CFD DEM Analysis of a Dry Powder Inhaler with containerization MFiX on Cloud

Vinod Kumar, V M Krushnarao Kotteda, Antara Badhan

University of Texas at El Paso

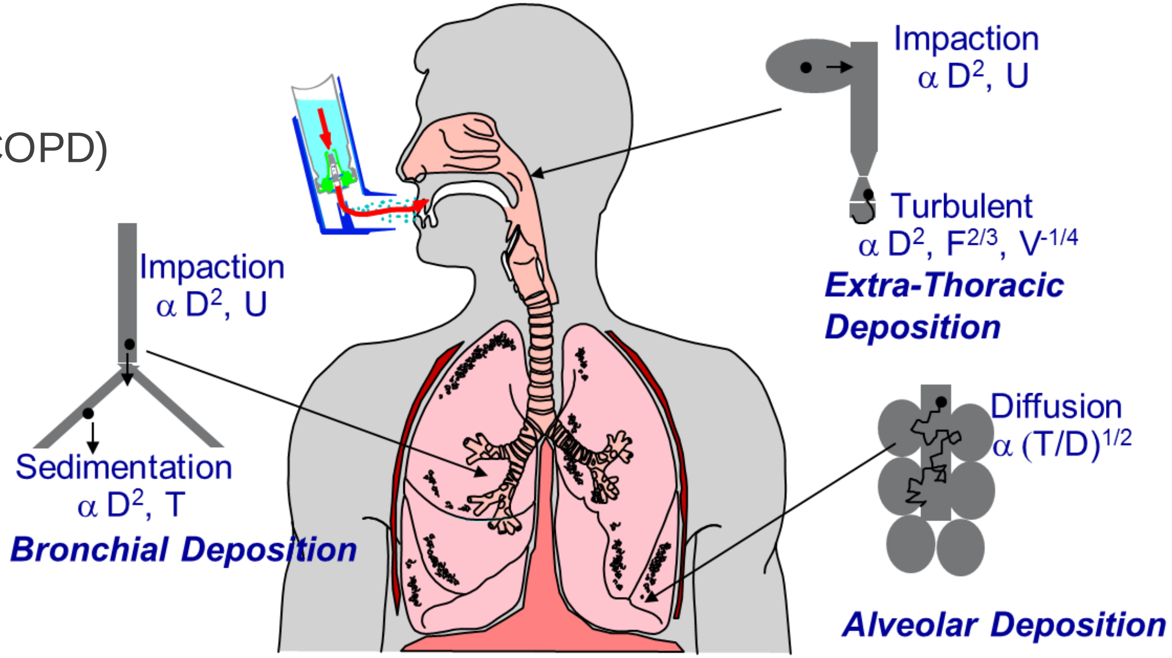
2019 NETL Workshop on Multiphase Flow Science, August 6-8, 2019

Outline

- Introduction
  - DPI
  - MFiX
  - Dakota
- Framework to implement MFiX in Dakota
- Verification and Validation
- Results

Introduction

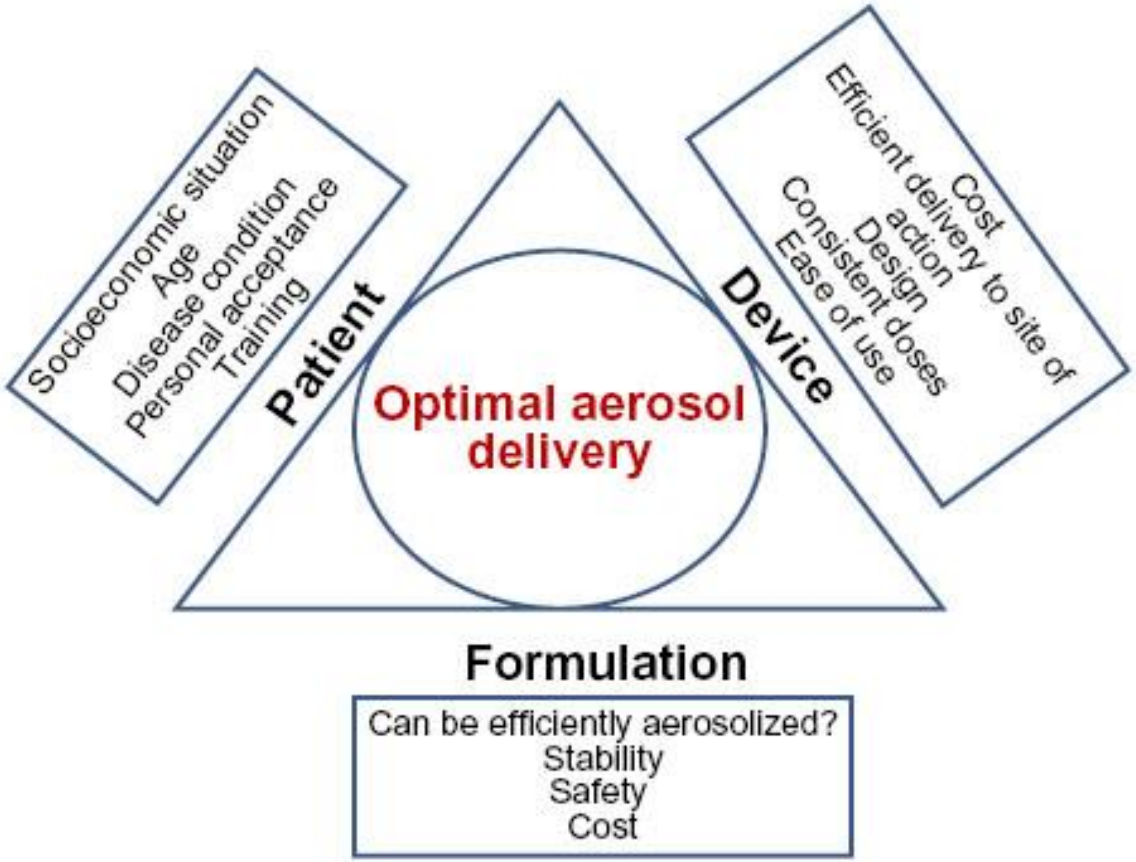
- Inhalation Therapy refers to direct delivery of the medications to/via the lungs by inhalation
  - **Regional Therapeutic Effect**
    - Respiratory Disease
      - Asthma and Chronic obstructive pulmonary disease (COPD)
    - Pulmonary Hypertension
- Advantages of Inhalation Therapy
  - **Delivery of the Medications Directly to the Action Site**
  - **Rapid Onset**
  - **Enhanced Bioavailability by Avoiding First Pass Effect**



https://www.catalent.com/index.php/thinking/science/formulation-of-inhaled-products

Introduction

Inhaler Considerations



Types of Inhaler

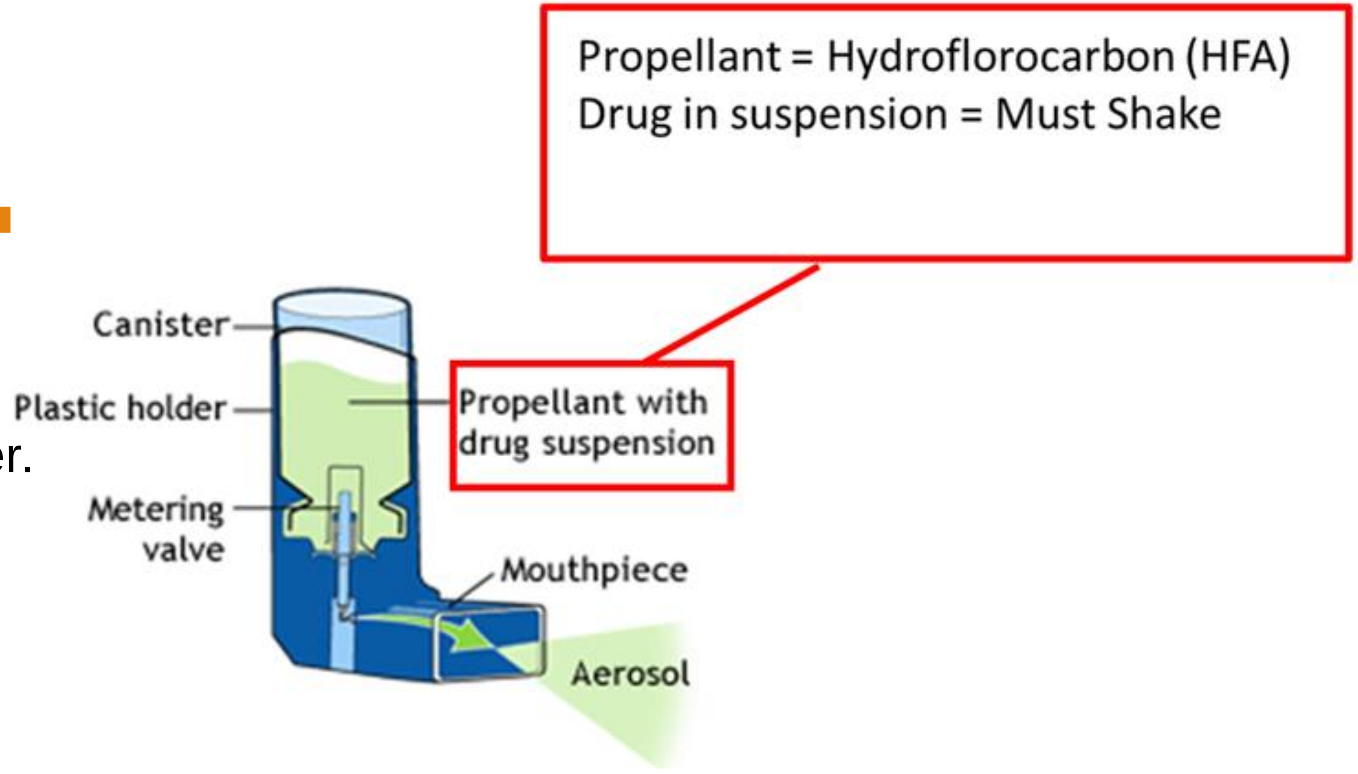
Inhaler

- Nebulizer
- Breath Activated Inhaler
- Pressurized Metered Dose Inhaler (pMDI)
- Dry Powder Inhaler (DPI)

Image sourcess: http://www.whitehousepharmacy.co.za/medicine-usage-guides/breath-actuated-inhalers/
Google images

Introduction

- Most common form of inhalers.
- Medication stored in solution in a pressurized canister.
- Propellants should be nontoxic, nonflammable, and compatible with drugs

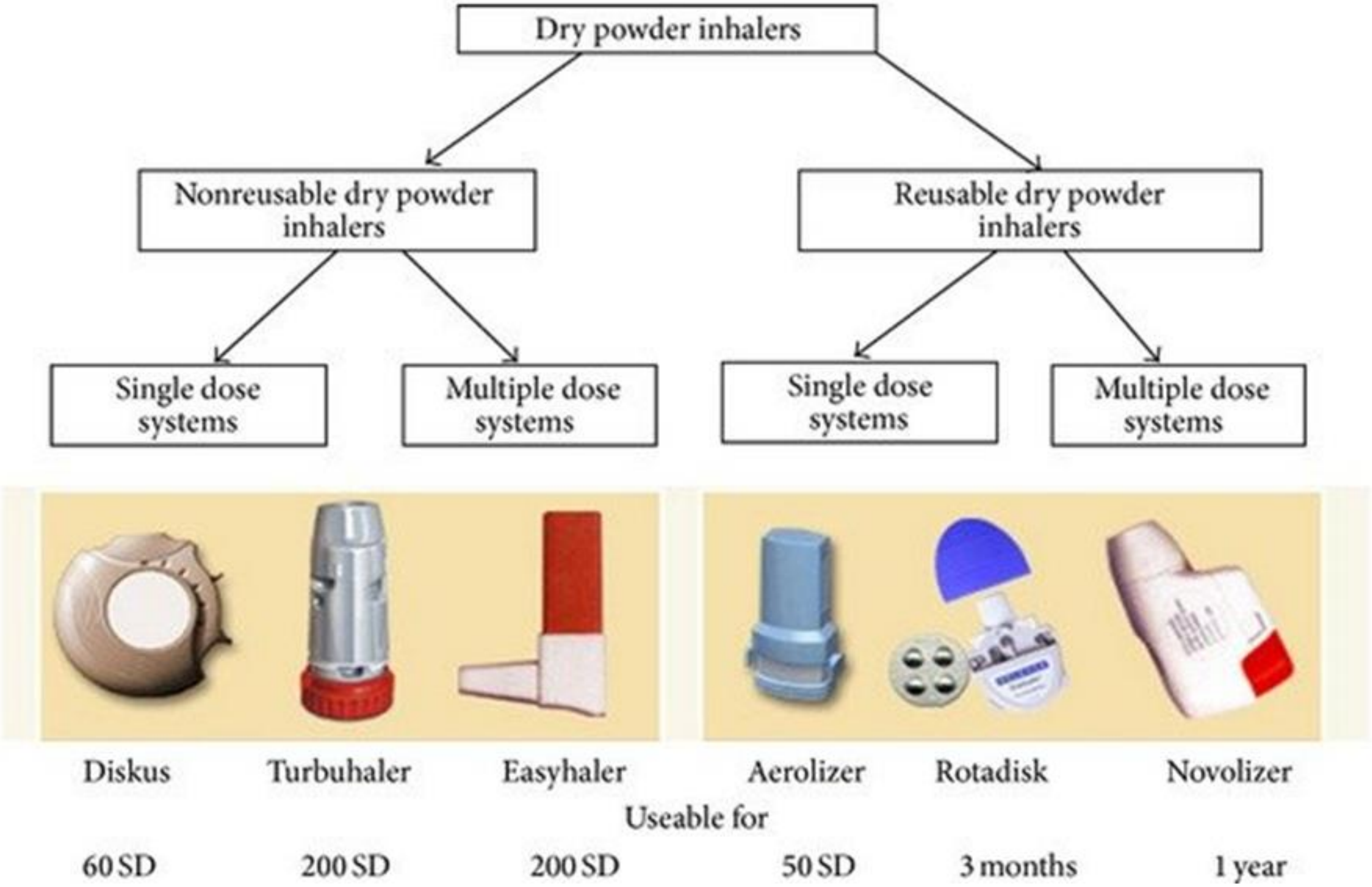


- Breath-activated inhaler
- Works immediately
- DPI does not contain a propellant

- Strong inhalation is required
- Drug in loose powder form
  - Micronized drug particles(1-5µm)

Image: http://www.asthma.ca/adults/treatment/meteredDoseInhaler.php

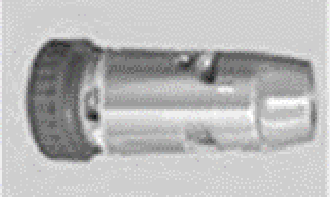
Introduction

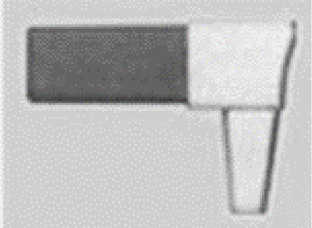


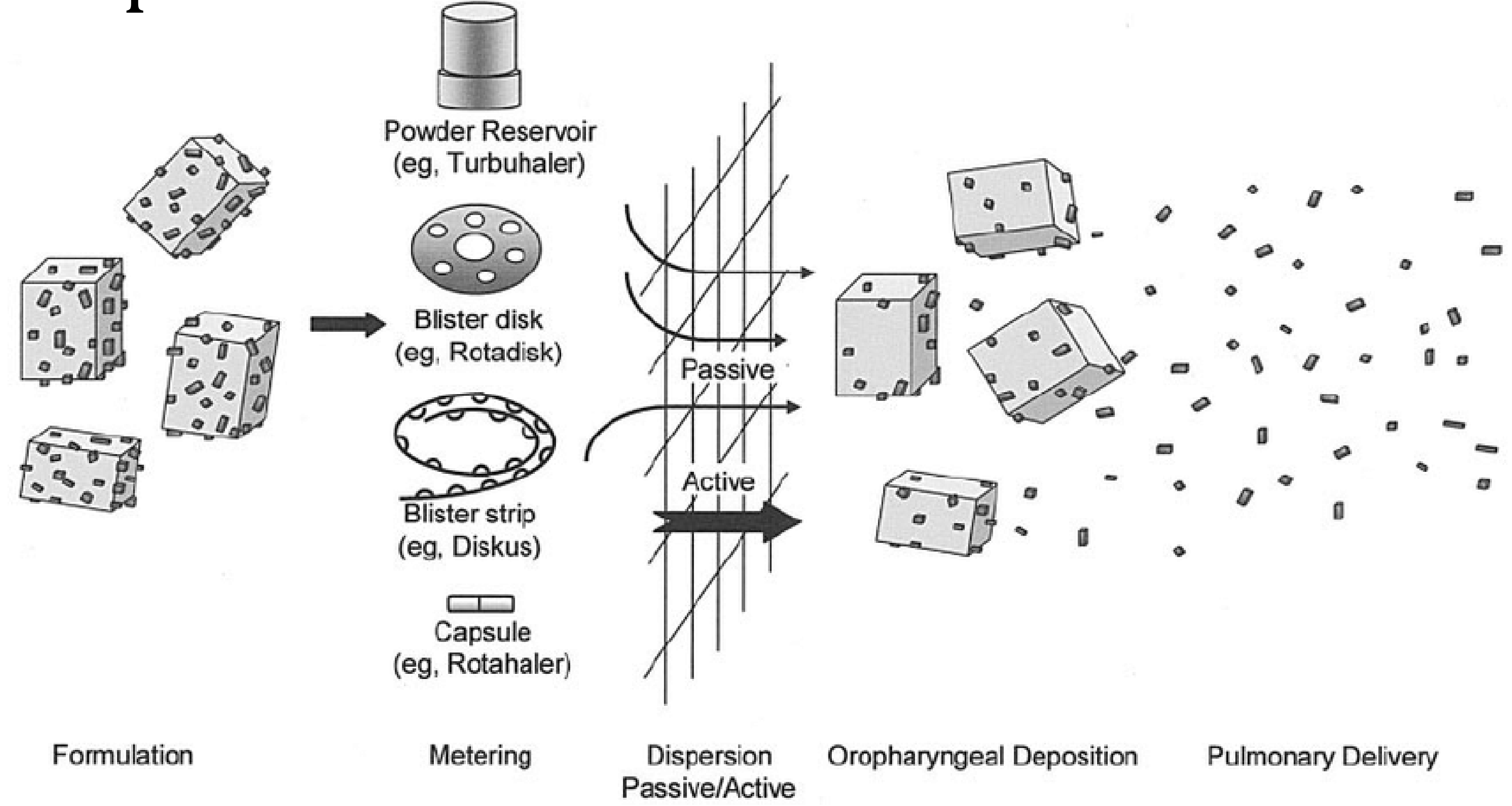
SD : singledose

Introduction

Working principle of a DPI







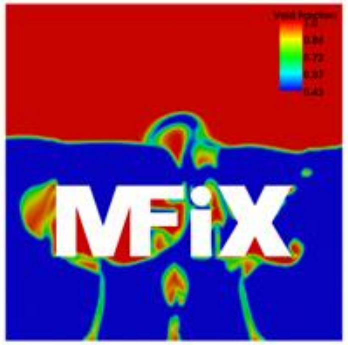
Future Challenges of DPI

Challenge/objective	Solution
Reducing patient errors	Simple self-intuitive DPI design Minimal number of handling steps The same inhaler for all inhaled medication
Improving patient compliance with the inhalation instruction	Simple, self-intuitive DPI design Feedback on inhalation performance
Improving patient adherence to the therapy	Minimizing the number of inhalations per dose Simple, compact DPI design Minimal number of handling steps
Improving safety	No unnecessary excipients Disposal inhalers for special applications e.g. hygroscopic drugs, vaccines, antibiotics (when the risk of bacterial resistance development in the DPI)
Improving efficacy	More powerful inhaler design (balancing between inter particulate, dispersion, and disposition forces)
Specialized inhalation	Patient (group) tailored DPI design
Reducing the costs of inhaled therapy	Simple and cheap (but effective) DPI design Simple drug formulation technologies

MFiX

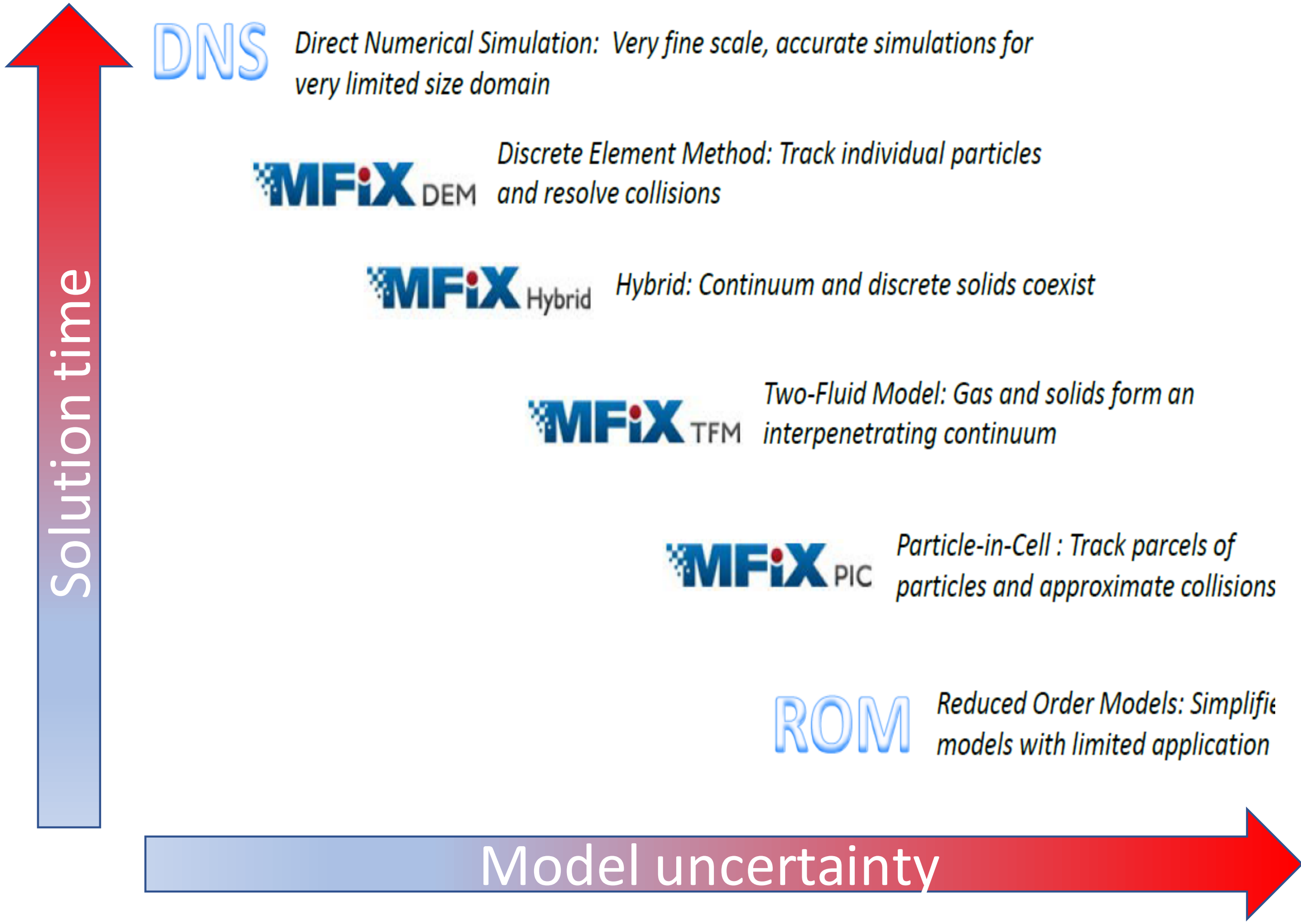
MFiX is

- a multiphase CFD software
- developed by NETL (Opensource)
- a legacy code written in Fortran



Provides a suite of models that treat the carrier phase (gas phase) and disperse phase (solids phase) differently.

- MFIX-TFM (Two-Fluid Model)
- MFIX-DEM (Discrete Element Model)
- MFIX-PIC (Multiphase Particle in Cell)



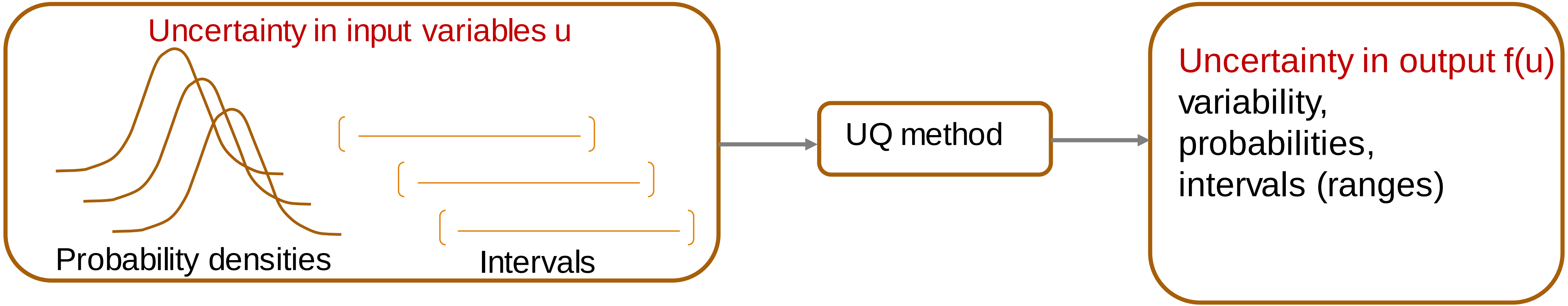
DAKOTA

Explore and predict with confidence.

Dakota has grown significantly beyond an optimization toolkit.

- state-of-the-art optimization methods,
- methods for sensitivity analysis, parameter estimation, uncertainty quantification, and verification

The toolkit provides a flexible and extensible interface between simulation codes and iterative analysis methods.



UQ methods

Sampling (Monte Carlo, LHS)
- ✓ Robust, understandable, and applicable to any model
- ✓ Slow to converge
- ✓ Moments, PDF/CDF, correlations, min/max

Stochastic Expansions
- ✓ Surrogate models tailored to UQ for continuous variables
- ✓ Highly efficient for smooth model responses
- ✓ Moments, PDF/CDF, Sobol indices

Reliability
- Goal-oriented; target particular response or probability levels
- Efficient local (require derivatives) / global variants
- Moments, PDF/CDF, importance factors

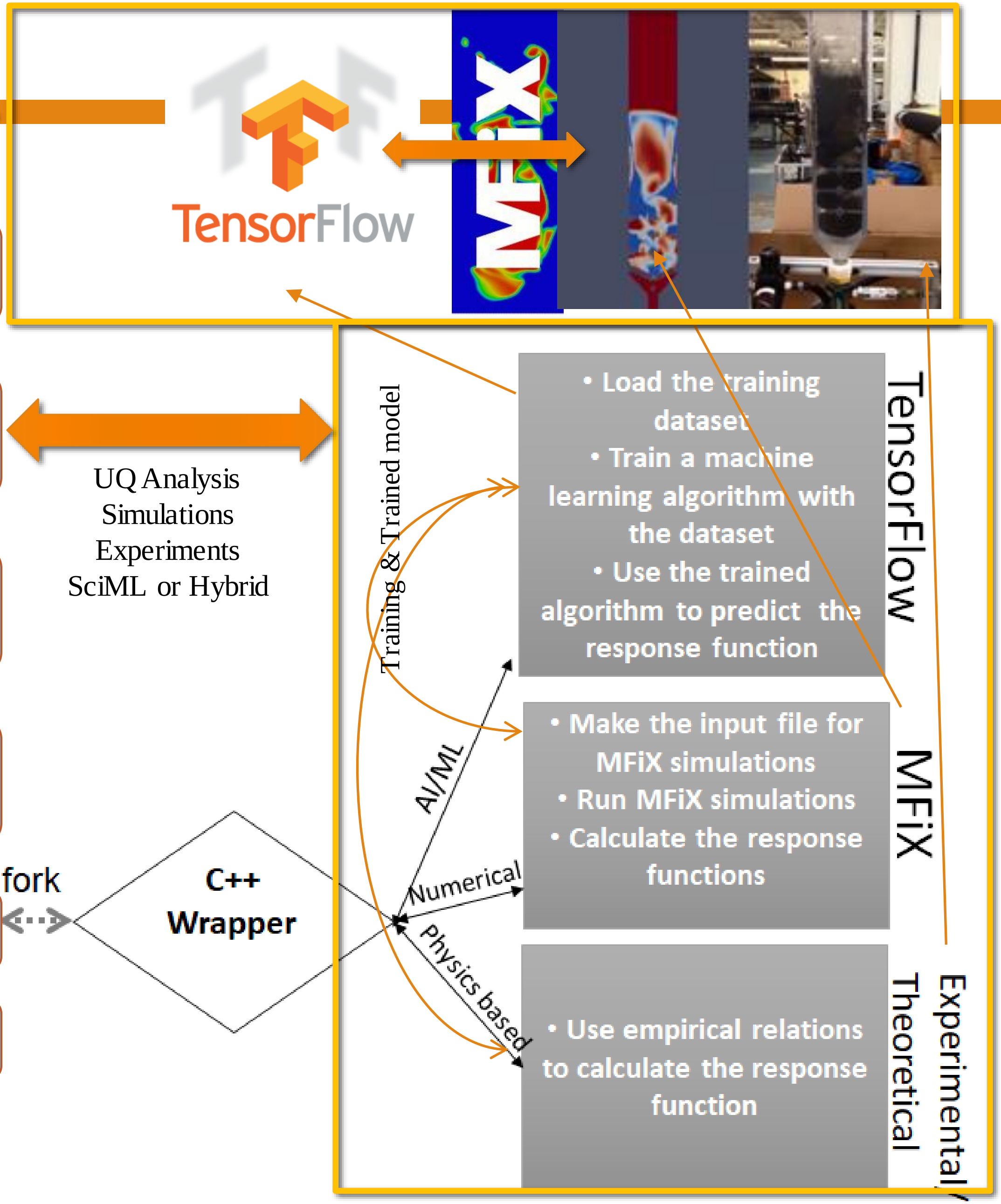
Epistemic
- Non-probabilistic methods
- Generally applicable, can be costly when no surrogate
- Belief/plausibility, intervals, probability of frequency

Consider variable characterizations, model properties, ultimate UQ goal to choose a method

A Practical Process for UQ

DAKOTA

- Identify uncertain input parameters
- Characterize input uncertainties and map them into Dakota variable specifications
- Select a method appropriate to variables, goal, and problem
- Set up Dakota input file and interface to simulation
- Run study
- Interpret the results




```
environment

method
   sampling
   sample_type lhs
   samples = 1000
  seed = 98765 rng rnum2

variables
  normal_uncertain = 2
  means            = 0.80 0.80
  std_deviaions  = 0.10 0.10
  descriptors        'x1' 'x2'

interface
  fork
    analysis_driver = 'mfix'

responses
  response_functions = 1
  no_gradients
  no_hessians
```

UQ results with Dakota

Case #	Input1 $e_{p,n}$	Input 2 $e_{w,n}$	Bed height Sample mean	Bed height Sample Std deviation
1	N(0.8,0.1)	N(0.8,0.1)	14.374	1.7e-01
2	N(0.8,0.1)	N(0.8,0.05)	14.372	1.6e-1

Flow in the fluidized bed

$e_{p,n}$ = particle-particle restitution co-efficient

$e_{w,n}$ = Particle-wall restitution co-efficient

UQ results with PSUADE

MCS with 100,000 samples

Case #	Input1 $e_{p,n}$	Input 2 $e_{w,n}$	Bed height Sample mean	Bed height Sample Std deviation
1	N(0.8,0.1)	N(0.8,0.1)	14.371	1.7e-1
2	N(0.8,0.1)	N(0.8,0.05)	14.367	1.5e-1

Response function (Bed height) =

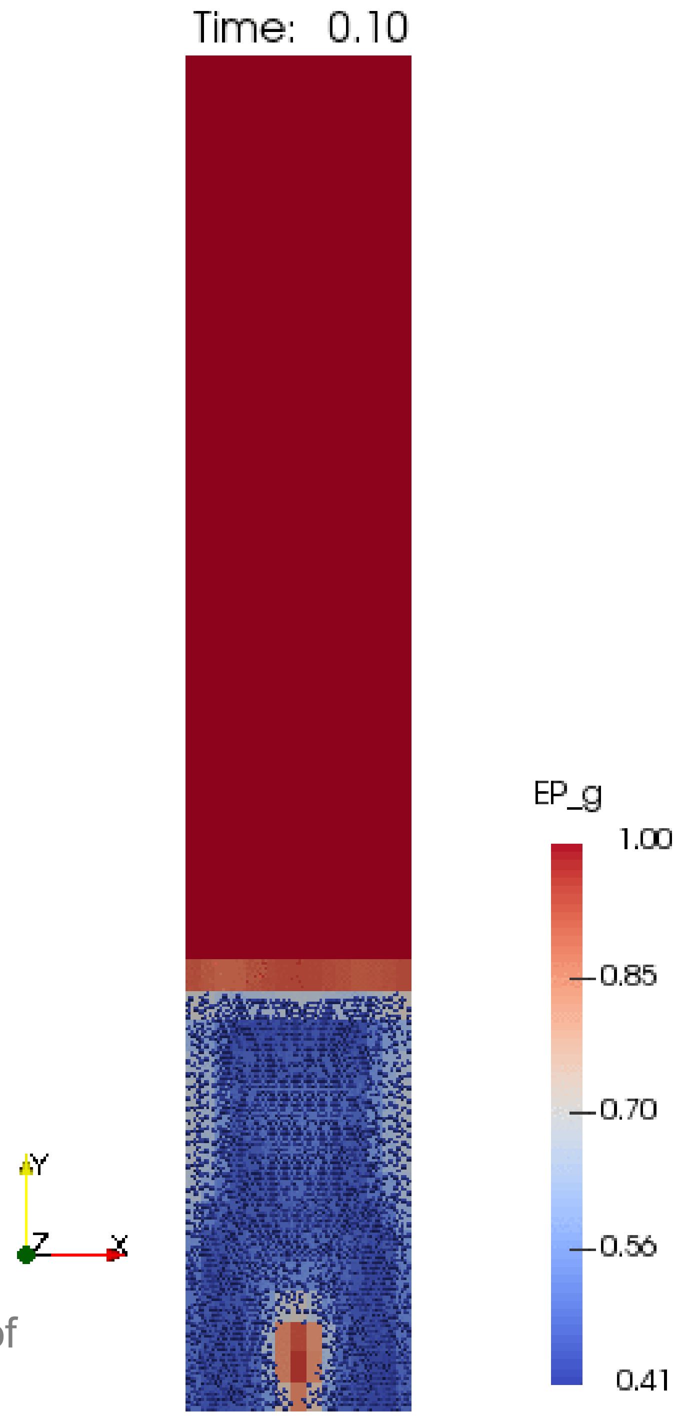
$$= 17.026 - 7.767\, e_{p,n} - 0.46428 e_{w,n} + 5.6644\, e_{p,n}^2 + 0.18379\, e_{p,n}\, e_{w,n} + 0.20556\, e_{w,n}^2$$

Gel, A., Garg, R., Tong, C., Shahnam, M. and Guenther, C., 2013. Applying uncertainty quantification to multiphase flow computational fluid dynamics. *Powder technology*, *242*, pp.27-39.

Flow in a fluidized bed

Central jet fluidized bed

- The air is injected at a speed of 4200 cm/s through a narrow inlet having width of 1 cm and located exactly at the geometric center of the bottom wall.
- cells size: 1 cm x 2 cm
- Number of cells: 675 (=15x45) computational cells.
- The bed is initialized with 217.15 g of particles with a diameter of 0.4 cm and density of 2.7 g/cm3, resulting in total of 2400 spherical particles.
- DEM
- Non reacting flow



VMK Kotteda, A Stephens, W Spotz, and V Kumar, and A Kommu, 'Uncertainty quantification of fluidized beds using a data-driven framework', Powder Technology 354, 709-718 (2019)

Flow in a fluidized bed: parameters for UQ analysis

	D_p (cm)	U_{inlet} (cm/s)	$e_{p,n}$	$e_{w,n}$	KN (g/s^2)	KN_W (g/s^2)	μ	μ_W	μ_g (g/ cm s)
mean	0.34	4200	0.8	0.8	1000000	1000000	0.1	0.1	0.00018
std	0.0297	367.5	0.07	0.07	87500	87500	0.0087	0.0087	0.00001575

D_p = Particle diameter

U_{inlet} = Velocity of the fluidizing agent at the inlet

$e_{p,n}$ = particle-particle restitution co-efficient

$e_{w,n}$ = particle-wall restitution co-efficient

KN = particle – particle normal collision spring constant

KN_W = particle – wall normal collision spring constant

μ = particle - particle friction co-efficient

μ_W = particle – wall friction co-efficient

μ_g = viscosity of the fluidizing agent at the inlet

Response function

Average bed height

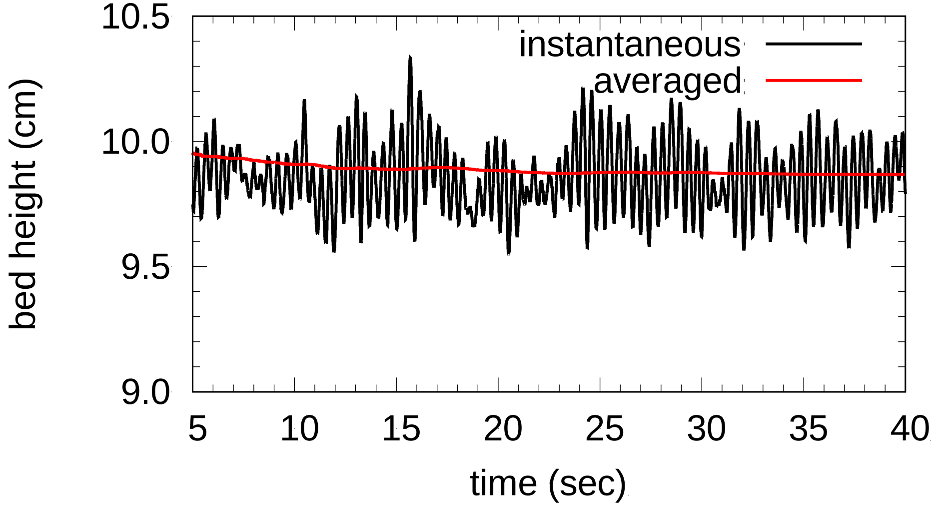
$$H_p(t) = \sum_{n=1}^{N_p} Y^n / N_p$$

UQ results: Flow in a fluidized bed

	D_p (cm)	U_{inlet} (cm/s)	$e_{p,n}$	$e_{w,n}$	KN (g/s^2)	KN_W (g/s^2)	μ	μ_W	μ_g (g/ cm s)
mean	0.34	4200	0.8	0.8	1000000	1000000	0.1	0.1	0.00018
std	0.0297	367.5	0.07	0.07	87500	87500	0.0087	0.0087	0.00001575

Response function

Average bed height

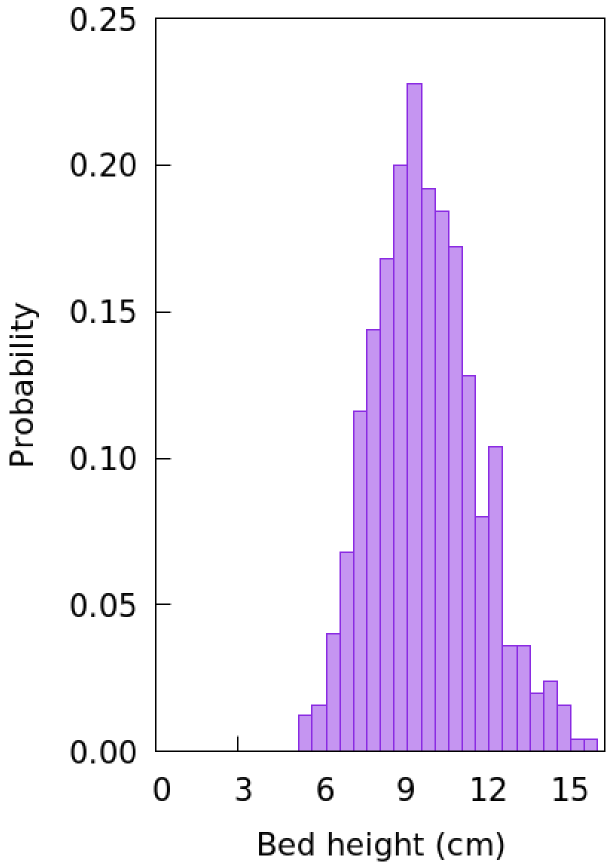


Bed height at t=40 is 9.86838 cm

Number of samples = 500

Mean: 9.6826836828

Std: 1.9528769373

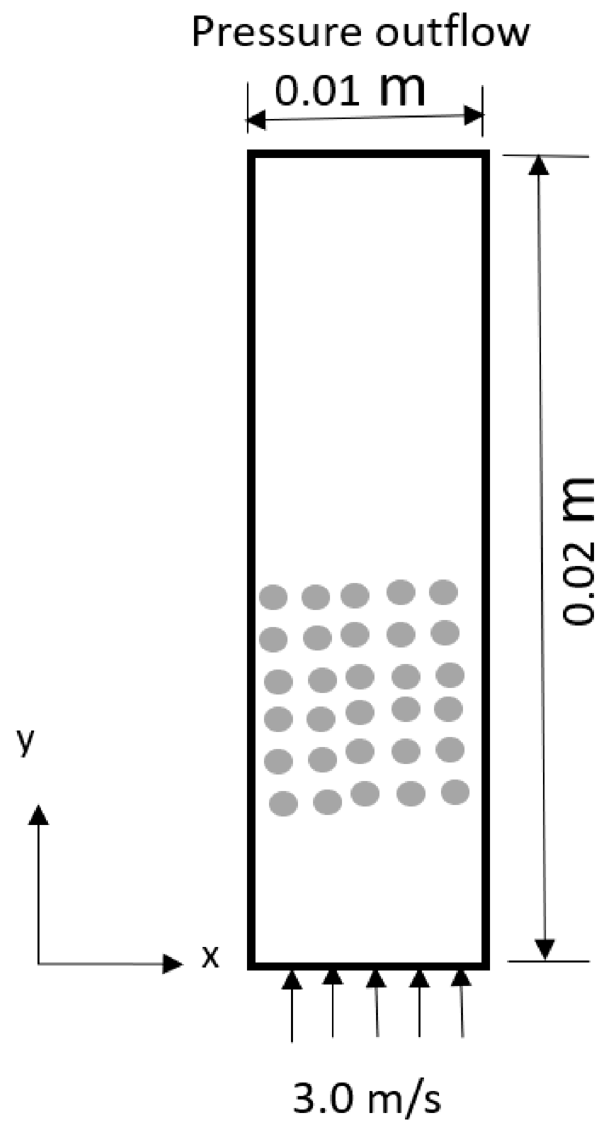


	Bed height
D_p	9.87853e-01
U_{inlet}	7.65915e-01
$e_{p,n}$	1.26841e-03
$e_{w,n}$	-2.19558e-02
KN	-5.44667e-02
KN_W	-4.08984e-02
μ	-1.03671e-02
μ_W	6.74702e-02
μ_g	-1.76986e-02

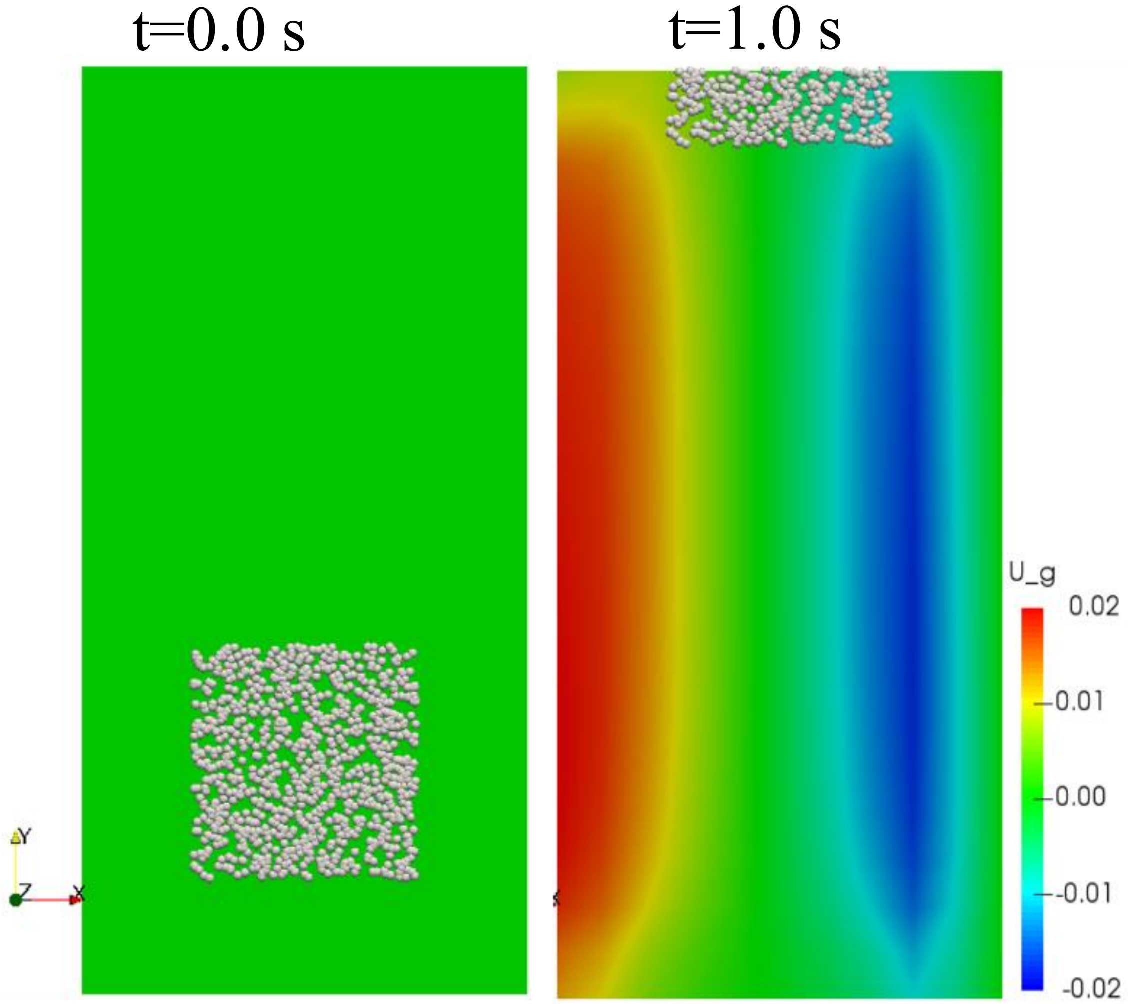
Partial Correlation Matrix between inputs and output

DPI: Problem definition

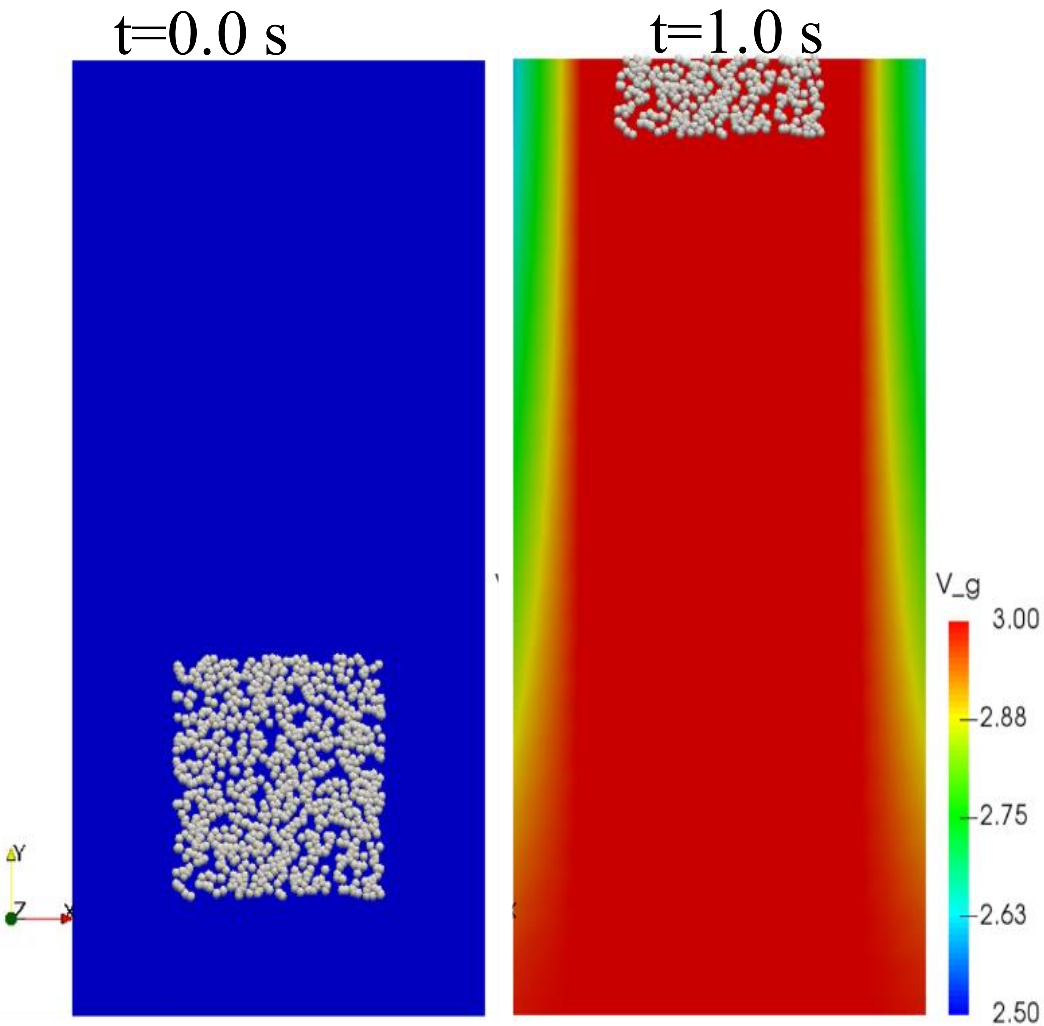
- 20 equi-spaced discretized cells in the axial direction
- 10 equi-spaced discretized cells in the normal direction
- 500 drug particles
    - Size: 3.2 μm
    - Density: 1520 kg/m^3
- 500 carrier particles
    - Size: 52.5 μm and
    - Density:2.650 kg/m^3
- Velocity of air: 3.0 m/s,
- Density of air: 1.205 kg/m^3



Results



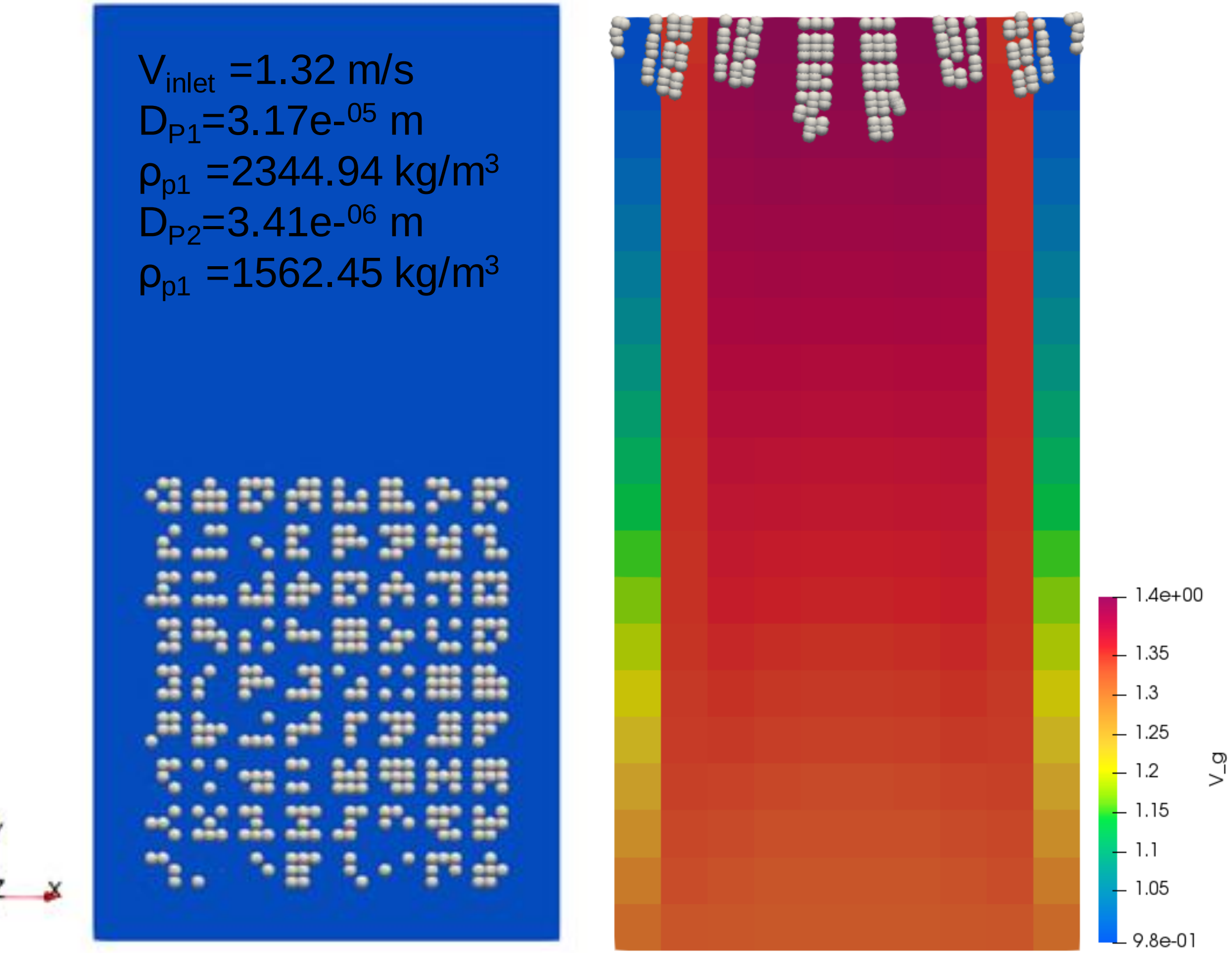
Velocity fields along the x-direction



Velocity (y-direction) fields along the y-direction

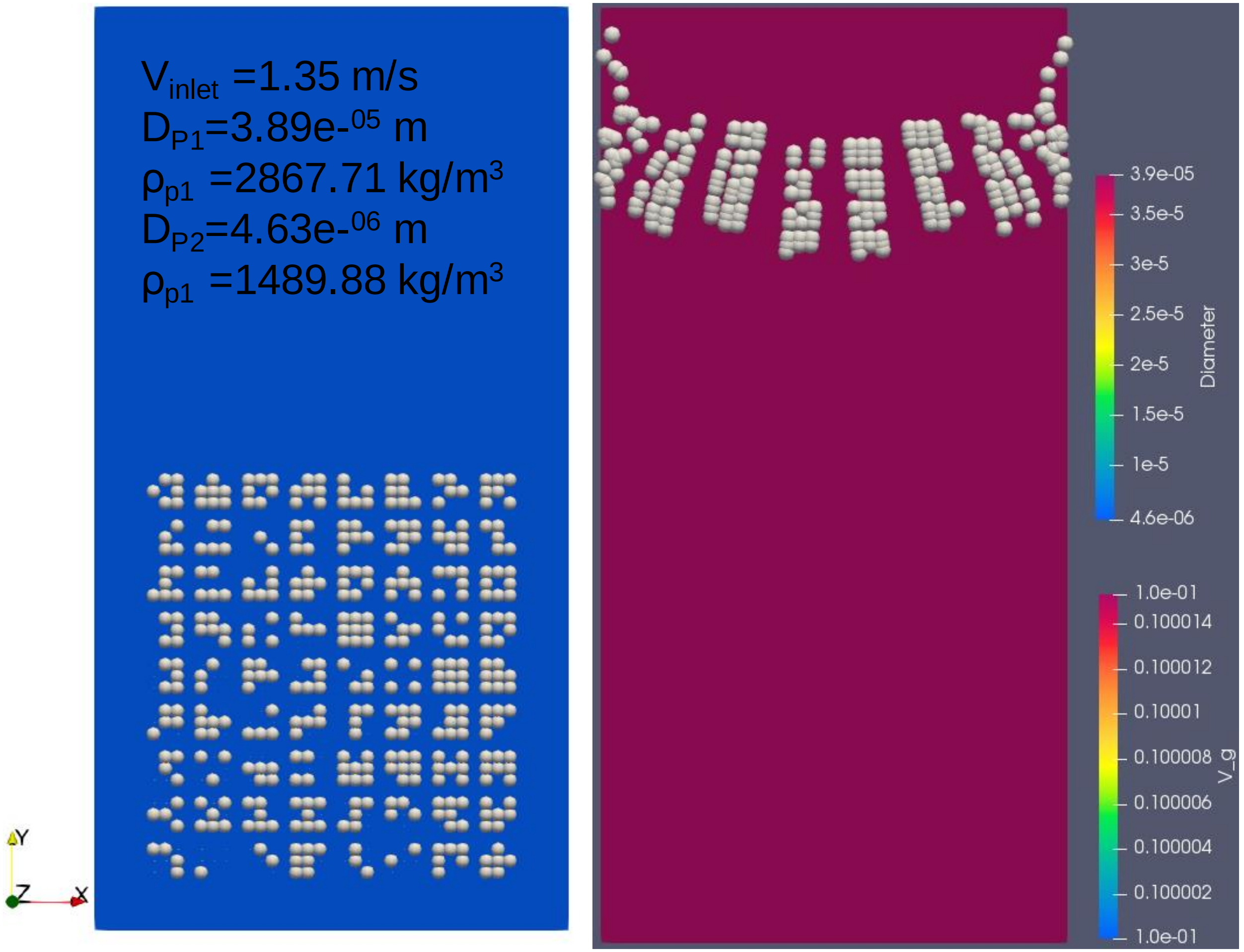
Results: Effect of particles diameter

t=0.0 s t=2.0 s



axial velocity (y-direction) fields

t=0.0 s t=3.0 s



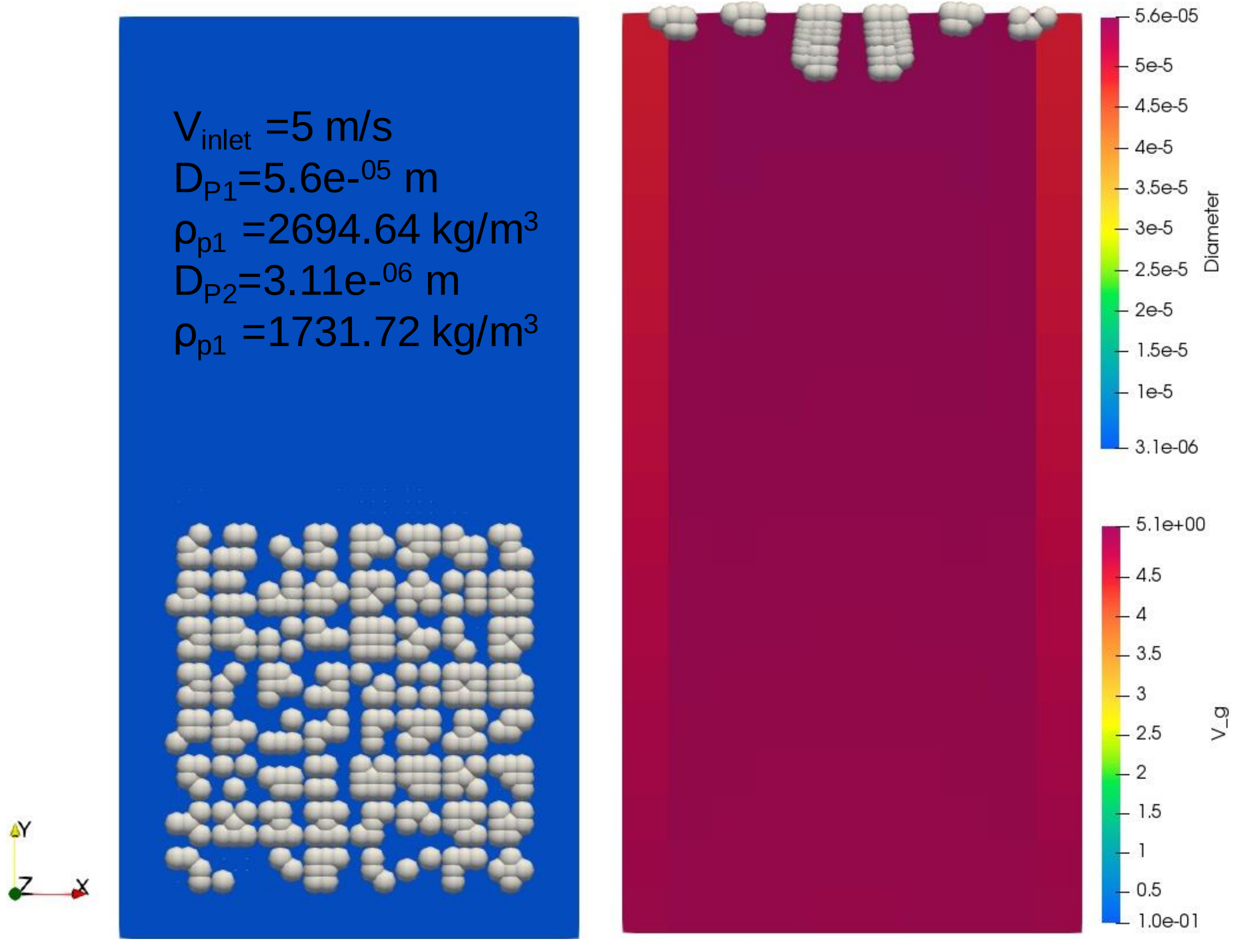
axial velocity (y-direction)

Results: Effect of velocity at the inlet

t=0.0 s   t=3.0 s

axial velocity (y-direction) fields

t=0.0 s   t=2.0 s



axial velocity (y-direction)

Summary

- A framework is used to implement MFiX in Dakota-UQ toolkit
- The framework has been validated on various test cases.
- 2D simulations are carried out with MFiX to simulate flow in an inhaler.
- Particles residence time increases with the particle diameter
- Particle residence time decreases with an increase in the inflow velocity.

Multi- physics & scale Computational Lab

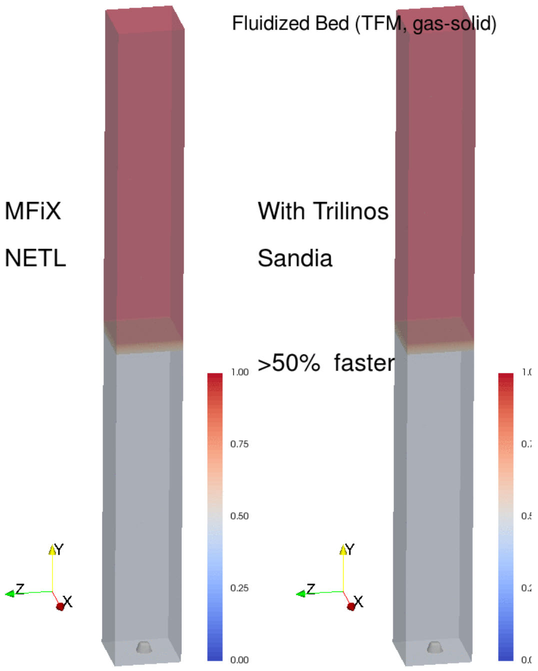
engineering.utep.edu/mu3com

Fluidized Bed (TFM, gas-solid)

MFiX
NETL

With Trilinos
Sandia

>50% faster

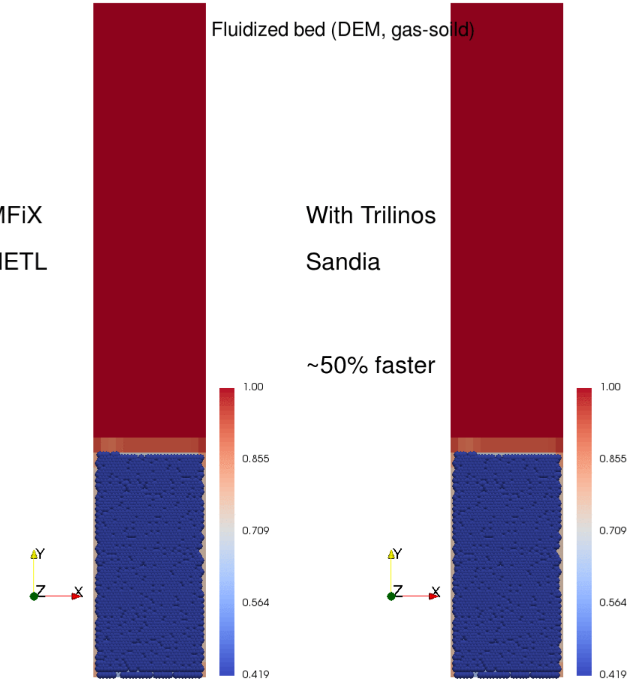


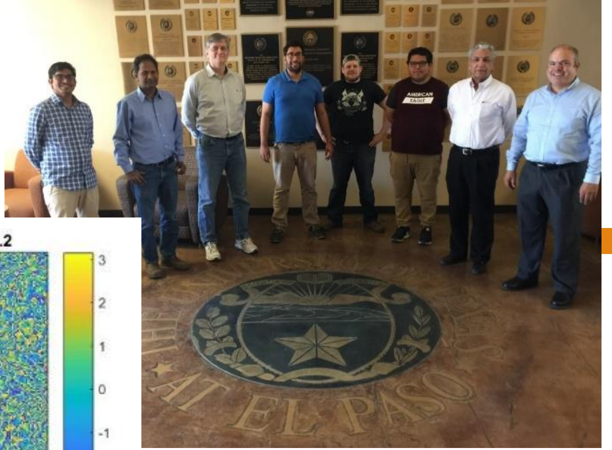
Fluidized bed (DEM, gas-solid)

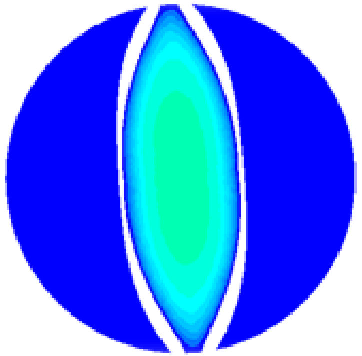
MFiX
NETL

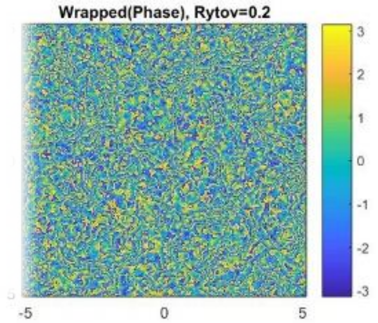
With Trilinos
Sandia

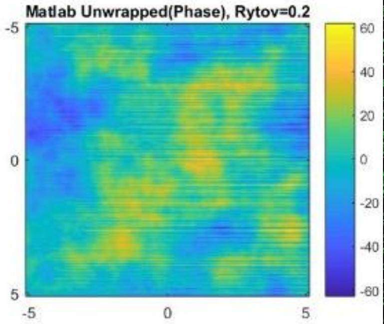
~50% faster

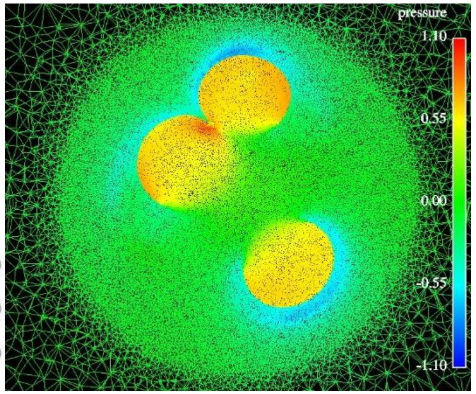


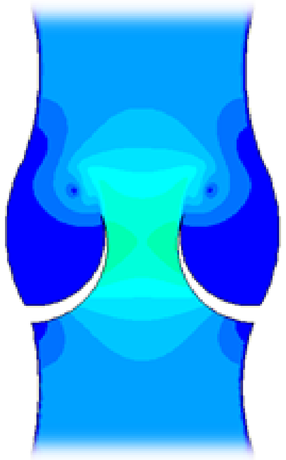




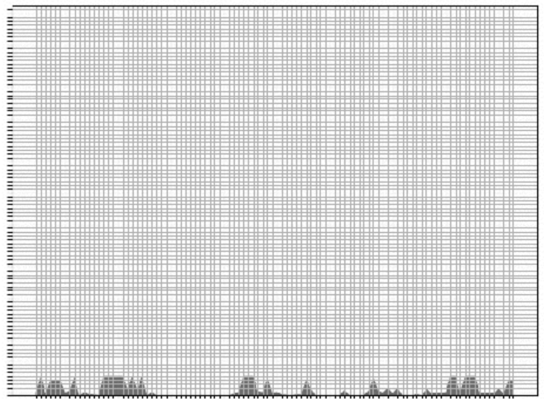




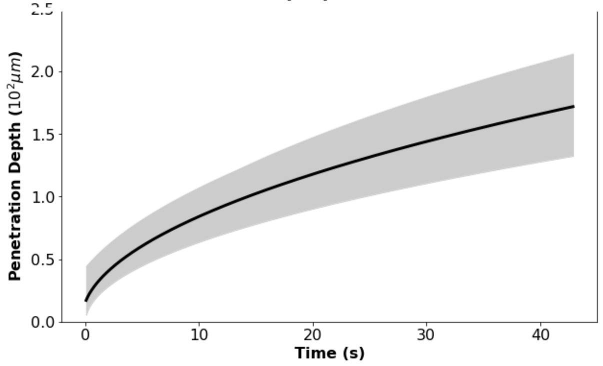


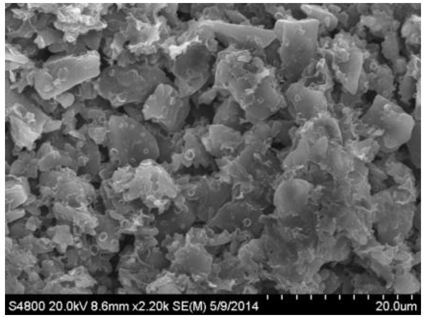


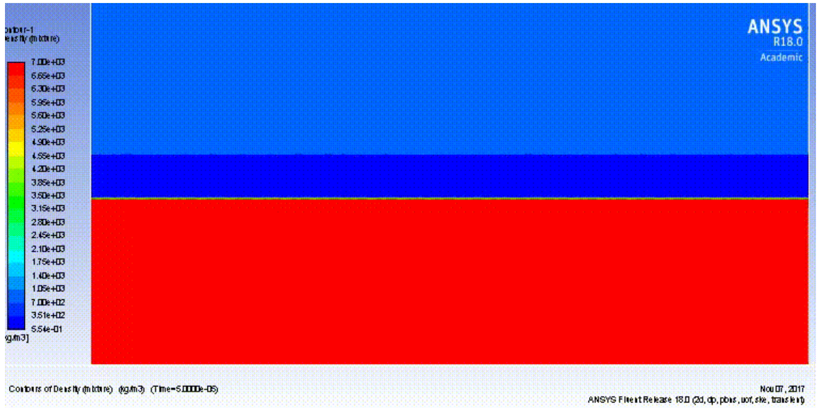
Exa-scale Pore Network Simulator (EXPNS):
High viscosity fluid invading through porous media



Uncertainty quantification







Acknowledgement

UTEP

UNIVERSITY OF WYOMING

THANK YOU ....

QUESTIONS ?