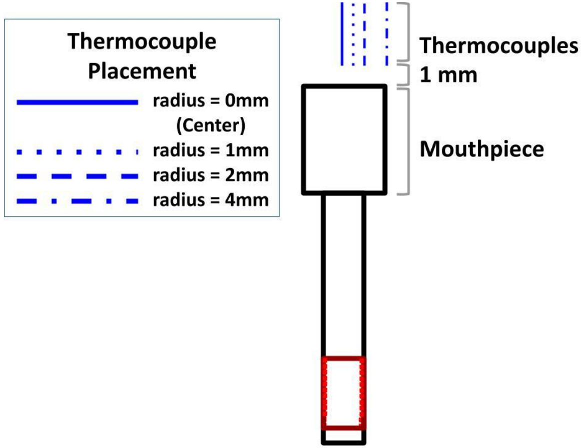
Operating Conditions

- Inlet Volumetric Flow Rate = 0.5 L/min
- Transient State
- Power Applied for 10 seconds
  - Max Power = 1 Watt
- 3 Replicate Experiments (n=3)

Type T thermocouples

- Diameter = 0.127 mm (0.005 in)
- Data Processing = OMB-DAQ-3000





Credibility > Validation > Comparator

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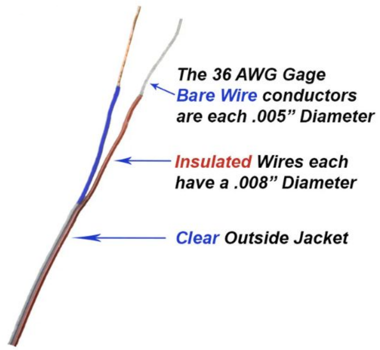
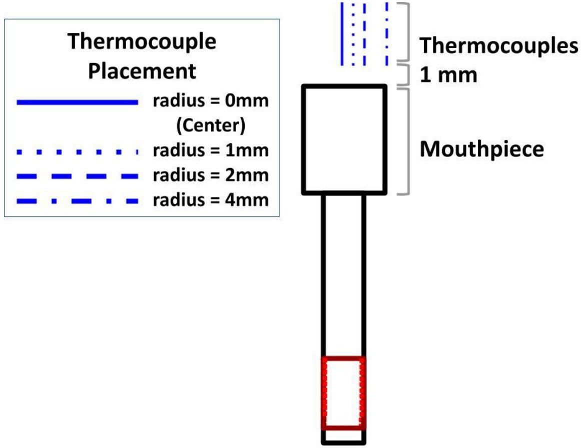


System doesn't guarantee exact thermocouple placement.



Credibility > Validation > Comparator

Sources of Experiment SRQ Uncertainties

b_1 : Standard Thermocouple Measurement Uncertainty
b_2 : Calibration Uncertainty
b_3 : Replicates (3)

SRQ Uncertainty*:

$$u_D = \sqrt{b_1^2 + b_2^2 + b_3^2} = 0.1667$$

*ASME V&V 20-2009 (R2021): Standard for Verification and Validation in Computational Fluid Dynamics and Heat Transfer, (2022).

Credibility > Validation > Comparator

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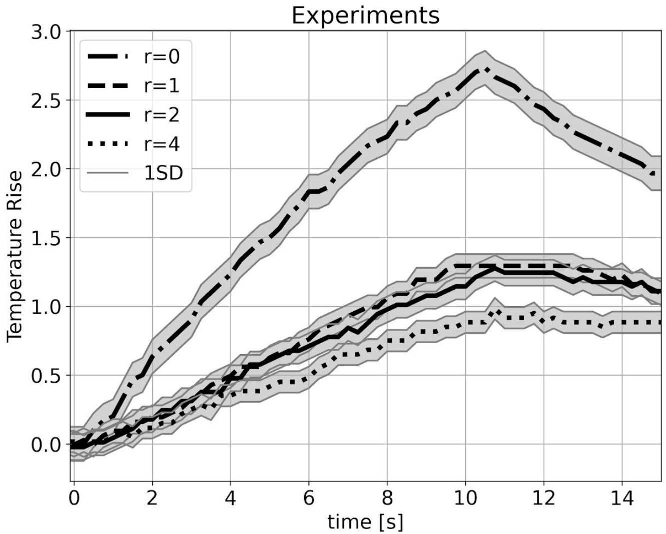

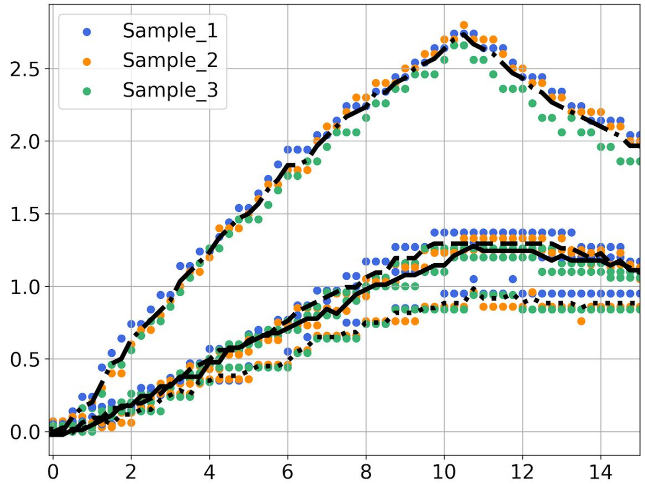

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Credibility > Validation > Comparator

Both 1mm and 2mm radial position are within one SD of each other.

Sources of Experiment SRQ Uncertainties

b_1 : Standard Thermocouple Measurement Uncertainty
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SRQ Uncertainty*:

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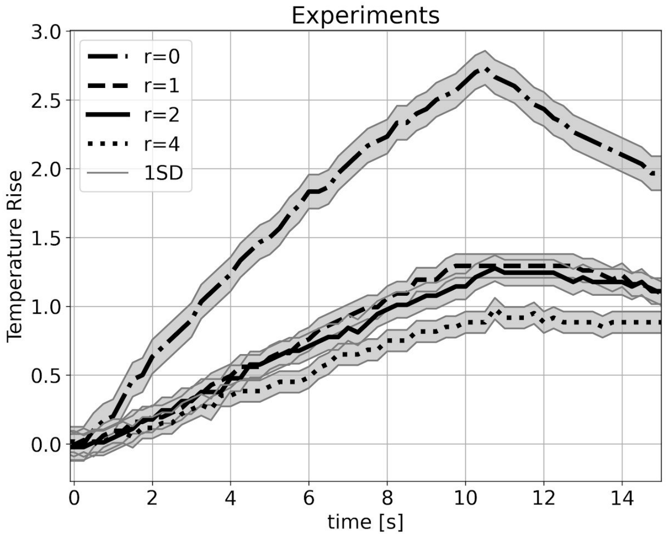

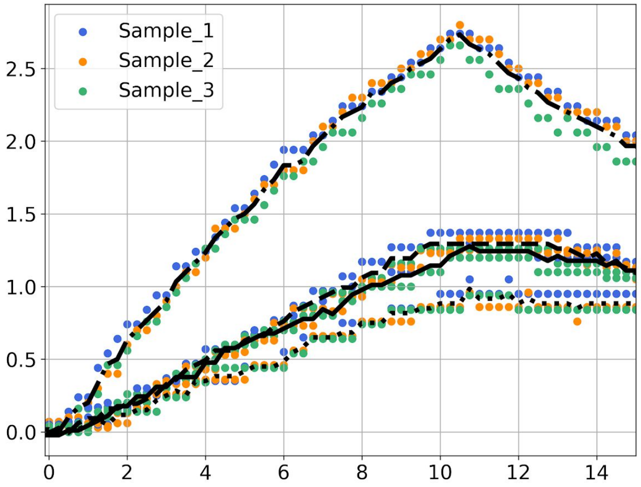

*ASME V&V 20-2009 (R2021): Standard for Verification and Validation in Computational Fluid Dynamics and Heat Transfer, (2022).

Credibility > Validation > CM&S

Comparator

- Quantification of test samples
- Quantification of test conditions

Computational Model & Simulation (CM&S)

- Model Form
- Mode Input
    - Quantification of Sensitivities
    - Quantification of Uncertainties

Assessment

- Equivalency of input parameters
- Output comparison

Credibility > Validation > CM&S > Model Input

Comparator

- Quantification of test samples
- Quantification of test conditions

Computational Model & Simulation (CM&S)

- Model Form
- **Mode Input**
  - **Quantification of Sensitivities**
  - Quantification of Uncertainties

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- Equivalency of input parameters
- Output comparison

Quantification of Sensitivities

Local Sensitivity Analysis

Credibility > Validation > CM&S > Model Input

Comparator

- Quantification of test samples
- Quantification of test conditions

Computational Model & Simulation (CM&S)

- Model Form
- **Mode Input**
  - Quantification of Sensitivities
  - **Quantification of Uncertainties**

Assessment

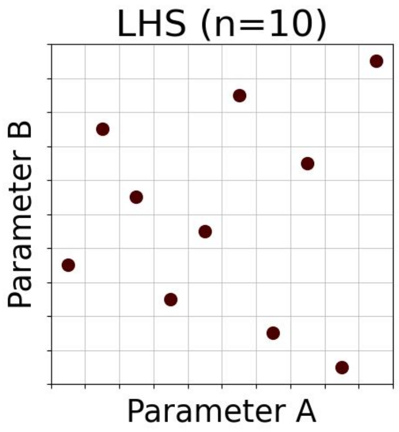
- Equivalency of input parameters
- Output comparison

Quantification of Sensitivities

Local Sensitivity Analysis

Quantification of Uncertainties

Latin Hypercube Sampling (LHS)



Credibility > Validation > CM&S > Uncertainties

Sensitivities: Most influential parameters

- Inlet Airflow
- Time to Maximum Power
- Maximum Power

Uncertainties: Measurement Accuracy

- Input Volumetric Flow Rate: [0.49, 0.51]
- Applied Power: [0.9995, 1.0005]
- Time to Max Power: [1, 3]

Fluke 87 III True RMS Digital Multimeter

Thermal Mass Flowmeter TSI 4100

Credibility > Validation > CM&S > Sampling

Sensitivities: Most influential parameters

- Inlet Airflow
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- Maximum Power

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- Input Volumetric Flow Rate: [0.49, 0.51]
- Applied Power: [0.9995, 1.0005]
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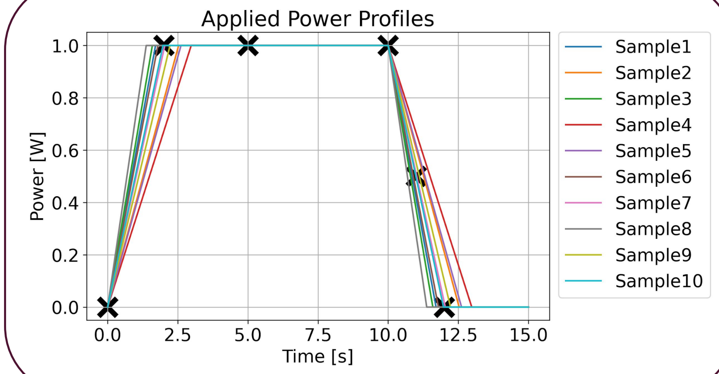
Latin Hypercube Sampling

- Commercial Software
  - n = 10 samples @ 10 hrs/sample
- Open Source Software (Planned)
  - n = 30 samples

DAKOTA
Explore and predict with confidence.

	VFR [L/min]	Power[W]	Time to Max Power[s]
Sample1	0.49444	0.999854	1.708276
Sample2	0.497275	1.000266	2.531816
Sample3	0.506627	0.999797	1.593601
Sample4	0.509589	1.000491	2.981642
Sample5	0.491796	1.000308	2.616563
Sample6	0.494134	0.999897	1.793473
Sample7	0.507415	1.000018	2.036836
Sample8	0.508372	0.999688	1.375442
Sample9	0.499768	1.000112	2.223488
Sample10	0.491104	0.999987	1.973276



Credibility > Validation > CM&S > Sampling

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Latin Hypercube Sampling

- Commercial Software
  - n = 10 samples @ 10 hrs/sample
- Open Source Software (Planned)
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DAKOTA
Explore and predict with confidence.

Automation is **not** possible with ANSYS

	VFR [L/min]	Power[W]	Time to Max Power[s]
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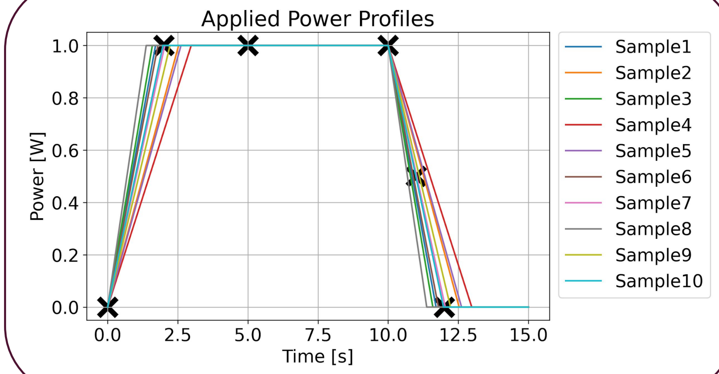
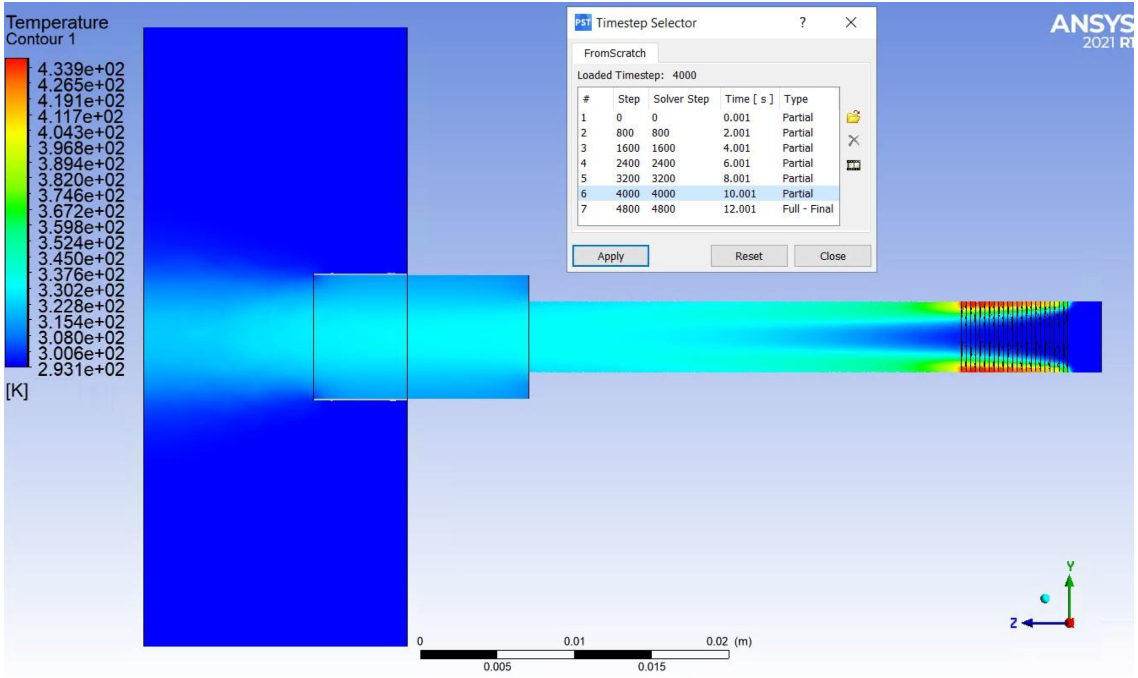


Credibility > Validation > CM&S



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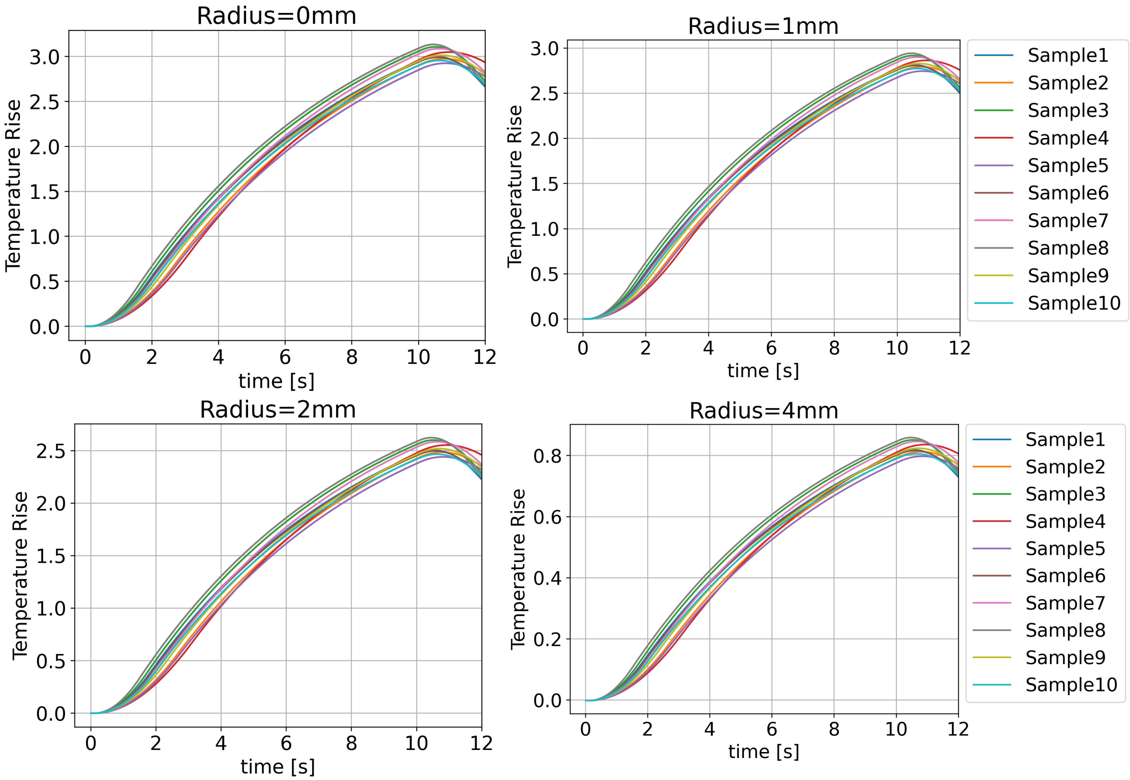

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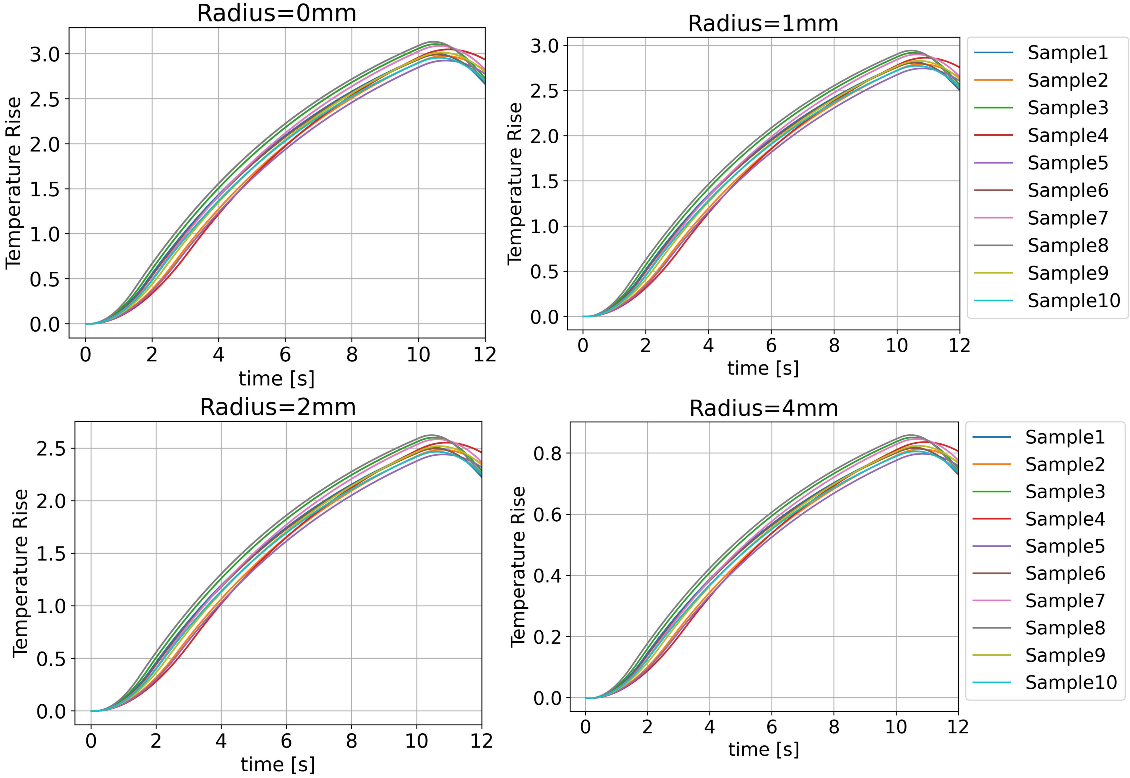
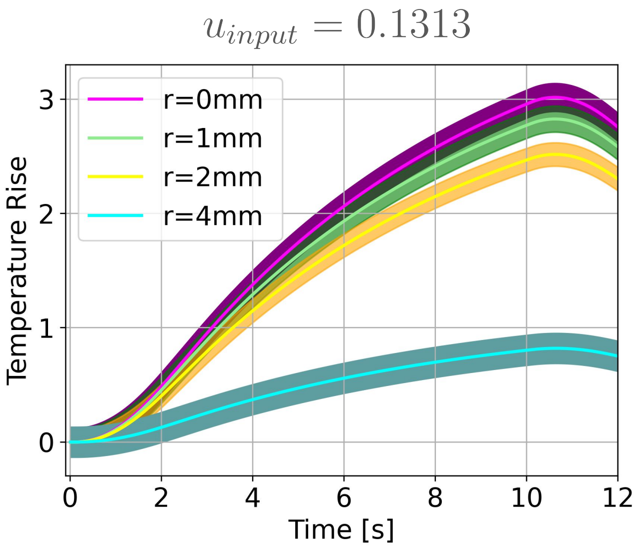
Credibility > Validation > CM&S





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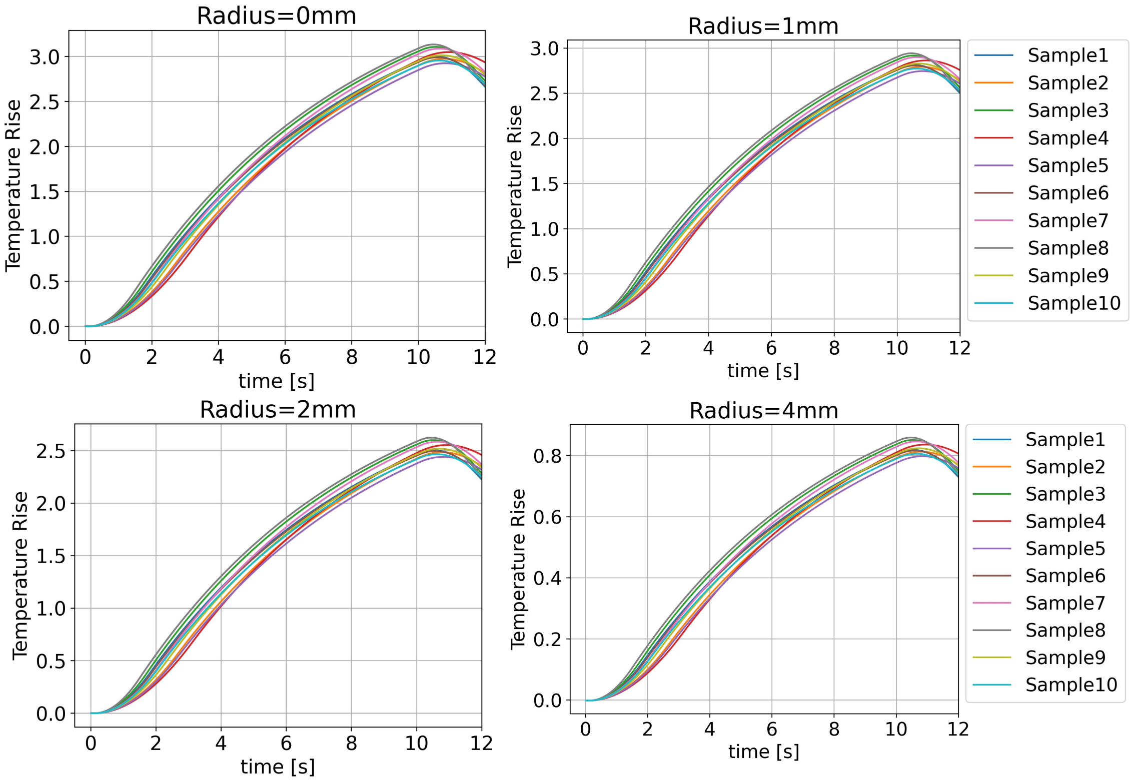
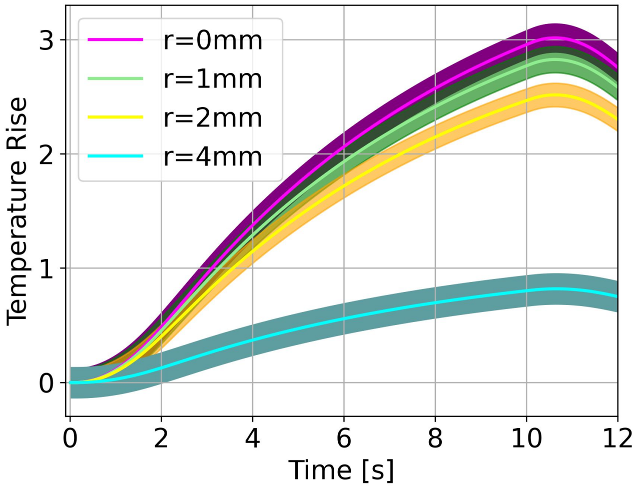


CM&S uncertainty is comparable to comparator uncertainty

$$u_{input} = 0.1313$$



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Credibility > Validation > Assessment

Comparator

- Quantification of test samples
- Quantification of test conditions

Computational Model & Simulation (CM&S)

- Model Form
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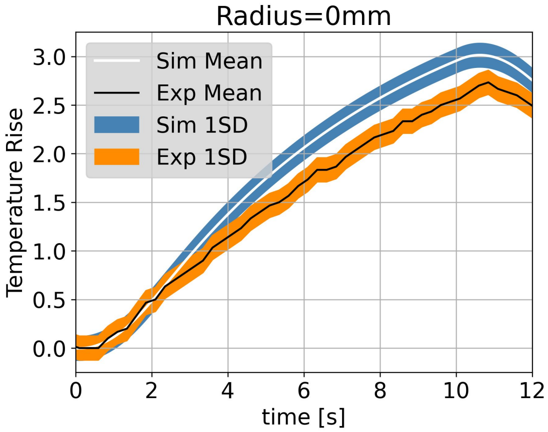
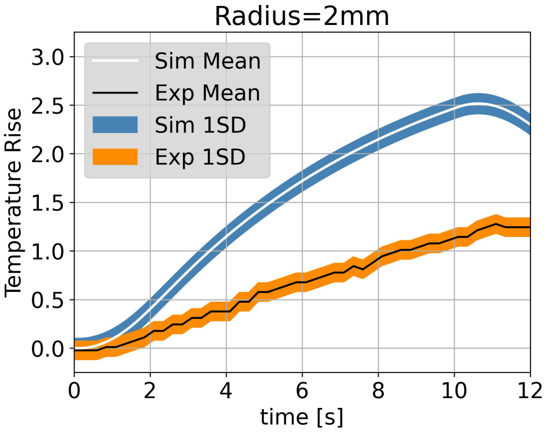
  - Quantification of Uncertainties

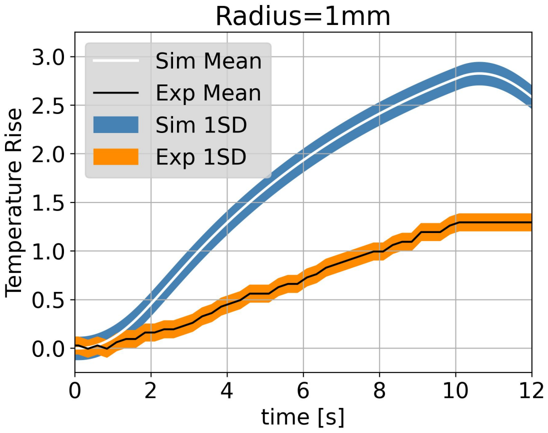
Assessment

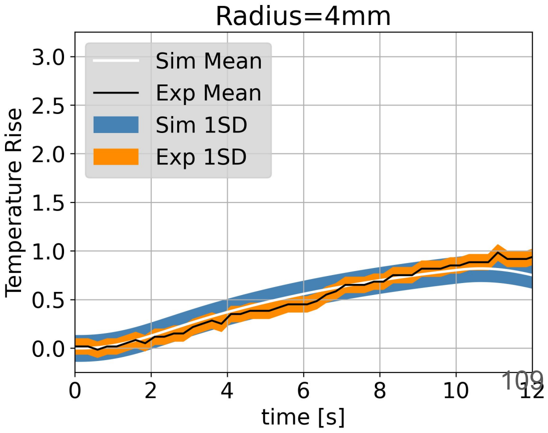
- Equivalency of input parameters
- Output comparison

Credibility > Validation > Assessment > Comparison









Credibility > Validation > Assessment > Comparison

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D. S. Moore, The Basic Practice of Statistics, W. H. Freeman, 4th edition (2007).
National Institute of Standards and Technology (NIST). Tolerance intervals for a normal distribution. NIST Engineering Statistics Handbook.

Credibility > Validation > Assessment > Comparison

Comparator

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Computational Model & Simulation (CM&S)

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Validation Metrics

Deterministic

- RMSE

Probabilistic

- Area Metric
- Confidence Interval
- Tolerance Interval

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National Institute of Standards and Technology (NIST). Tolerance intervals for a normal distribution. NIST Engineering Statistics Handbook.

Validation > Assessment > Comparison > Multi-Metric

Area Validation Metric

(Completed)

Area difference between two Cumulative Distribution Functions

$$d = \int_{-\infty}^{\infty} |F(x) - S_n(x)| dx$$

Confidence Interval (CI)

(Planned)

Difference between two CI centered at the mean

$$CI = \bar{x} \pm z \frac{s}{\sqrt{n}}$$

Tolerance Interval (TI)

(Planned)

Difference between two TI within a certain proportion of the data

$$TI = \bar{x} \pm k_2 s$$

$$k_2 = z_{(1+p)/2} \sqrt{\frac{\nu(1 + 1/n)}{\chi^2_{1-\alpha,\nu}}}$$

D. S. Moore, The Basic Practice of Statistics, W. H. Freeman, 4th edition (2007).
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Credibility > Validation > Assessment > Comparison

Comparator

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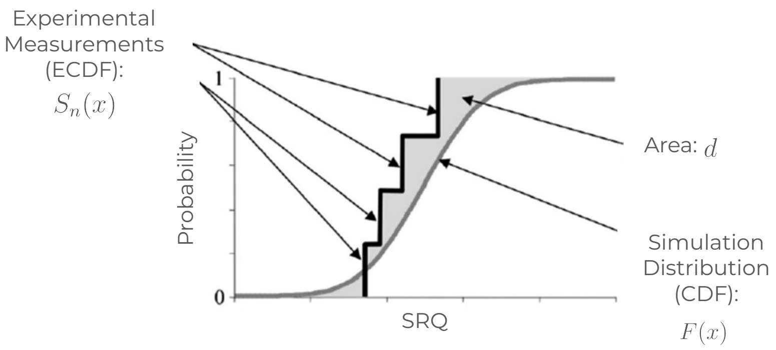
Assessment

- Equivalency of input parameters
- **Output comparison**

Area Validation Metric

Area difference between two Cumulative Distribution Functions (CDF)

$$d = \int_{-\infty}^{\infty} |F(x) - S_n(x)| dx$$



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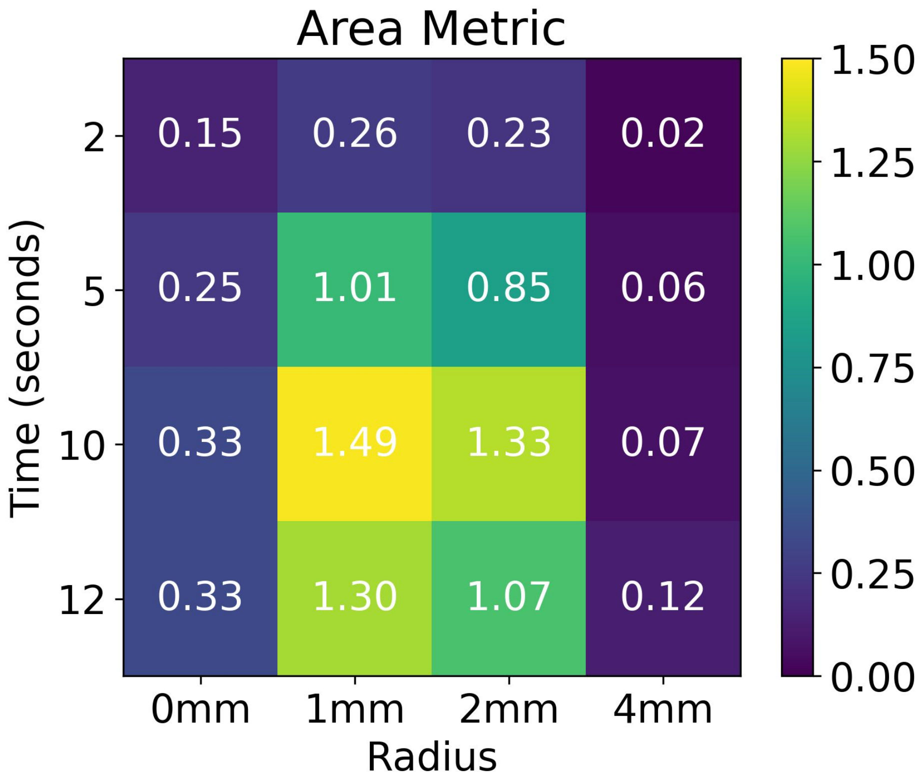
Credibility > Validation > Assessment > Comparison



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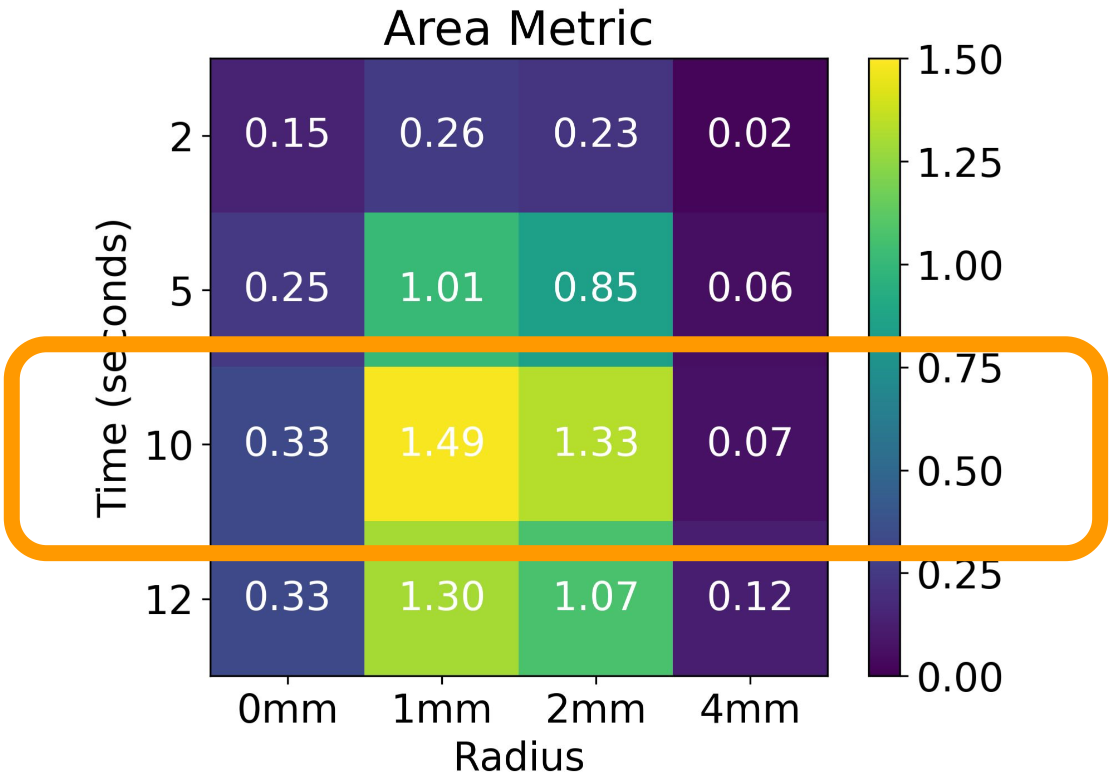

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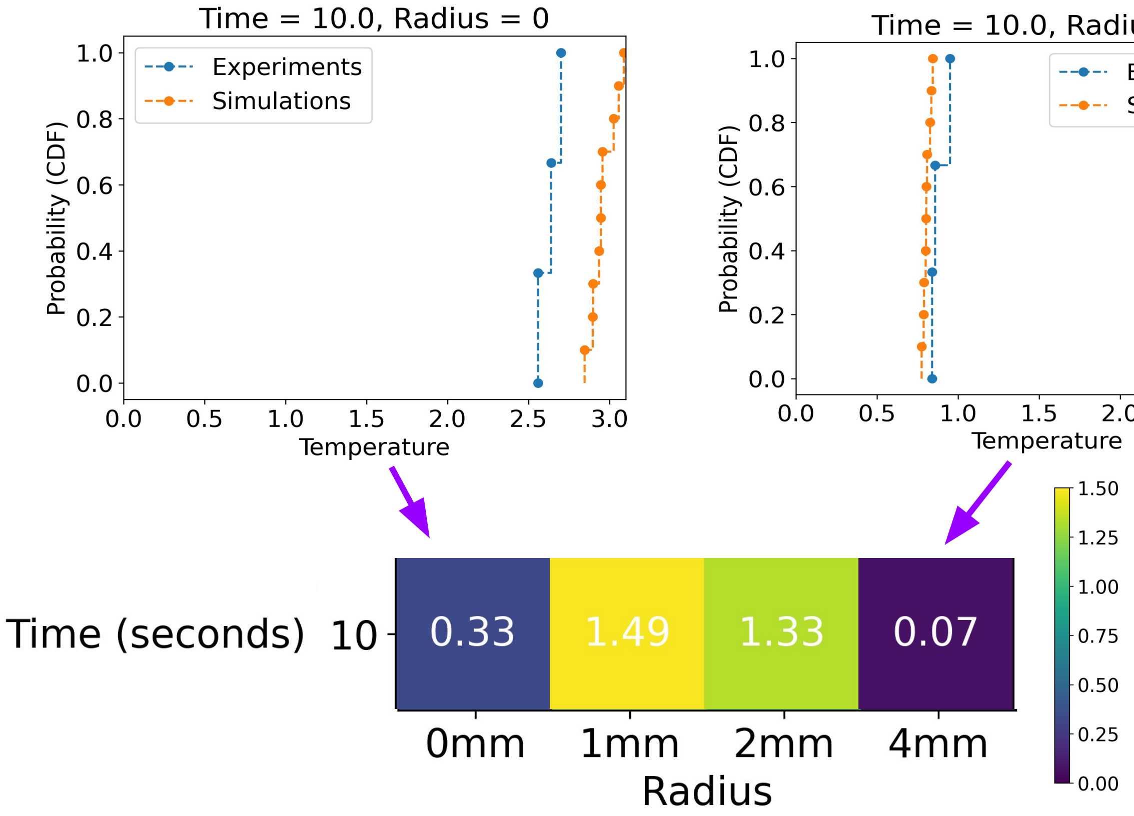

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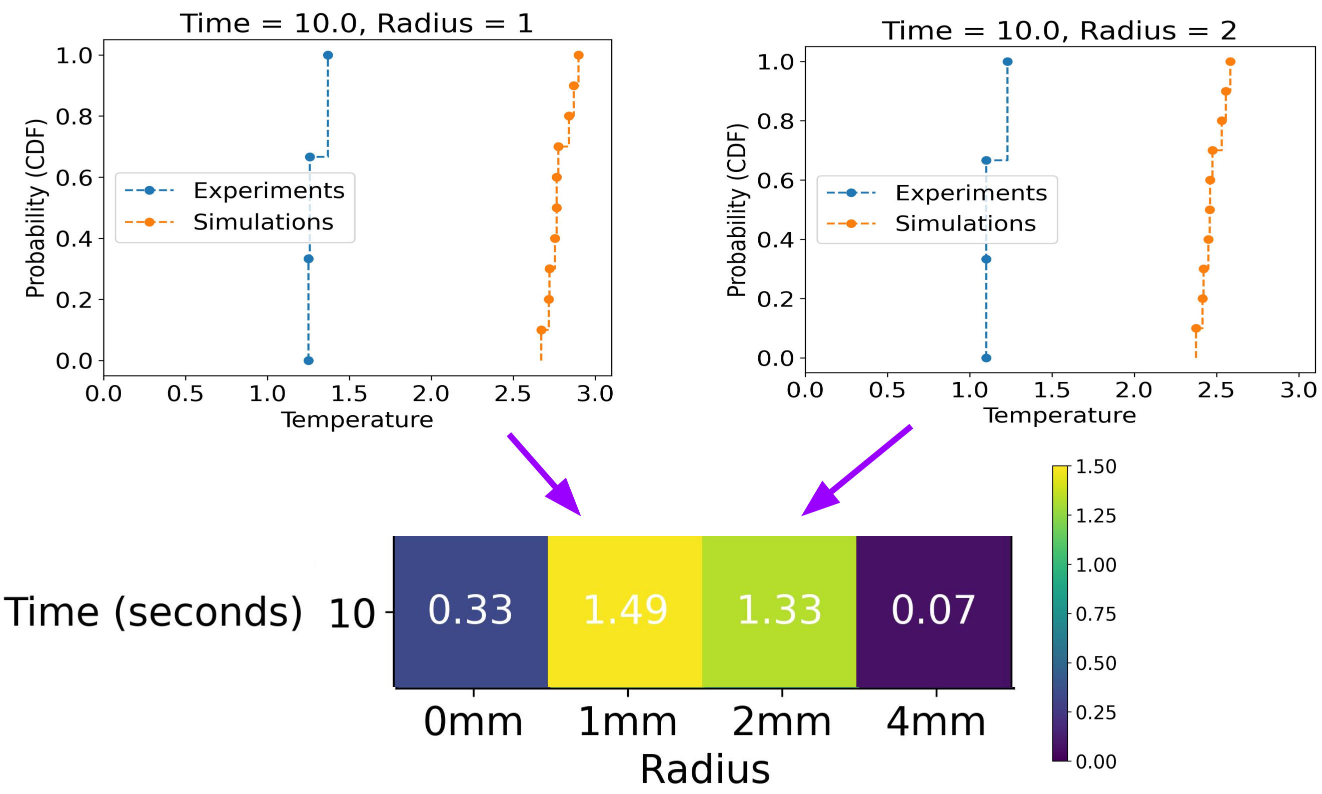
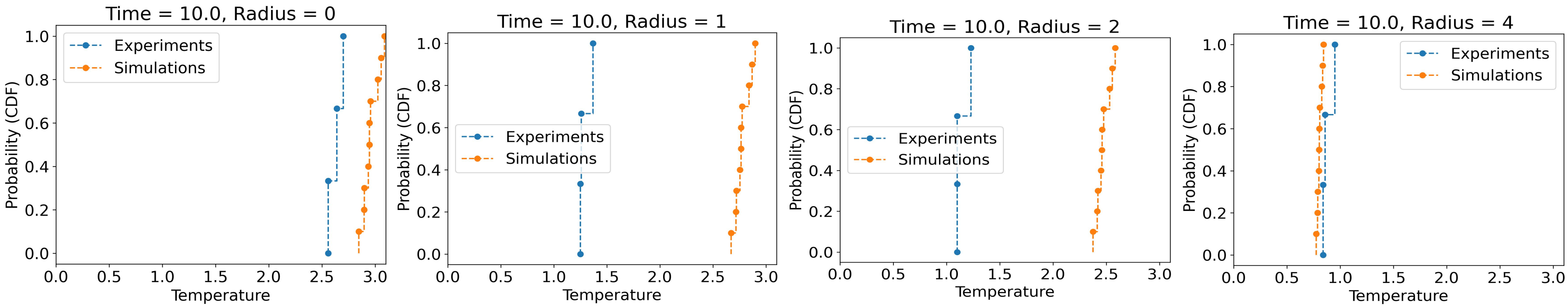
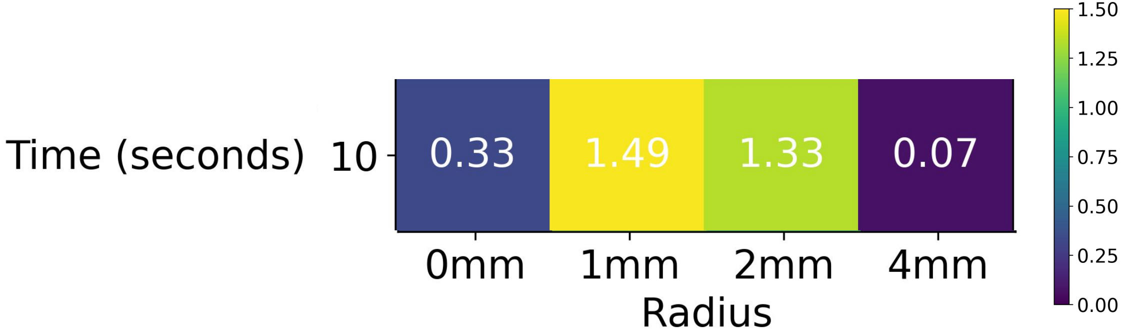


Credibility > Validation > Assessment > Comparison





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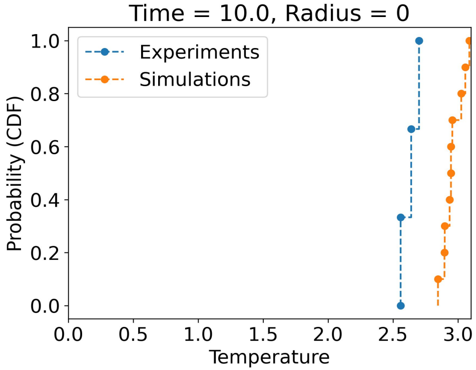

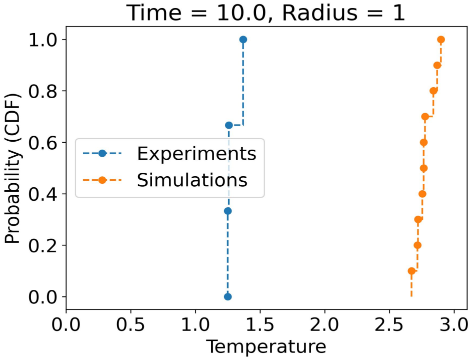

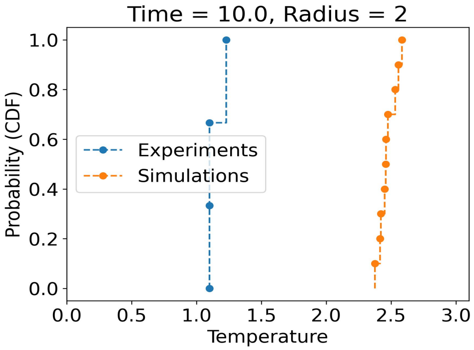

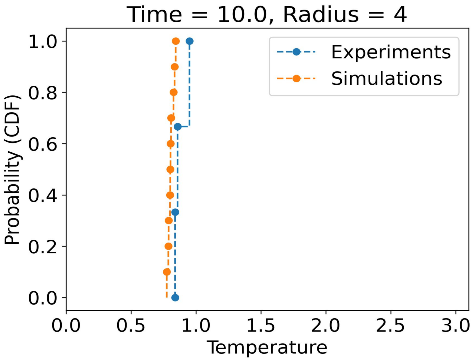

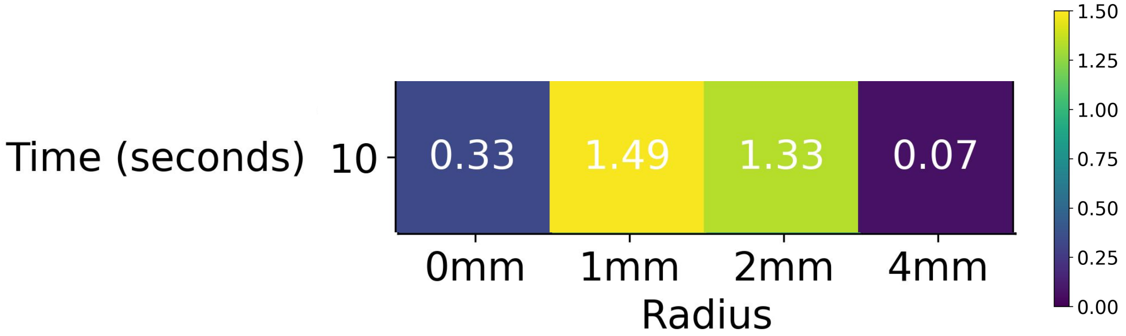

Area Metric doesn’t demonstrate overestimation or underestimation

Credibility > Validation > Assessment > Comparison

Deterministic

- Root Mean Square Error (RMSE)

$$d_{rmse} = \sqrt{\frac{1}{N}\sum(P_i - D_i)^2}$$

		r = 0 (Center)	r = 1 mm	r =2 mm	r = 4 mm
Max Temperature Rise	Difference	0.28061	1.53140	1.23841	-0.16487
	RMSE	0.19842	1.08286	0.87569	0.11658
Mean Temperature Rise	Difference	0.19322	0.89454	0.75116	-0.07778
	RMSE	0.13662	0.63253	0.53115	0.05500

Credibility > Validation > Assessment > Comparison

Deterministic

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	RMSE	0.19842	1.08286	0.87569	0.11658
Mean Temperature Rise	Difference	0.19322	0.89454	0.75116	**-0.07778**
	RMSE	0.13662	0.63253	0.53115	0.05500

Credibility > Validation > Assessment > Comparison

Deterministic

- Root Mean Square Error (RMSE)

$$d_{rmse} = \sqrt{\frac{1}{N}\sum(P_i - D_i)^2}$$

		r = 0 (Center)	r = 1 mm	r =2 mm	r = 4 mm
Max Temperature Rise	Difference	0.28061	1.53140	1.23841	-0.16487
	RMSE	**0.19842**	1.08286	0.87569	**0.11658**
Mean Temperature Rise	Difference	0.19322	0.89454	0.75116	-0.07778
	RMSE	**0.13662**	0.63253	0.53115	**0.05500**

Validation Study Summary

Qualitative Agreement is adequate for

- Center (Maximum)
- 4mm radius (Minimum)

Deterministic RMSE:

- SRQ Mean @ Center: 0.13662
- SRQ Mean @ r = 4mm: 0.05500

Area Metric

- SRQ Mean @ Center: d = [0.15 , 0.33]
- SRQ Mean @ r = 4mm: d = [0.02, 0.12]

Uncertainties

$$u_{num} = 5.8719 \times 10^{-5}$$
$$u_{input} = 0.1313$$
$$u_D = 0.1667$$

Relevant Notes

Thermocouple placement is not guaranteed

Sample generation automation is not possible with ANSYS

The 1mm and 2mm radial position are within a SD

CM&S uncertainty is comparable to comparator uncertainty

$$u_{exp} = 0.1667 \qquad u_{sim} = 0.1313$$

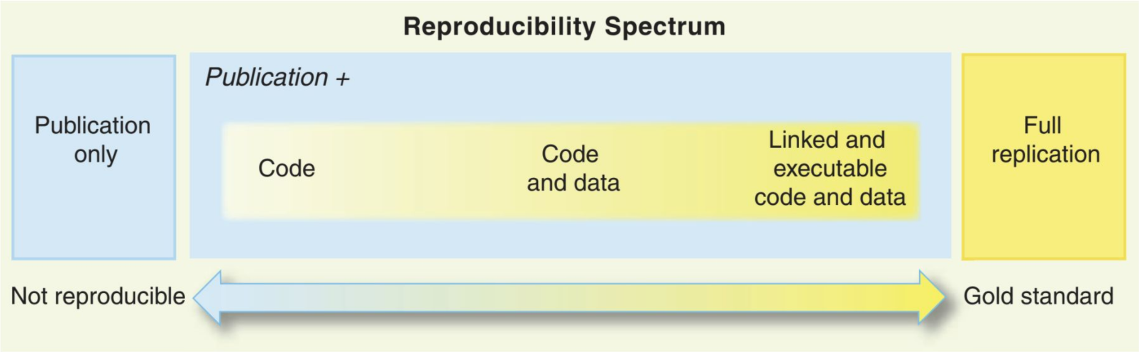
The Area Metric doesn't show overestimation or underestimation.

Credibility Activities Performed

	ANSYS	OpenFOAM
Validation - EDDS	**X**	

Reproducibility

Reproducibility

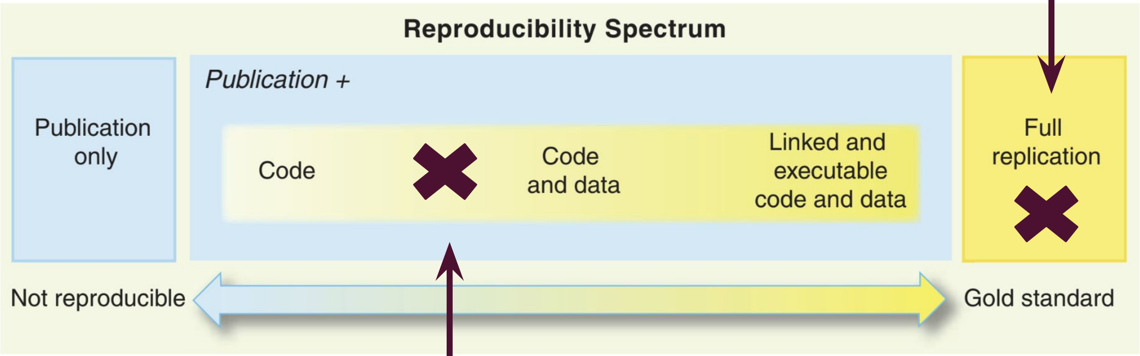


R. D. Peng, Reproducible Research in Computational Science, Science 334, 1226– 1227 (2011).

Reproducibility

Commercial Solver (ANSYS)

- AFM
- HAFM



Open Source Solver (OpenFOAM)

- AFM
- HAFM

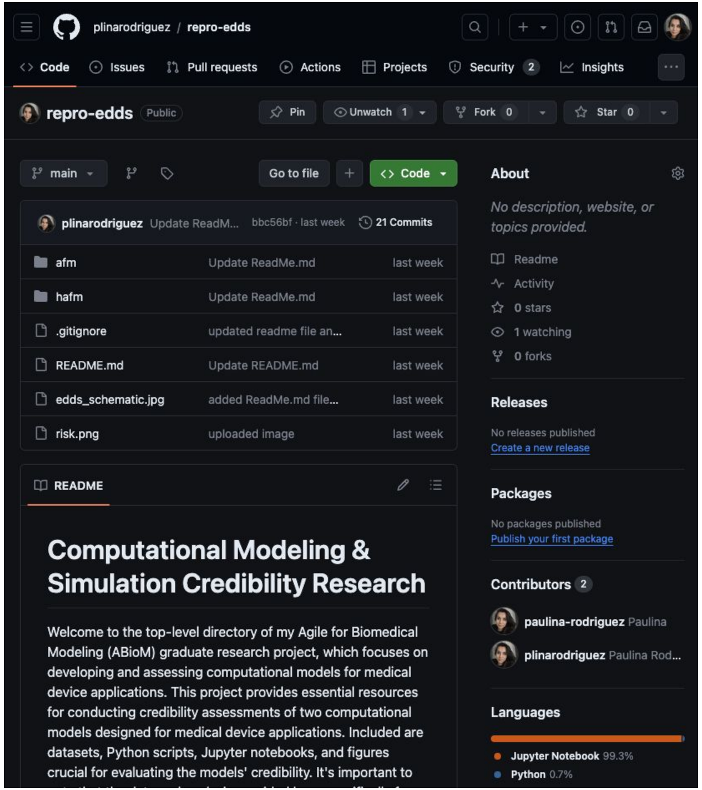
National Academies of Sciences and Medicine, Reproducibility and Replicability in Science, The National Academies Press, Washington, DC (2019).

Reproducibility > Commercial Software (ANSYS)

Prioritize post-processing and credibility analysis.

GitHub repository (**`repro-edds`**):

```
repro-edds
├ AFM
│ ├ model_experiments
│ │ ├ data
│ │ ├ figures
│ │ ├ airflow_model-experiments.ipynb
│ │ ├ data_processing.py
│ │ └ problem_description.py
│ ├ verification
│ └ validation
└ HAFM
  ├ model_experiments/
  ├ sampling/
  └ validation/
```



Reproducibility > Open Source Software (OpenFOAM)

Entire end-to-end reproducibility

- Container
  - Computational Model
  - System Configurations
- Zenodo for large files
  - Mesh
  - Container Image as an archive
- Github repository (**`repro-edds`**)
  - Credibility Assessment
  - Post-Processing
  - Guidance for Accessing Workflow

Reproducibility > Assessment (Planned)

1. Recruit Student Participant(s)
   - Find graduate or undergraduate students
2. Reproducibility Walk Through
   - Provide overview of commercial and open-source workflows
3. Execution
   - Have students go through each workflow and document experiences
4. Qualitative Survey
   - Administer a survey on usability and overall experience
5. Usability Evaluation
   - Assess feedback and compare workflow performance

Summary

Current Efforts

Status of Aims

Status of Publications

Timeline

Current Work

Transitioning to OpenFOAM

- Mesh Conversion ANSYS to OpenFOAM

Validation Metrics

- Implement confidence intervals on ANSYS HAFM
- Implement tolerance intervals on ANSYS HAFM
- Reviewing validation metrics for small sample datasets

Containerization Feasibility

- Docker
- Aptainer (Singularity)
- Podman

HPC Environment

- OpenFOAM Installation
    - Starting with pipe flow test case
    - Run mesh decomposition and solution reconstruction

High Performance Computing (HPC)

Sandia National Laboratories Solo cluster

13,464 compute cores

374 compute nodes

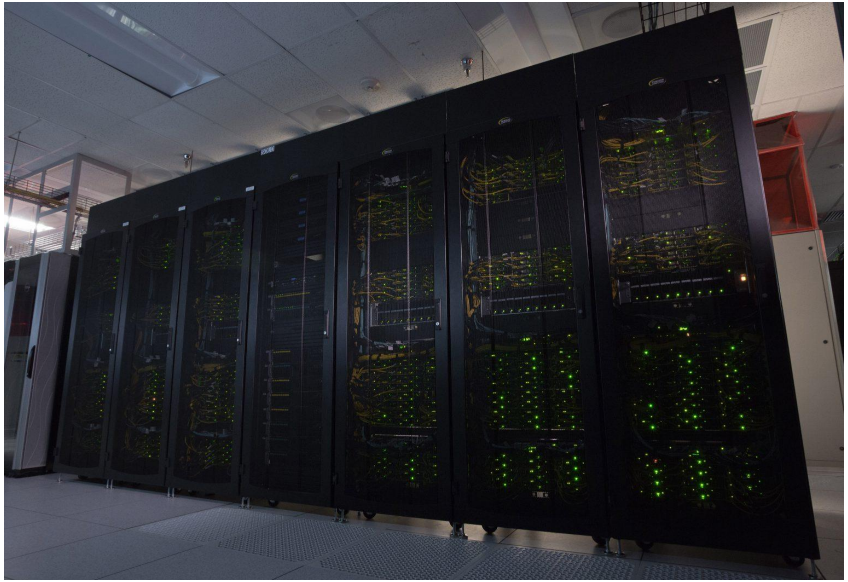
36 cores per node

Linux 7 operating system

Modules for configuring environment

- *Dakota for automating UQ*

Message Passing Interface (MPI)



Timeline - Micro - Aim 1: Computational Case Study

		Not Started	In Progress	Completed
Aim 1.1: Credibility Plan	Define medical device system			X
	Define COU, QOI, and risk			X
	Define Sources of Evidence			X
	Choose SRQ's			X
Aim 1.2: Computational Model	CM&S: AFM & ANSYS			X
	CM&S: AFM & OpenFOAM	X		
	CM&S: HAFM & ANSYS			X
	CM&S: HAFM & OpenFOAM	X		
Aim 1.3: Reproducibility	Reproducible Workflow: AFM & ANSYS			X
	Reproducible Workflow: AFM & OpenFOAM	X		
	Reproducible Workflow: HAFM & ANSYS			X
	Reproducible Workflow: HAFM & OpenFOAM	X		
Aim 1.4: HPC	Mesh Decomposition: pipe flow & OpenFOAM		X	
	Mesh Decomposition: HAFM & OpenFOAM	X		
	Scalability study: pipe flow & OpenFOAM		X	
	Scalability study: HAFM & OpenFOAM	X		

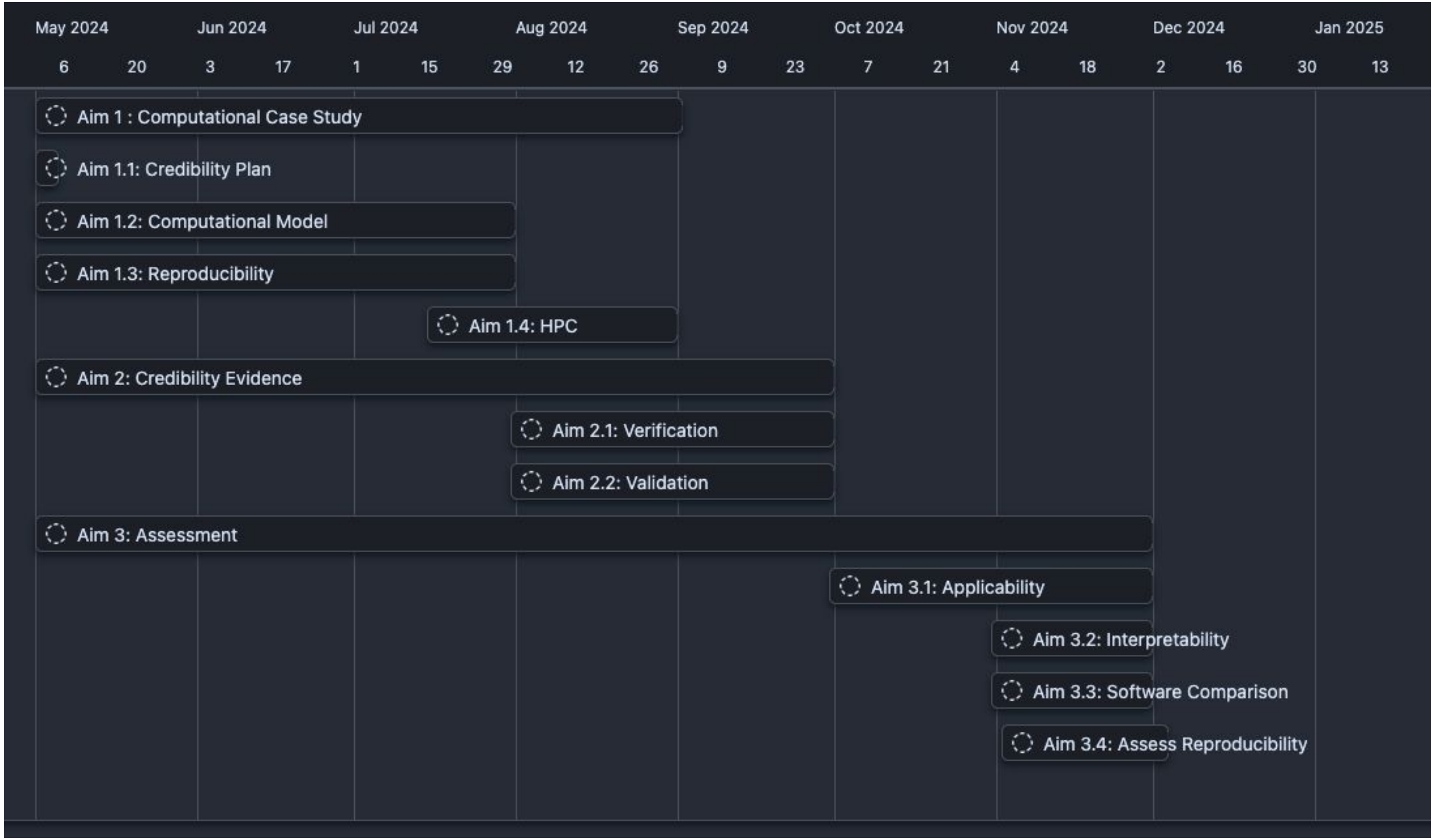
Timeline - Micro - Aim 2: Credibility Evidence

		Not Started	In Progress	Completed
Aim 2.1: Verification	Code Verification - ANSYS			X
	Code Verification - OpenFOam	X		
	Calculation Verification - ANSYS			X
	Calculation Verification - OpenFOam	X		
Aim 2: Validation	Validation experiments - AFM			X
	Validation experiments - HAFM			X
	Propagate uncertainties - AFM - ANSYS	N/A	N/A	N/A
	Propagate uncertainties - AFM - OpenFOAM	X		
	Propagate uncertainties - HAFM - ANSYS			X
	Propagate uncertainties - HAFM - OpenFOAM	X		
	Multi-metric validation - AFM - ANSYS			X
	Multi-metric validation - AFM - OpenFOAM	X		
	Multi-metric validation - HAFM - ANSYS			X
	Multi-metric validation - HAFM - OpenFOAM	X		
	Novel modified metrics	X		

Timeline - Micro - Aim 3: Assessment

		Not Started	In Progress	Completed
Aim 3.1: Applicability	Modified CM&S - HAFM & ANSYS		X	
	Modified CM&S - HAFM & OpenFOAM	X		
Aim 3.2: Interpretability	Report for Regulator	X		
Aim 3.3: Software Comparison	ANSYS CM&S - AFM			X
	ANSYS CM&S - HAFM		X	
	OpenFOAM CM&S - AFM	X		
	OpenFOAM CM&S - HAFM	X		
	Comparison	X		
Aim 3.4: Assess Reproducibility	Consolidate Study - ANSYS			X
	Consolidate Study - OpenFOAM	X		
	Test Reproducibility - ANSYS	X		
	Test Reproducibility - OpenFOAM	X		

Timeline - Macro



Publication Plan

Topic	Journal	Status	Date
ANSYS HAFM V&V Analysis	JVVUQ	In Progress	06/2024
Multi-Metric Validation	JVVUQ	Planned	12/2024
Applicability Analysis HAFM OpenFOAM	JVVUQ	Planned	01/2025
Commercial vs. Open-Source Software	SIAM	Planned	01/2025

Why is this work important?

CM&S Trustworthiness

Why is this work important?

CM&S Trustworthiness

- Credibility (risk informed)
- Reliability

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What credibility activities to perform & with what level of rigor?

Why is this work important?

CM&S Trustworthiness

- Credibility (risk informed)
- Reliability

⬇

Interpretability

What credibility activities to perform & with what level of rigor?

Why is this work important?

CM&S Trustworthiness

- Credibility (risk informed)
- Reliability

⬇

Interpretability

⬇

Informed Decision Making

What credibility activities to perform & with what level of rigor?

Why is this work important?

CM&S Trustworthiness

- Credibility (risk informed)
- Reliability

⬇

Interpretability

⬇

Informed Decision Making

What credibility activities to perform & with what level of rigor?

How to communicate the results to non-expert decision makers?

Thank You!

Questions?

This research was funded by the Department of Energy Computational Science Graduate Fellowship (DE-SC0022158).

Backup Slides

DISSERTATION PROPOSAL COMMITTEE

Dr. Lorena A. Barba (Advisor), Department of Mechanical and Aerospace Engineering, The George Washington University

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Dr. Matthew Myers, Division of Applied Mechanics, U.S. Food and Drug Administration

Dr. Brian Carnes, Department of VVUQ and Credibility Processes, Sandia National Laboratories

Aim 1: Computational Case Study

Aim 1.1: Credibility Plan. Establish credibility-building practices following FDA guidelines,ASME V&V 10, 20, 40 standards that include:

- Defining the Context of Use(COU),Question of Interest(QOI),medical device system for an Electronic Drug Delivery System (EDDS), and risk assessment.
- Developing the computational model plan and identify primary vs. secondary sources of evidence.
- Defining system response quantities (SRQs) relevant for assessment.

Aim 1.2: Computational Model. Develop and implement a physics based computational model of the EDDS medical device. This includes an implementation using a commonly used commercial and open source software by the medical device industry.

- Develop a computational model of an electronic drug delivery system (EDDS) by breaking down the physics complexity into an Airflow EDDS and Heated Airflow EDDS model.
- Develop computational models using both commercial (ANSYS) and open- source (OpenFOAM) software.

Aim 1.3: Reproducibility. Develop and implement a reproducible workflow tailored to the computational model software, addressing its limitations in shareability.

- Establishareproducibleworkflowforbothcommercia landopen-sourcemod- els.
- Implement Reproducibility Documentation Including Post-processing data,Python scripts, and Jupyter notebooks.

Aim 1.4: High-Performance Computing (HPC). Utilize HPC resources for improving CM&S quality.

- Optimize mesh decomposition for parallelization. (OpenFOAM CM&S)
- Perform a scalability study on the OpenFOAM model. (Note that higher quality meshes are required for OpenFOAM results to be comparable to ANSYS.)

Aim 2: Credibility Evidence

Aim 2.1: Verification. Perform and assess CM&S verification by examining the mathematical and numerical methods, ensuring correctness and accuracy in representing the underlying physical phenomena.

- Conduct and assess Code Verification, encompassing Software Quality Assurance (SQA) and Numerical Code Verification (NCV).
- ConductandasseessCalculationVerification,encompassing DiscretizationEr- ror, Numerical Solver Error (NSE), and Use Error.

Aim 2.2: Validation. Perform and assess the CM&S capabilities to accurately depict real-world phenomena, using laboratory experiments as a reference point, and accounting for inherent uncertainties in the validation process.

- Conduct and document validation experiments, capturing all measurements, uncertainties, and operating conditions for the device.
- Apply Latin Hypercube Sampling (LHS) to propagate input uncertainties to generate statistically significant samples for the CM&S.
- Implement a multi-metric approach to compare the CM&S with physical laboratory experiments, using both deterministic and probabilistic validation metrics.
- Investigate the creation of novel modified metrics addressing small sample sizes and safety considerations specific to biomedical datasets.

Aim 3: Assessment

Aim 3.1: Applicability. Modify the CM&S for applicability to the COU and conduct an assessment of its capabilities to inform the QOI.

Aim 3.2: Interpretability. Create a comprehensive CM&S credibility evidence report, complete with an applicability analysis, to provide non-experts with the necessary information for making informed decisions regarding medical devices based on risk assessment.

Aim 3.3: Software Comparison. Conduct a comparative analysis of commercial and open-source software performance, considering their respective applications in the medical device industry. Identify and highlight any shortcomings that may impact regulatory decision-making for medical devices.

Aim 3.4: Assess Reproducibility. Evaluate the reproducibility plan by testing whether a user can achieve consistent results in the CM&S study by following the digital workflow. Conduct a qualitative usability assessment survey to gauge the usability of the workflow while confirming consistent outputs.

Status of Aims

Aim 1: Computational Case Study

Credibility Plan Development

- Developing comprehensive credibility plans
- Ensuring credibility objectives are met throughout the process

Model Creation with ANSYS

- Creating Computational Models (CM&S) using ANSYS
- Developing models for Airflow Model (AFM) and Heated Airflow Model (HAFM) systems

Reproducibility Workflow Implementation

- Establishing reproducibility workflows for AFM and HAFM
- Executing reproducibility plans using ANSYS CM&S

Aim 2: Credibility Evidence

Verification, Validation, and Uncertainty Quantification (VVUQ)

- Conducting verification and validation studies
- Performing uncertainty quantification for AFM and HAFM models using ANSYS CM&S

Aim 3: Assessment

Comparative Software Analysis

- Comparing software tools for computational modeling
- Assessing reproducibility workflows across different platforms

Interpretability and Performance Evaluation

- Generating interpretable reports to assess CM&S usability
- Evaluating applicability, interpretability, and performance of computational models

ANSYS CFX (Coupled Solver):

Mesh Generation then Overlay Mesh on Governing Equations: The mesh data (cell locations, volumes, faces) is used within the governing equations (momentum, continuity) during the solution process.

Initialize: Set initial conditions for velocity, pressure, and other variables on the mesh cells.

Momentum Equation: Solve the momentum equation for a predicted velocity field that may not satisfy continuity, using the mesh information.

Pressure Correction Equation: Derive a pressure correction equation from the continuity equation and predicted velocity, considering the mesh cell connectivity.

Solve Pressure Correction: Solve the pressure correction equation to obtain a pressure field update on the mesh.

Correct Velocity: Update the velocity field using the pressure correction to ensure mass conservation throughout the mesh.

Solve Scalar Equations (optional): Solve transport equations for other variables like temperature or turbulence quantities using the corrected velocity field and mesh information.

Convergence Check: Check for convergence of residuals (imbalances) in velocity, pressure, and other variables on the mesh.

Iterate: If not converged, return to step 4 with the updated solution fields on the mesh.

OpenFOAM (Segregated Solver with PIMPLE):

Mesh Generation:

Initialize: Set initial conditions for velocity, pressure, and other variables on the mesh cells.

Predictor Step:

Solve momentum equation for a predicted velocity field (similar to CFX step 2), using mesh information.

Update other variables (like turbulence) based on the predicted velocity on the mesh.

Pressure Correction Step:

Derive a pressure correction equation from the continuity equation using the predicted velocity and considering mesh connectivity.

Solve the pressure correction equation to obtain a pressure field update on the mesh.

Corrector Step:

Correct the velocity field using the pressure correction (similar to CFX step 5).

Optionally, perform a second corrector step for better convergence (PISO-like).

Solve Scalar Equations: Solve transport equations for other variables like temperature or turbulence quantities using the corrected velocity field and mesh information.

Convergence Check: Check for convergence of residuals in velocity, pressure, and other variables on the mesh.

Iterate: If not converged, return to step 2 with the updated solution fields on the mesh.

ANSYS CFX (Coupled Solver):

Mesh Generation: Create a mesh encompassing both the fluid and solid domains.

Overlay Mesh on Governing Equations: The mesh data is used within the governing equations (momentum, continuity, energy) for both fluid and solid regions.

Define Material Properties: Assign material properties (density, viscosity, thermal conductivity, etc.) to fluid and solid regions based on their mesh elements.

Define Heat Source: Specify the heat source term in the energy equation for the solid region, considering its mesh distribution.

Initialize: Set initial conditions for velocity, pressure, temperature (in both fluid and solid) on the mesh cells.

Momentum Equation: Solve the momentum equation for a predicted velocity field that may not satisfy continuity, using the mesh information.

Energy Equation (Fluid): Solve the energy equation for the fluid domain to determine temperature distribution, considering the mesh and velocity field.

Energy Equation (Solid): Solve the energy equation for the solid domain to determine temperature distribution, incorporating the heat source term and mesh data.

Pressure Correction Equation: Derive a pressure correction equation from the continuity equation and predicted velocity, considering the mesh cell connectivity.

Solve Pressure Correction: Solve the pressure correction equation to obtain a pressure field update on the mesh.

Correct Velocity: Update the velocity field using the pressure correction to ensure mass conservation throughout the mesh.

Interface Coupling: Exchange temperature information between the fluid and solid at their interface based on the mesh connectivity.

Convergence Check: Check for convergence of residuals (imbalances) in velocity, pressure, and temperature (both fluid and solid) on the mesh.

Iterate: If not converged, return to step 6 with the updated solution fields on the mesh.

OpenFOAM (Segregated Solver with PIMPLE):

Mesh Generation: Create a mesh similar to ANSYS CFX, encompassing both fluid and solid domains.

Define Material Properties: Assign material properties to fluid and solid regions based on their mesh elements.

Define Heat Source: Specify the heat source term in the energy equation for the solid region, considering its mesh distribution.

Initialize: Set initial conditions for velocity, pressure, and temperature (in both fluid and solid) on the mesh cells.

Predictor Step:

Solve momentum equation for a predicted velocity field (similar to CFX step 2), using mesh information.

Update other variables (like turbulence) based on the predicted velocity on the mesh.

Solve the energy equation for the fluid domain (similar to CFX step 7) on the mesh.

Solve a simplified energy equation for the solid domain (without pressure-velocity coupling) on the mesh.

Pressure Correction Step:

Derive a pressure correction equation from the continuity equation using the predicted velocity and considering mesh connectivity.

Solve the pressure correction equation to obtain a pressure field update on the mesh.

Corrector Step:

Correct the velocity field using the pressure correction (similar to CFX step 5).

Optionally, perform a second corrector step for better convergence (PISO-like).

Energy Equation (Full Solve): Solve the full energy equation for the solid domain, incorporating the heat source term, updated temperature from the fluid, and mesh data.

Convergence Check: Check for convergence of residuals in velocity, pressure, and temperature (both fluid and solid) on the mesh.

Iterate: If not converged, return to step 2 with the updated solution fields on the mesh.

ANSYS CFX Overview

Node-based Finite Volume Method

Coupled Solver

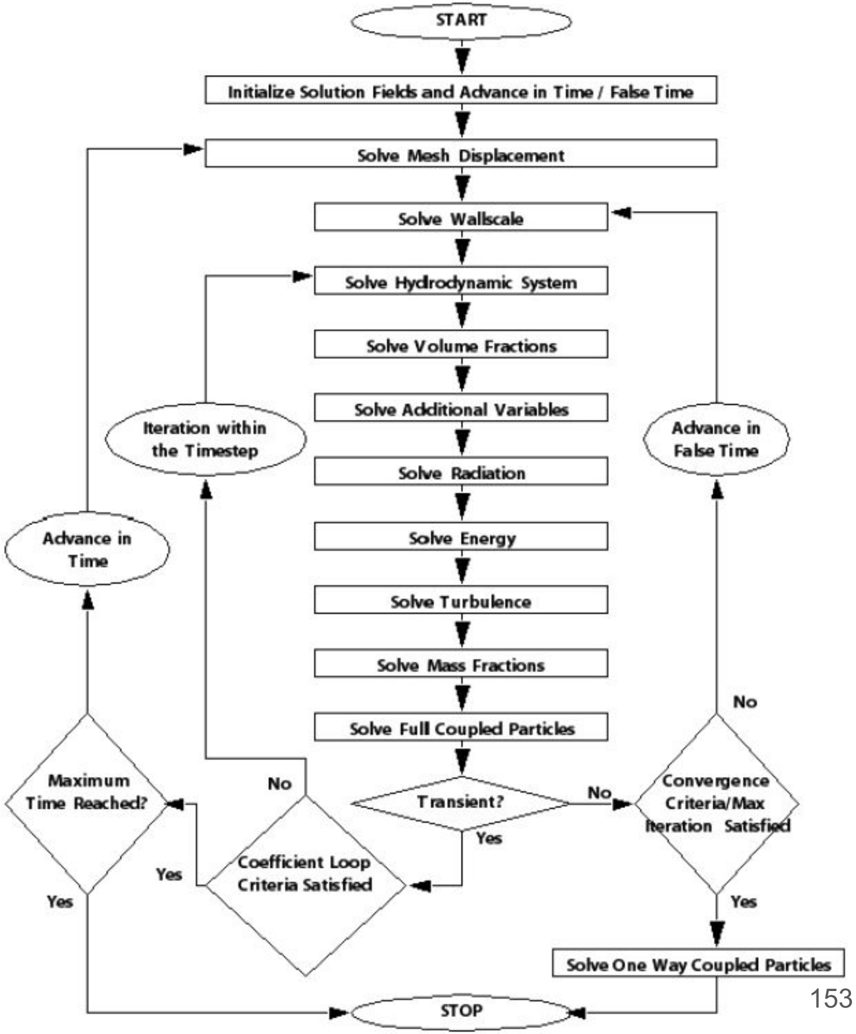
Second Order Backward Euler Transient Scheme

Temperature based Thermal Energy Equation

Conjugate Heat Transfer

High-Resolution Advection Scheme (explicit scheme)

Multigrid (MG) accelerated Incomplete Lower Upper (ILU) factorization



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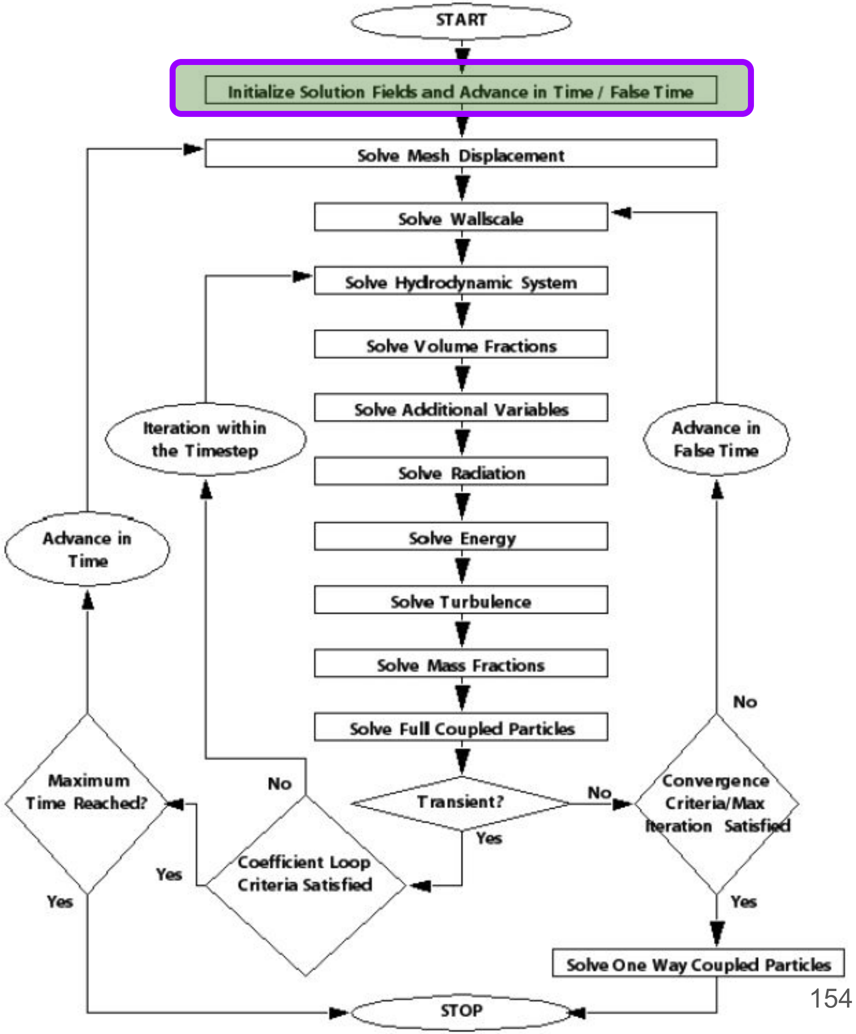


ANSYS CFX Control Volume Generation

Mesh Overlay

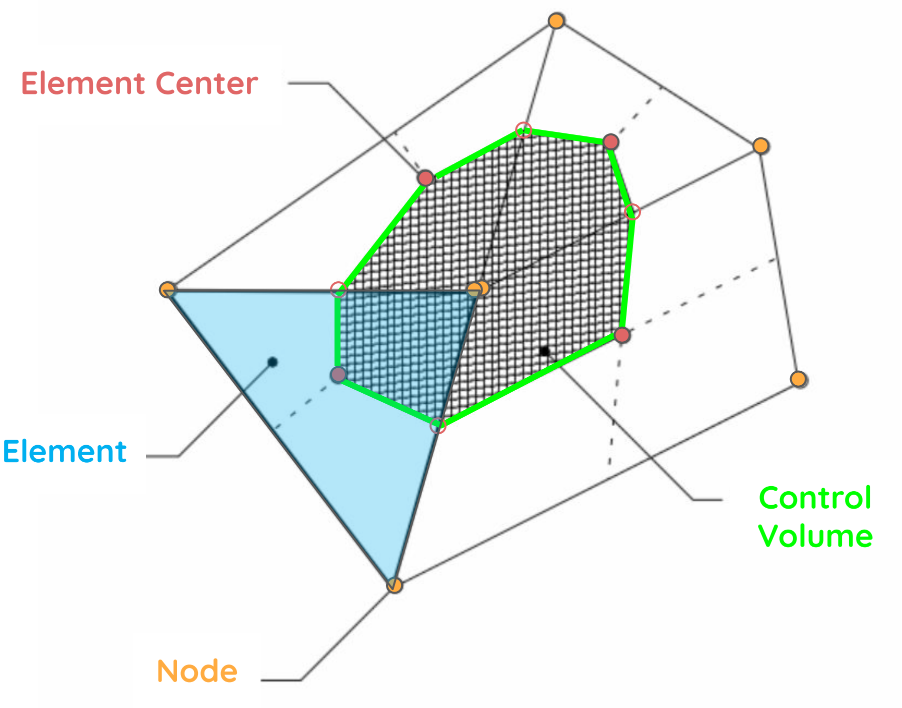
Start with a mesh: elements and nodes

- All solution variables and fluid properties are stored at the nodes

Control Volumes are constructed from the mesh

- Collect the center of each element
- Collect the center of each edge joining elements
- Connect all centers
- Generate a polygonal or polyhedral shape around each node

Conserve relevant quantities such as mass, momentum, and energy in control volume.



OpenFOAM Overview

Cell-Centered Finite Volume Method

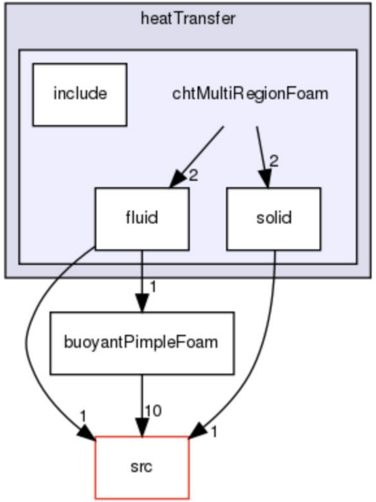
Segregated solution strategy (Sequential)

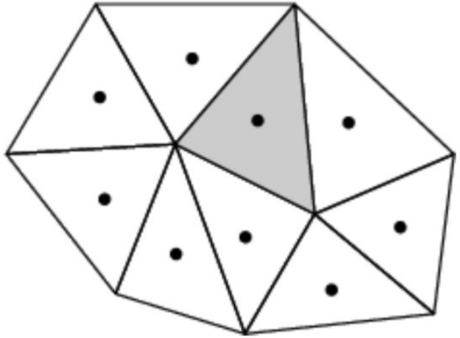
Solver: **`chtMultiRegionFoam.C`**

- Transient Solver
- Fluid Flow
- Solid Heat Conduction
- Conjugate Heat Transfer (Solid-Fluid)
- PIMPLE Algorithm Solver

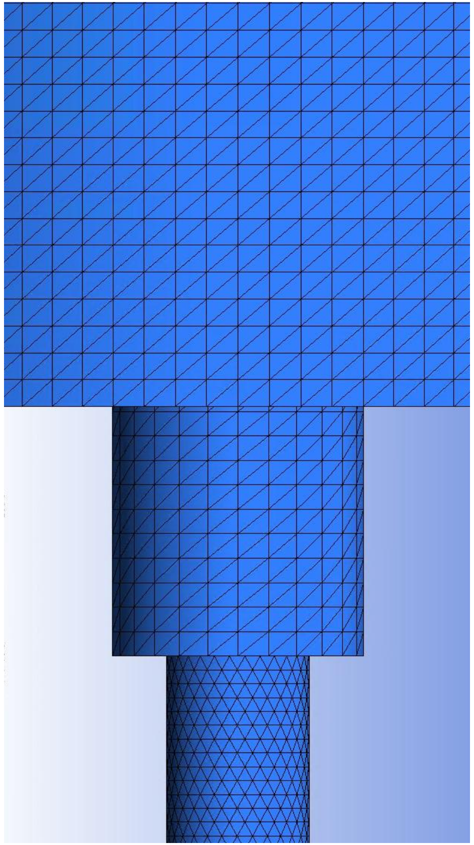
Mesh Decompose & Recompose:

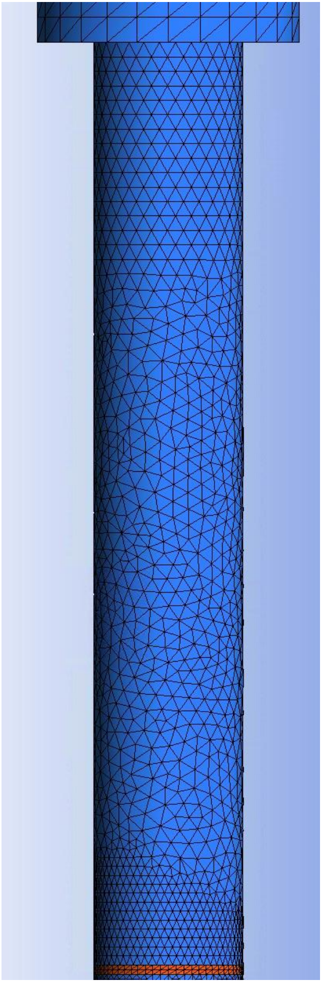
- **`simpleGeomDecomp`**
- **`multiLevelDecomp`**
- **`reconstructPar`**

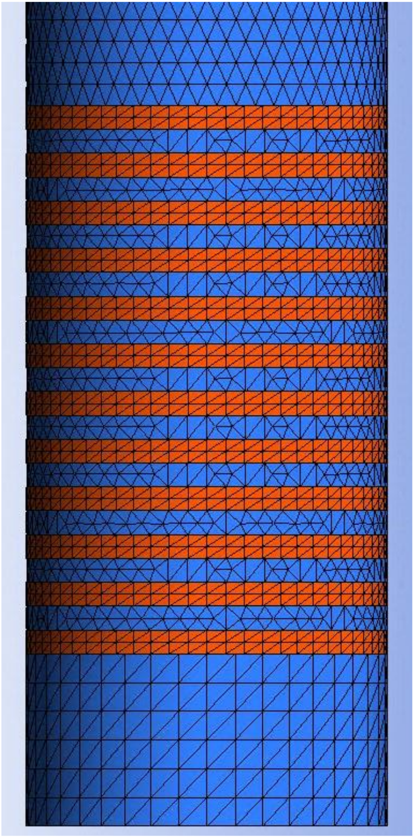




Mesh







Credibility > Verification

	Type		Credibility Goal
✓	Code	Software Quality Assurance (SQA)	SQA procedures were specified and documented.
+	Code	Numerical Code Verification (NCV)	NCV was not performed.
✓	Calculation	Discretization	Applicable grid or time-step convergence analyses were performed and their respective convergence behaviors were observed to be stable, but the discretization error was not estimated.
✓	Calculation	Numerical Solver Error	No solver parameter sensitivity was performed.
✓	Calculation	Use Error	Key inputs and outputs were verified by internal peer review.

Risk Assessment

Decision Consequence

Model Influence	Low	Medium	High
High	3	4	5
Medium	2	3	4
Low	1	2	3

Motivation

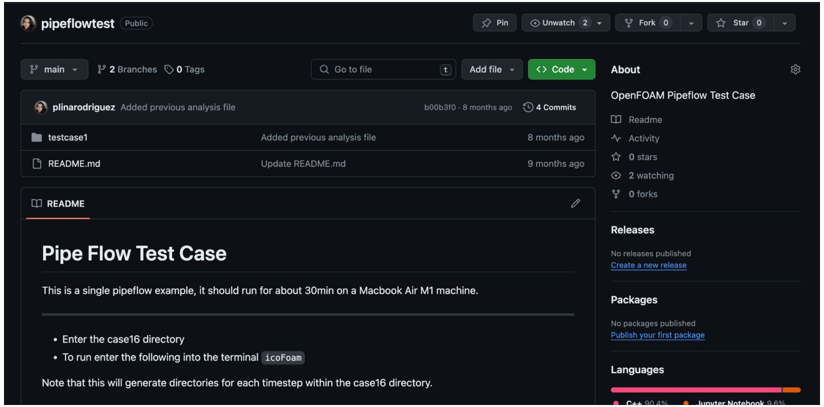
1. Accelerate the use of modeling in the product development and premarket review stages, where appropriate
2. Identify current gaps where M&S could play a meaningful and impactful role in FDA's regulatory mission, but currently does not due to lack of scientific expertise, personnel resources, regulatory guidelines, or knowledge of M&S technological capability
3. Harness FDA partners and collaborators (e.g., CERSIs, NIH IMAG group, NSF IUCRC Program) to advance external M&S efforts relevant to FDA's mission
4. Strengthen internal networks for sharing resources and modeling techniques within FDA and host training sessions to enhance hands-on experience with these resources, techniques and relevant software platforms
5. Consideration of the establishment of Good Simulation Practice to foster harmonization across the FDA, and where appropriate, across international regulatory bodies
6. Use M&S to enhance FDA's submission process and workload prediction to aid research optimization and resource allocations

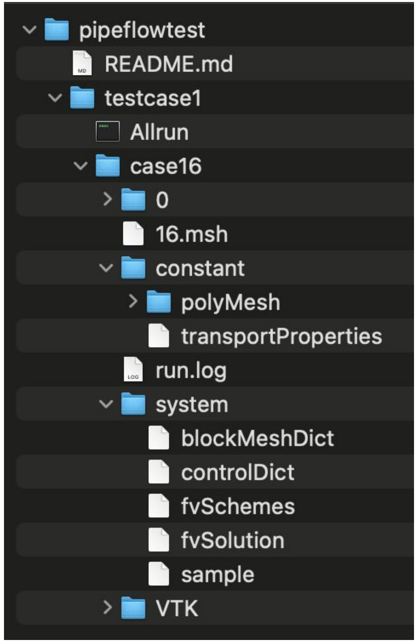
Purpose of M&S Opportunity	Description	Relevant modeling disciplines
To replace or augment clinical trials with *in silico* clinical trials	Develop M&S methods and frameworks for evaluating medical products using virtual cohorts of patients, sometimes referred to as *in silico* clinical trials. *In silico* clinical trials can be used to evaluate medical products when real clinical trials would be unethical (e.g., using the Virtual Family to assess thermal safety of implanted devices during MRI – see page 11), augment and potentially reduce the required size of clinical trials (see [53,54]), or ultimately even replace clinical trials.	Many
To reduce the need for clinical studies to support bioequivalence	Use M&S to inform product specific guidance development for bioequivalence of complex locally-acting drug products, such as dermal and ophthalmic topical products and orally inhaled and nasal drug-device combinations. *In vitro* experiments supported by M&S may be used to develop product-specific bioequivalence approaches that do not include comparative clinical endpoint or pharmacodynamic studies.	Fluid dynamics, physiologically-based pharmacokinetic modeling
To provide evidence supporting safety or effectiveness of medical imaging devices and computer-aided diagnostic software	Leverage radiation transport simulations to generate evidence that can assist in the regulatory process for medical imaging devices and computer-aided diagnostic software. Industry already invests heavily in developing tools that can simulate radiological devices for internal R&D. There is an opportunity to use these tools in the regulatory process, especially for submissions which do not normally require clinical data (e.g., some 510(k) devices).	Radiation transport
To provide a novel method for medical device manufacturers to support reprocessing	Investigate feasibility of, and if appropriate encourage the use of, M&S in medical device regulatory submissions as evidence supporting device sterilization or reprocessing (cleaning, disinfecting, sterilizing) effectiveness.	Fluid dynamics, solid mechanics, thermal

HPC Test Case

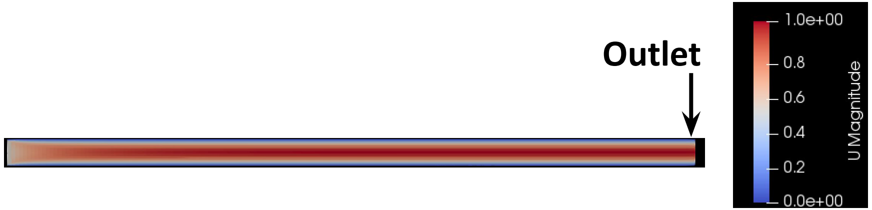
Pipe Flow Test Case

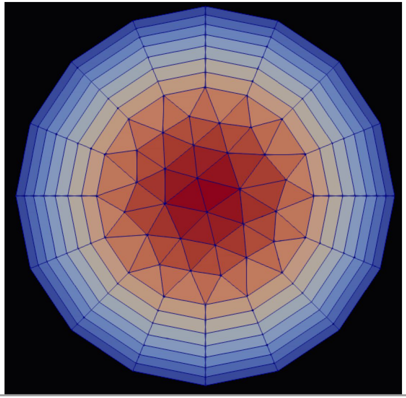
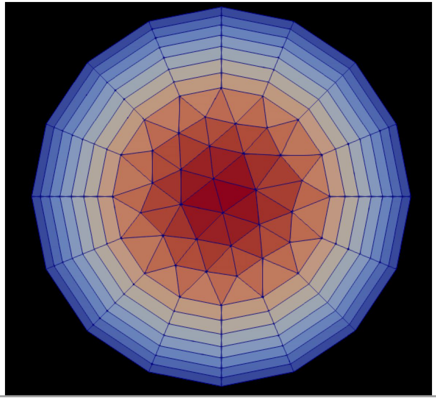
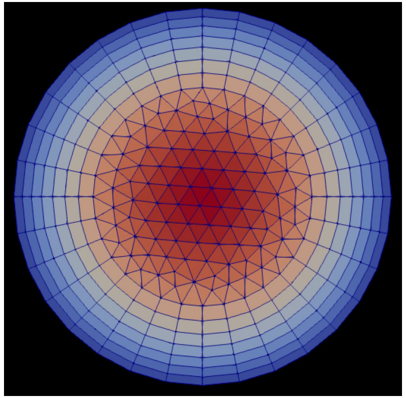
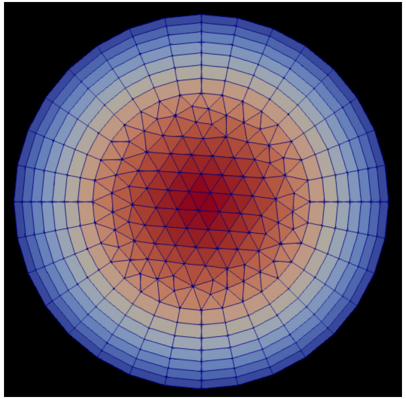
- Has 3 different meshes for performing a mesh convergence study
- Conduct a Cloud Computing comparison study (AWS, Google Cloud, and local machine M1 chip)
- Will be used to test the HPC environment



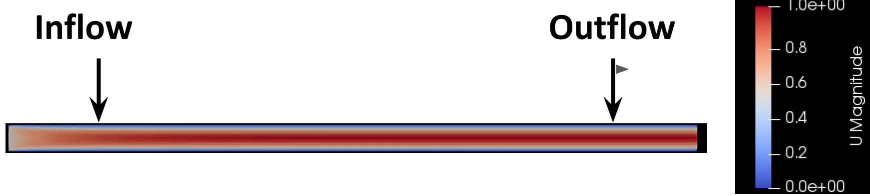


Results - Velocity Profile

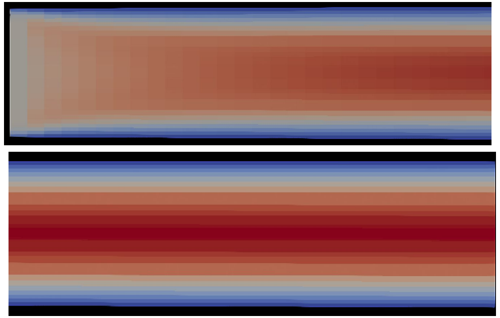


AWS Coarse Mesh			Local Machine Coarse Mesh
AWS Medium-Coarse Mesh			Local Machine Medium-Coarse Mesh

Results - Velocity Profile



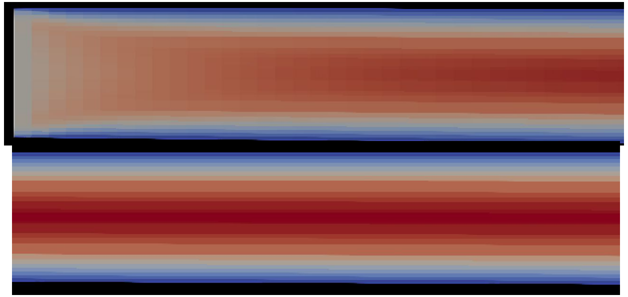
AWS Coarse Mesh



Inflow

Outflow

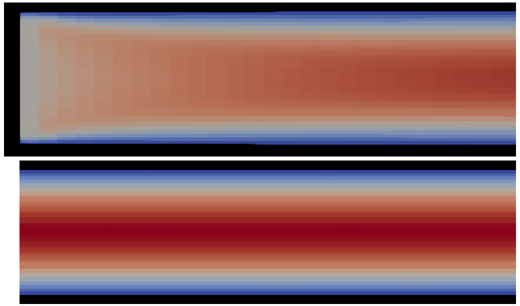
Local Machine Coarse Mesh



Inflow

Outflow

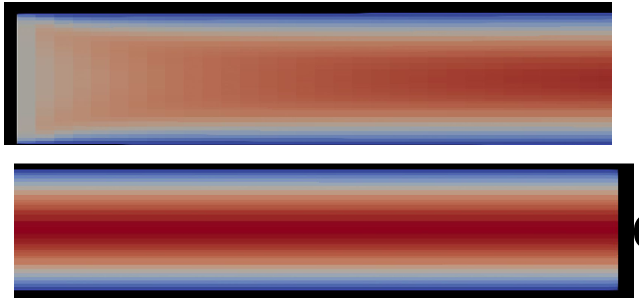
AWS Medium-Coarse Mesh



Inflow

Outflow

Local Machine Medium-Coarse



Inflow

Outflow

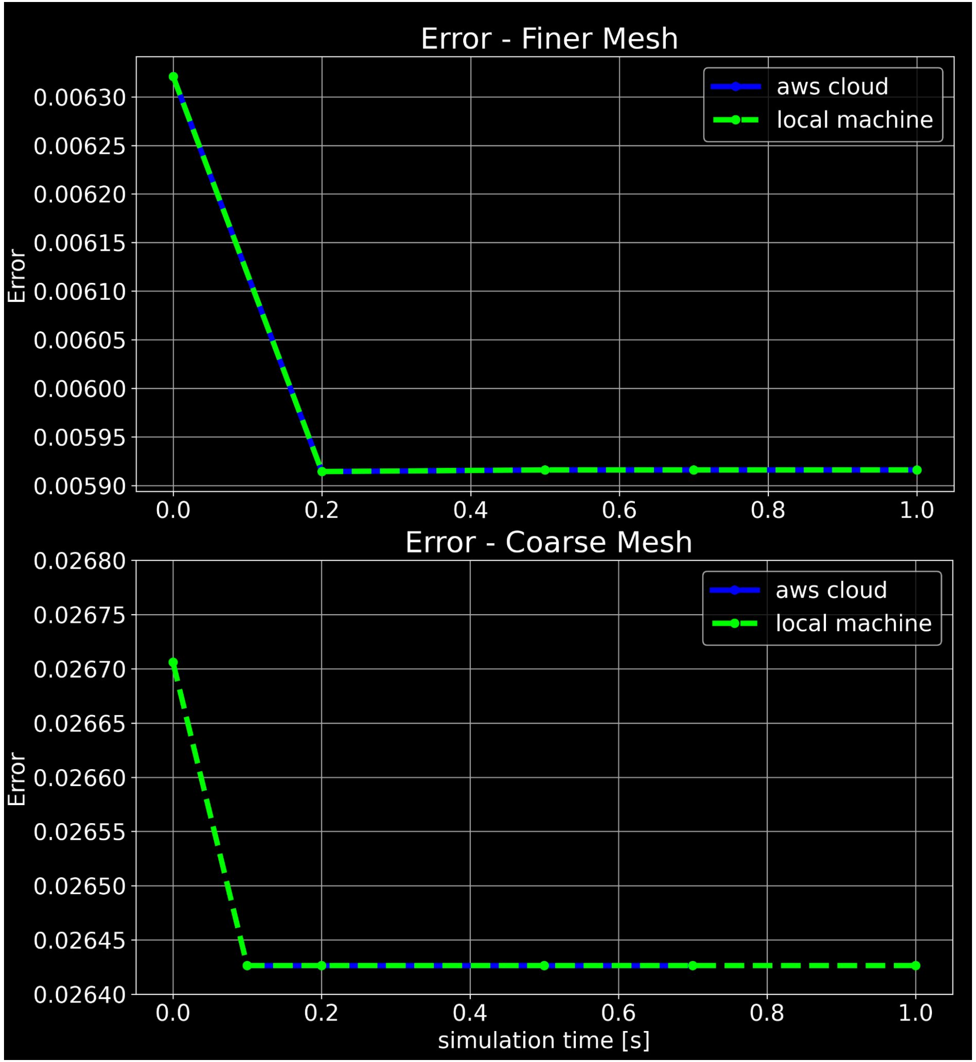
Results - Verification

Error = $V_{analytic}$ – $V_{simulation}$

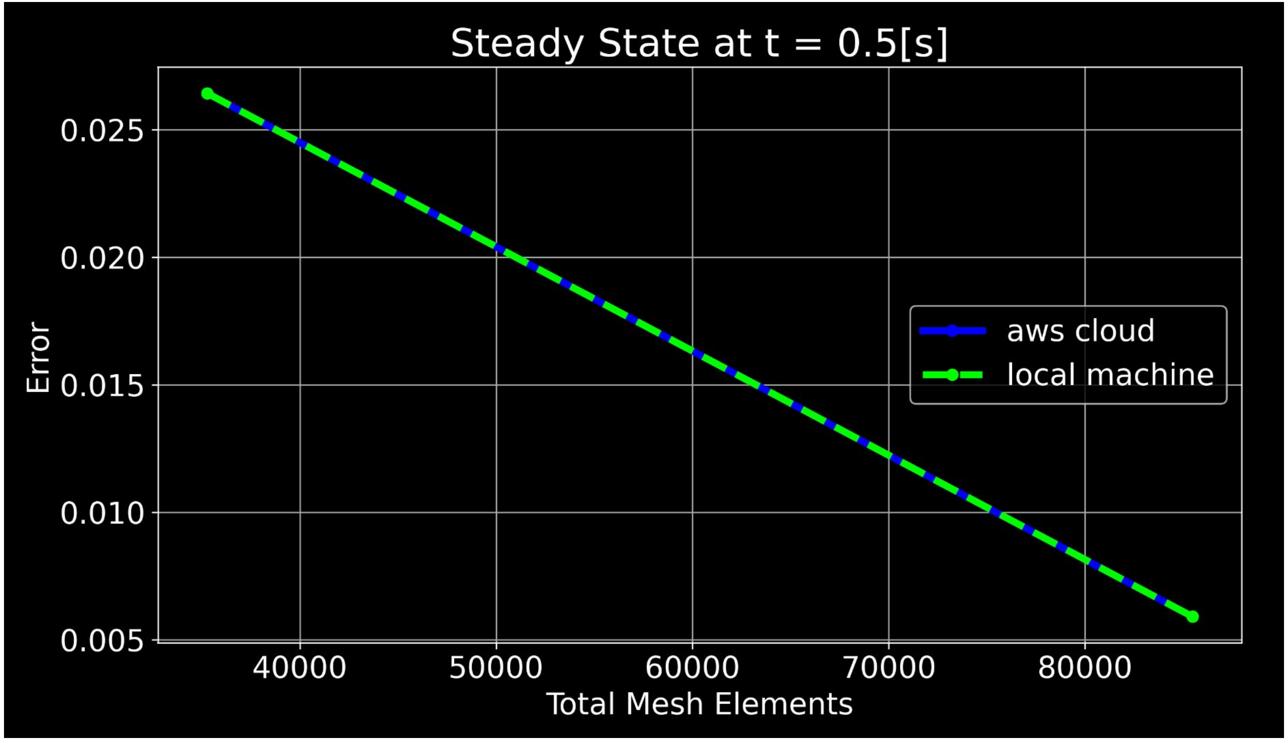
Both the coarse and fine mesh simulations reach steady state is reached after **0.2 seconds**

The error reaches convergences for both mesh resolutions

The coarse mesh has a larger **error (1e-2)** vs. finer mesh has **error (1e-3)**



Results - Verification



At steady state AWS and my local machine produce the same results.

Results - Performance

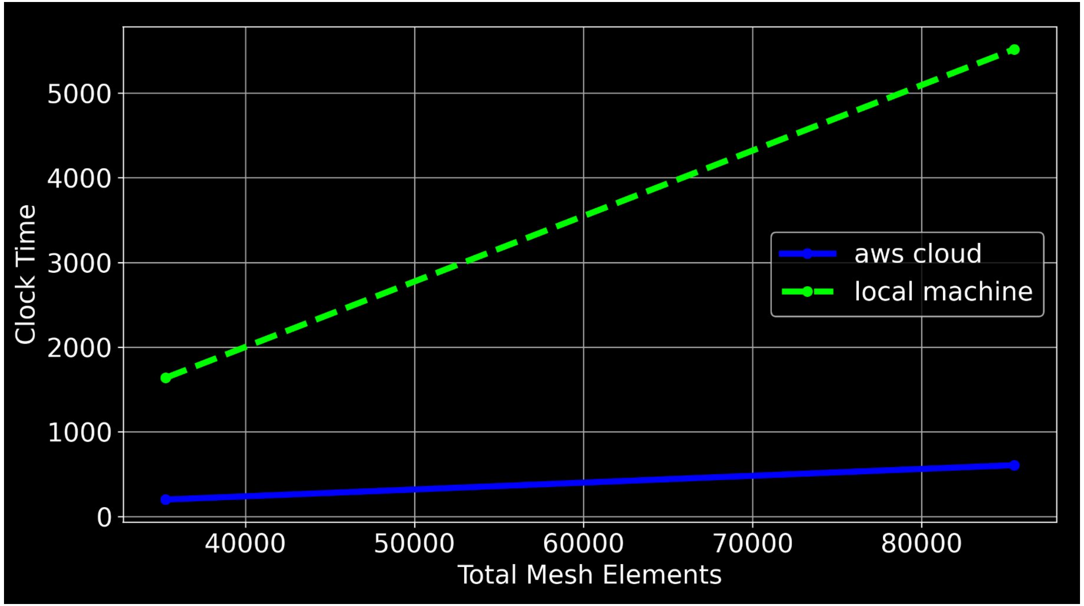
AWS is faster than my local machine

Coarse Mesh

- AWS is 716% faster

Fine Mesh:

- AWS is 810% faster



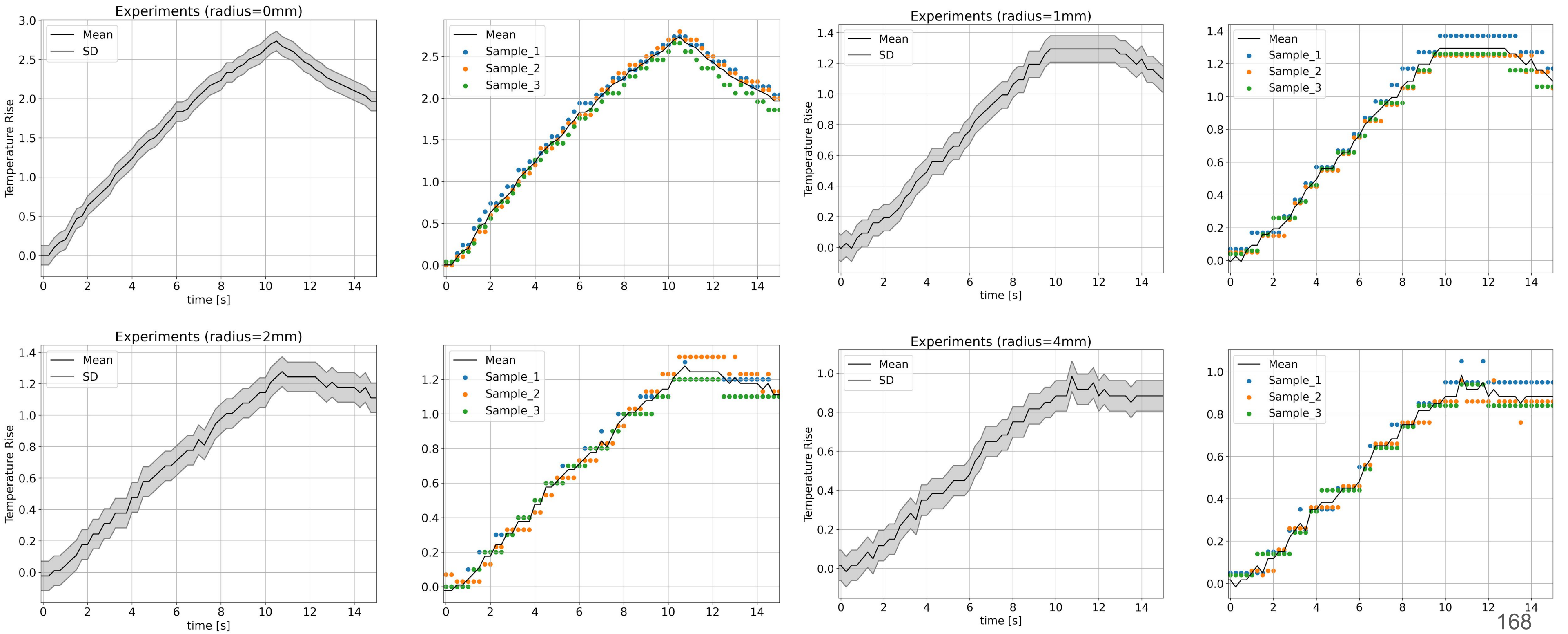
	Coarse Mesh (35276 Elements)	**Medium-Coarse Mesh** (85476 Elements)
AWS	3.34 minutes	10.11 minutes
Local Machine	27.29 minutes	91.97 minutes (~ 1.53 hours)
Difference	**23.94 minutes**	**81.86 minutes (~ 1.36 hours)**

ANSYS (backup slide)

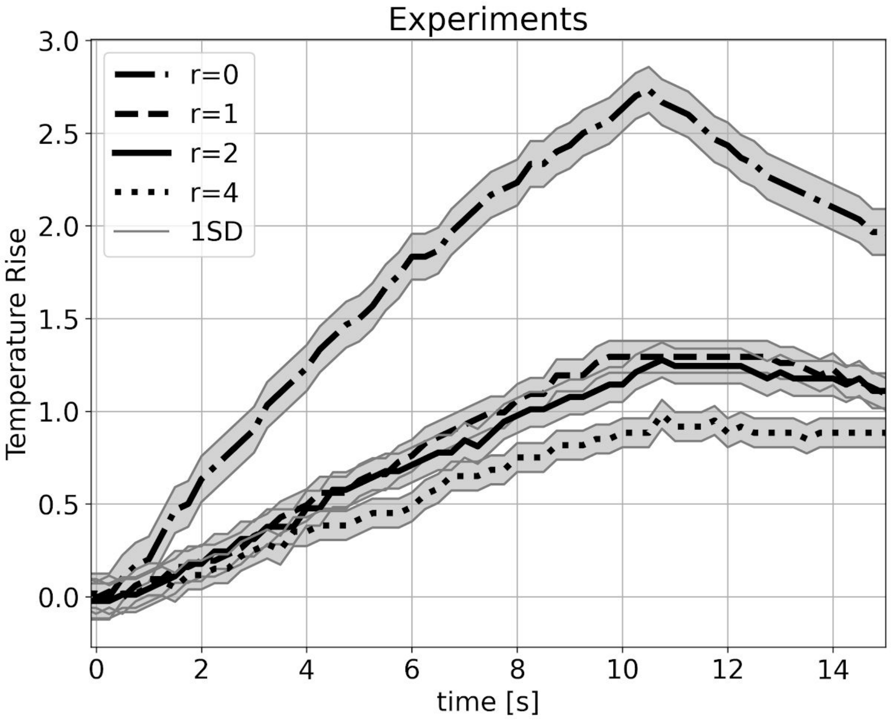
Interface (fluid - Solid)

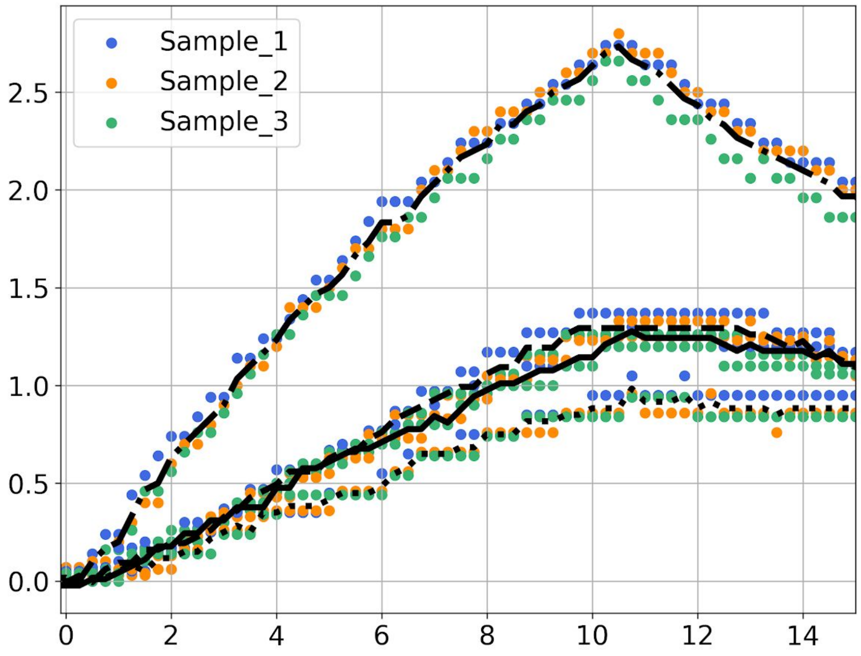
- General Grid Interface (GGI)
  - connections permit nonmatching of node location, element type, surface extent, surface shape and even non-matching of the flow physics across the connection.
  - For conjugate heat transfer, heat flow through fluid-solid interfaces is nonsymmetric
    - GGI samples both fluid and solid regions equally.
    - Better for accuracy and convergence.
  - Useful for rotating machinery systems

CM&S > Heated Air Flow (HAF) > Comparator



CM&S > Heated Air Flow (HAF) > Comparator





Sensitivity Analysis

Coils vs. No Coils -

- The higher the inlet velocity the bigger the difference in velocity profiles between coils vs. no coils.
  - 0.5 L/min: 1.8% diff in velocity
  - 1 L/min: 4.5% diff in velocity
  - 2 L/min: 6.5% diff in velocity

Open Air Dimensions: diameter = 10 - 80[mm] & height = 17 - 190[mm] (sensitive to height not diameter!

Impacts of inlet velocity on temperature profile!

Variations in geometry

Variations in outlet (opening vs. outlet)

Applied power source or temperature profile source

Applied Power on or Off and duration

Types of power profiles: linear, exponential, quadratic, cubic

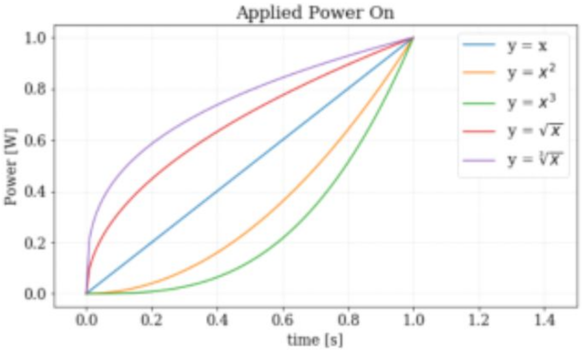
Explored geometry variability (device to device)

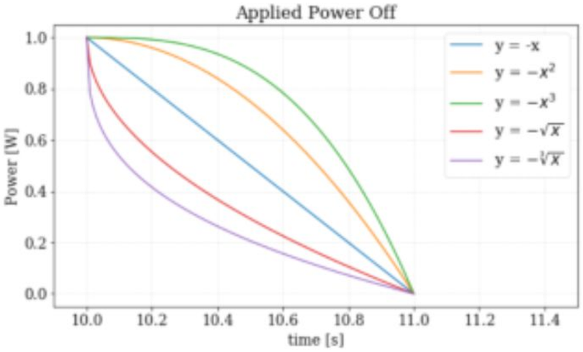
Adiabatic vs. Temperature boundary conditions

Volumetric Flow Rate vs. Inlet Velocity

Tolerance Calculations:

Power Profile





Power Profile

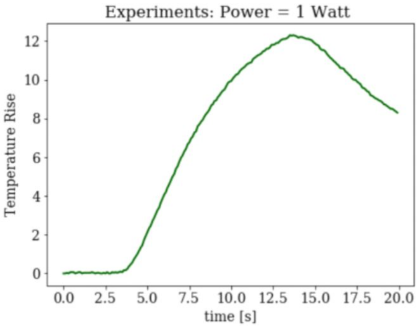
Geometry(mm)		Sample 1	Sample 2	Sample 3	Avg/Mean	SD
Mouthpiece	inner diameter	7.96	8.03	7.98	7.99	0.029439
	length	13	13.02	12.96	12.99333333	0.024944
	thickness	0.13	0.13	0.13	0.13	0
Tube Between	inner diameter	4.54	4.51	4.46	4.503333333	0.032998
	length	34.485	34.73	34.87	34.695	0.159112
	thickness	0.15	0.15	0.15	0.15	0
Wick	length	7.5	7.5	7.5	7.5	0
	thickness	0.155	0.15	0.155	0.153333333	0.002357
	inner diameter	4.54	4.51	4.46	4.503333333	0.032998
Coils	qty	10	10	10	10	0
	diameter outer	4.53	4.53	4.53	4.53	0
	coil diameter	0.3	0.3	0.3	0.3	0
	empty space between	0.5	0.5	0.15	0.383333333	0.164992
Inlet Tube	inner diameter	4.54	4.51	4.46	4.503333333	0.032998
	length	2.1	2.16	2.165	2.141666667	0.029533
	thickness	0.15	0.15	0.15	0.15	0

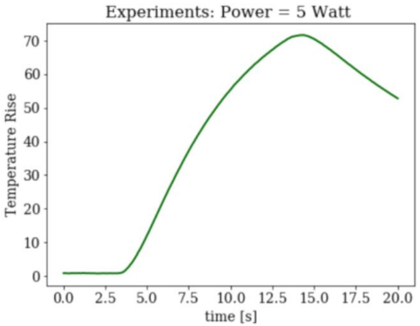
Inflow: Velocity = 1.65 [L/min] (Net Airflow through Wick = 1.18 [L/min], Net Airflow through the Air

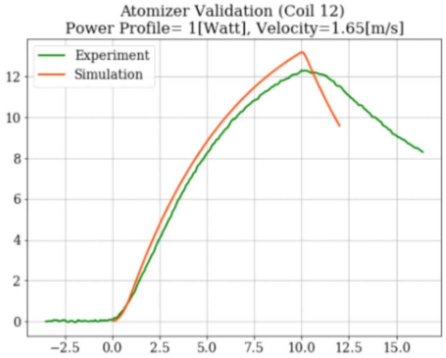
Channel = 1.07 [L/min])

Coils: Power = 1 [W] & 5 [W], Material = Nickle (continuous solid), # of Coils = 12

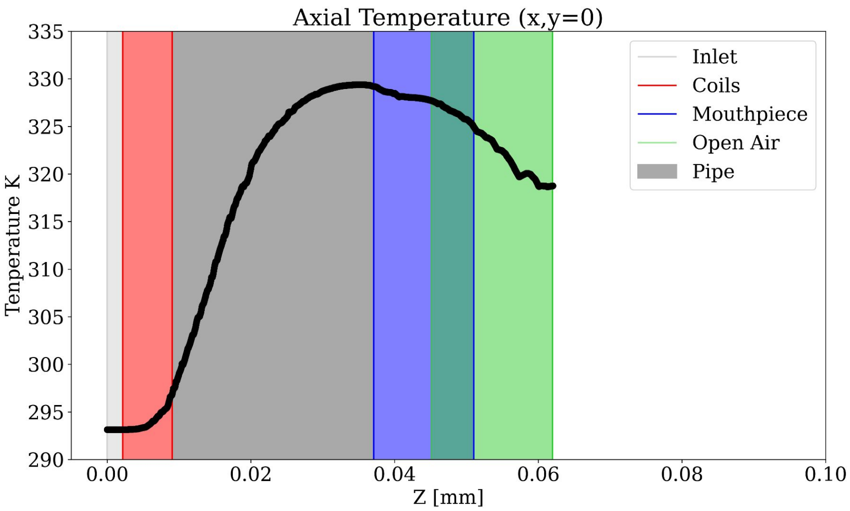
- Outputs Collected at 12th coil with thermocouple



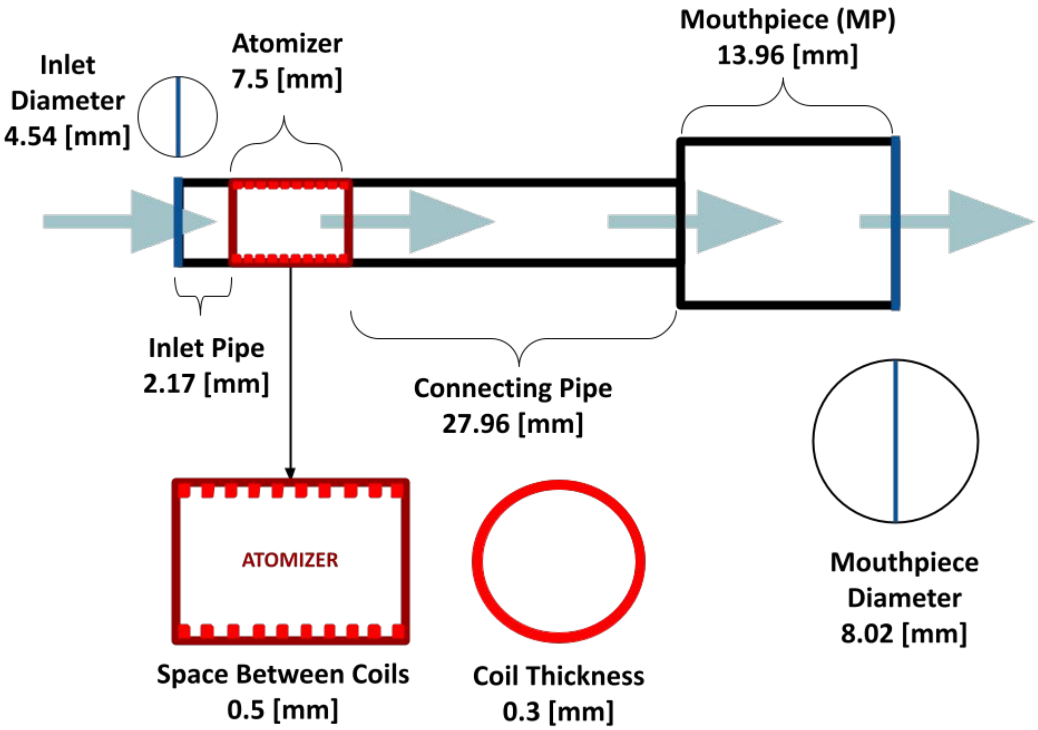




Applied airflow (LPM)	Net airflow through the wick (LPM)	Net airflow through the air channel (LPM)
1.65	1.18	1.07
3.30	2.40	2.20
6.60	5.34	4.78



Axial Temperature (x,y=0)
Temperature K
Z [mm]
335
330
325
320
315
310
305
300
295
290
0.00
0.02
0.04
0.06
0.08
0.10
Inlet
Coils
Mouthpiece
Open Air
Pipe


Inlet
Diameter
4.54 [mm]
Atomizer
7.5 [mm]
Mouthpiece (MP)
13.96 [mm]
Inlet Pipe
2.17 [mm]
Connecting Pipe
27.96 [mm]
ATOMIZER
Space Between Coils
0.5 [mm]
Coil Thickness
0.3 [mm]
Mouthpiece
Diameter
8.02 [mm]