Modeling of a Continuous Inclined Blender - Developing a Database of Model Parameters to Predict Future Performance

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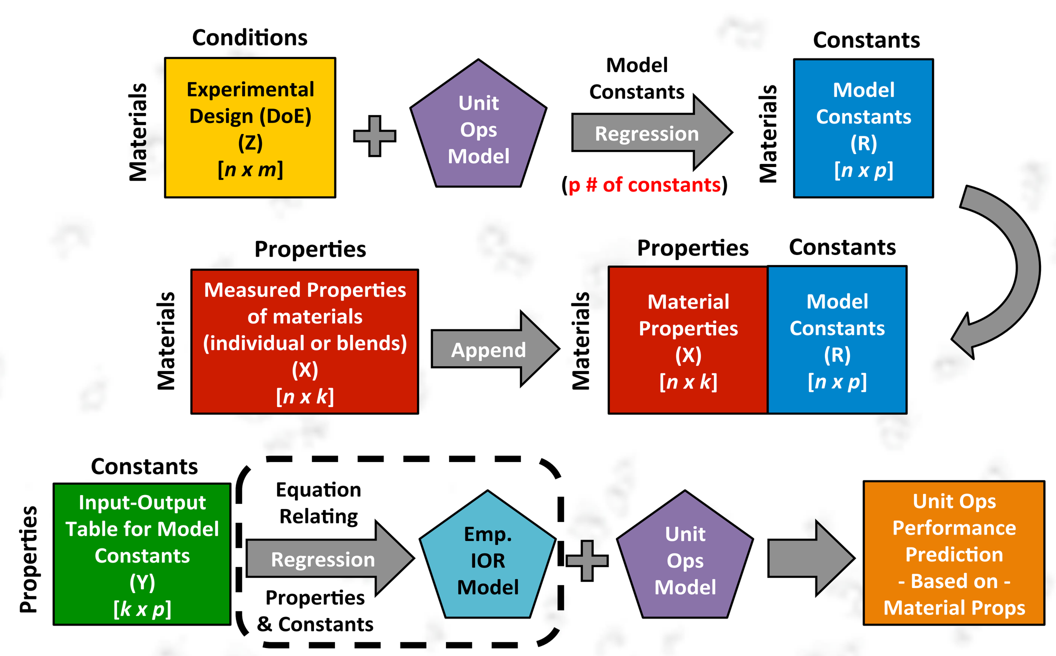
GOALS

- Develop a database of model parameters and correlate them to process parameters and material properties.
- Enable prediction of blender performance given the properties of the input materials or the blend.

DELIVERABLES

- Subject the blender to a variety of materials and operate it at a series of conditions performing RTD and dynamic holdup tests
- Fit the extracted data to suitable RTD and dynamic holdup models
- Correlate the model parameters to process parameters and material/blend properties
- Enable prediction of performance if the properties of the incoming materials/blends are known

DESCRIPTION

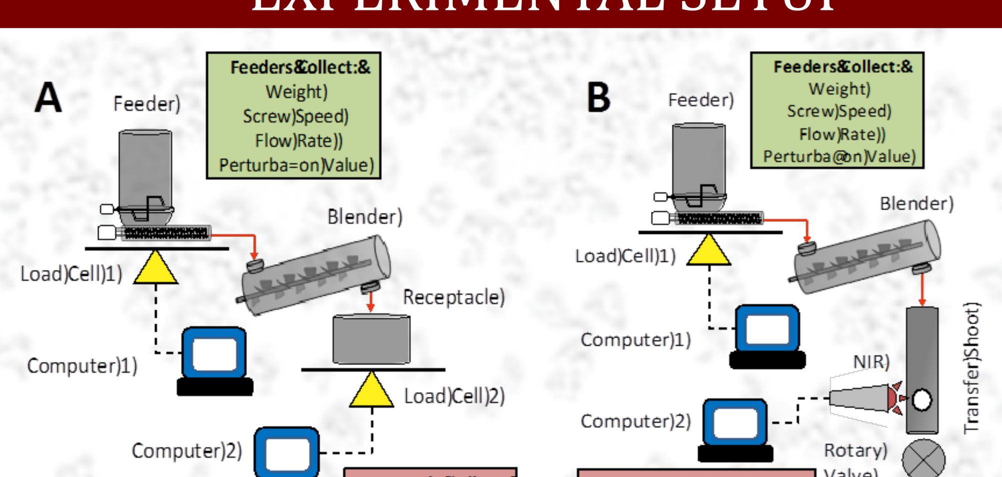


Experimental Design

Formulation	Material
Material Property Design Space Mapping (MPDSM)	Anhydrous Calcium Phosphate
	Metformin HCl
	Acetaminophen USP
	Prosolv HD90
	Avicel PH 102
	Croscarmellose Sodium
	Solka Floc
	Crospovidone (Poly XL 10)
	Magnesium Stearate

- Mass flowrate: 20 kg/hr and 40 kg/hr
- Impeller speed: 150, 250 and 350 rpm

EXPERIMENTAL SETUP



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MATERIAL SPARRING APPROACH TO DEVELOP CDC PRODUCTS

- A methodology based on API characteristics for screening formulations regarding their suitability for DCCM
- The methodology is data driven, where each question relates to a known product /process failure mode
- The methodology is fast - 1 week turnaround time
- The methodology is material sparing - less than 10 kg of blend
- The method distills in to the following six questions
  1. *Can we feed each ingredient at the required flow rate?*
  2. *Do ingredients stick or agglomerate?*
  3. ***Can we achieve blend homogeneity?***
  4. *Does the blend stick or agglomerate?*
  5. *Are blend flow properties good enough to achieve desired weight uniformity ?*
  6. *Will tablet attributes be adversely affected by the DCCM process?*

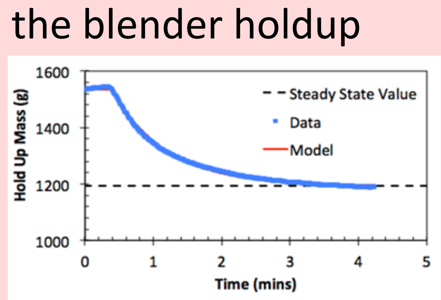
EXPERIMENTAL PROCEDURE

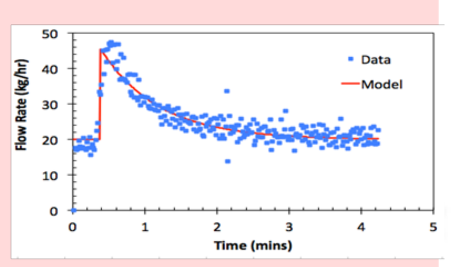
RTD Tests

- We begin with an empty blender set to the desired impeller speed
- Begin feeder, feeder data collection, NIR data collection and starting filling material in chute
- Allow the NIR data to show steady values
- Insert tracer
- Allow tracer to wash out – watch real time predictions
- Change to the next setting
- Allow for steady mass flow
- Repeat from Step 3

Holdup Tests

- We begin with an empty blender set to the desired impeller speed
- Begin feeder, feeder data and scale data collection
- Wait for the system to reach steady state
- Stop all units and measure weight of material in the collection bucket and weight of material dispensed by the feeder
- Difference between the weights is the blender holdup
- Resume operation
- Change to the next setting
- Repeat from Step 3





Holdup Models

Logistic function model – used for startup

$$F_{out}(t)=\frac{F_{in}}{1+Exp(-k(t-t_o))}$$

$$\frac{dM(t)}{dt}=F_{in}\left(1-\frac{1}{1+Exp(-k(t-t_o))}\right)$$

$$\therefore M(t)=\frac{F_{in}}{k}\left(kt+Ln(1+Exp[-kt_o])-Ln(1+Exp[kt-kt_o])\right)$$

First order model – used for startup

$$\tau\frac{-dM(t)}{dt}=Mss-M(t)$$

$$F_{out}(t)=F_{in}(t)-\frac{dM(t)}{dt}$$

$$\therefore F_{out}(t)=F_{in}(t)-\frac{Mss-M(t)}{\tau}$$

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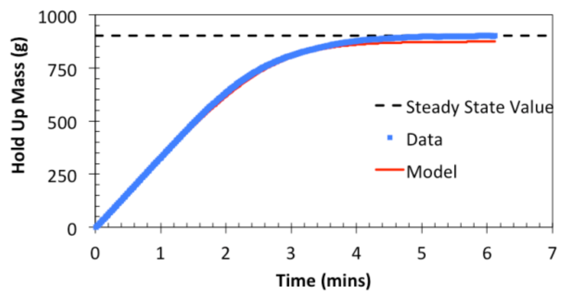
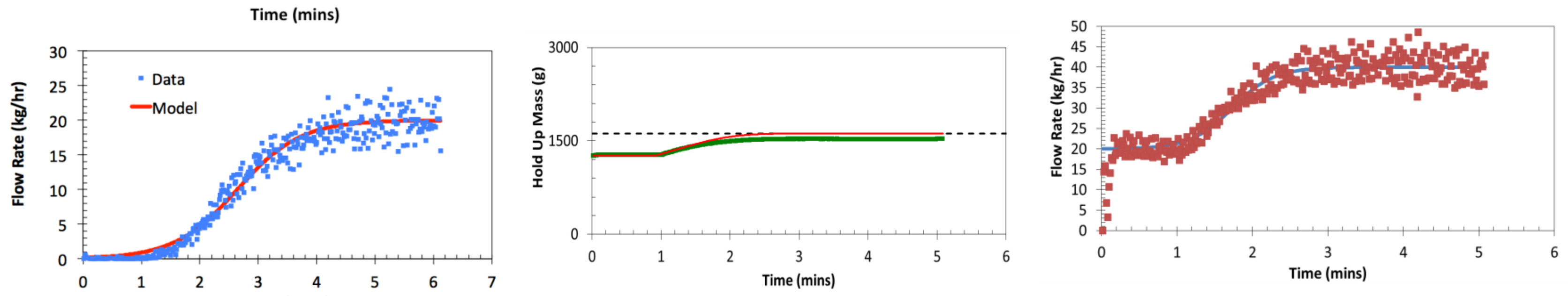
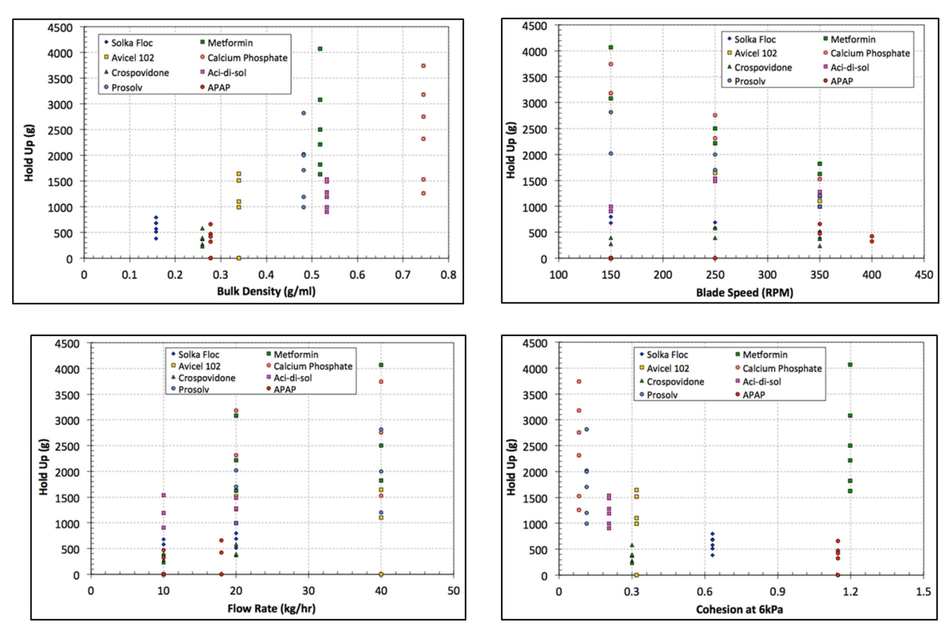
RESULTS

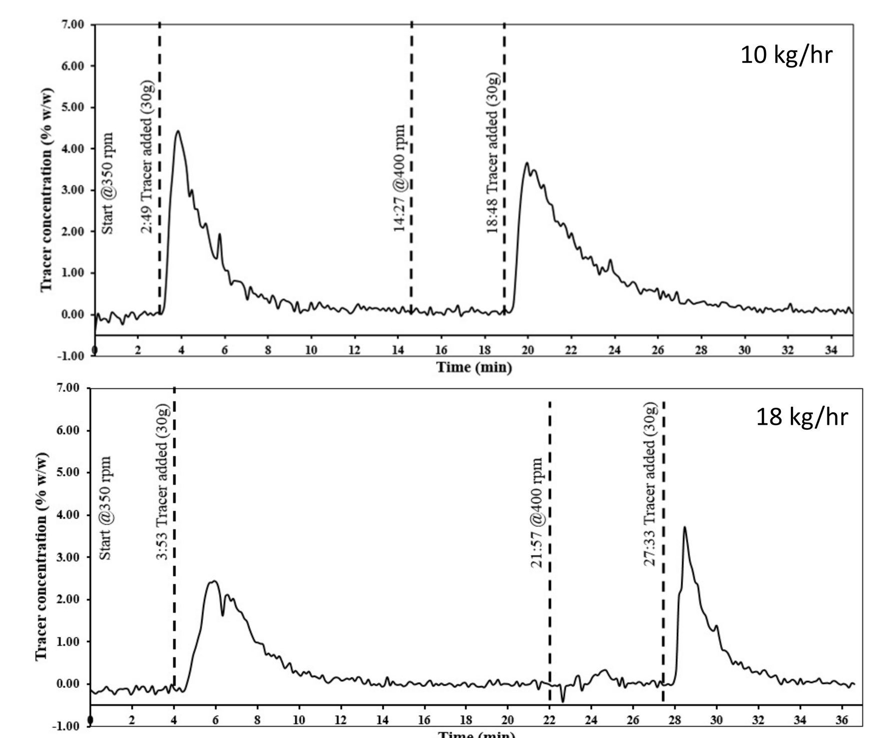


- Holdup experiments were performed for all materials are all conditions of the design space
- Data was fitted to the appropriate model and model parameters were extracted.





Material	Mass flow rate (kg/hr)	Impeller speed (rpm)	Holdup (kg)	Transition Time Constant (min) - τ	S-Rate Value (1/min)	Mid-Point Time (min)
Metformin	40	350	1.704	0.30	-	-
Metformin	40	250	2.282	0.62	-	-
Metformin	40	150	3.575	1.78	-	-
Metformin	20	150	3.090	-	1.83	9.27
Metformin	20	250	2.140	0.23	-	-
Metformin	20	350	1.576	0.29	-	-
APAP 0081	18	400	0.486	0.61	-	-
APAP 0081	18	350	0.711	0.99	-	-
APAP 0081	10	350	0.524	-	1.89	2.90
APAP 0081	10	400	0.382	0.37	-	-
SolkaFloc	10	150	0.684	-	3.06	2.30
SolkaFloc	10	250	0.584	0.32	-	-
SolkaFloc	10	350	0.401	0.25	-	-
SolkaFloc	20	150	0.773	0.76	-	-
SolkaFloc	20	250	0.658	0.71	-	-
SolkaFloc	20	350	0.467	0.48	-	-
Crospovidone	20	350	0.353	0.66	-	-
Crospovidone	20	250	0.576	0.81	-	-
Crospovidone	20	150	0.407	0.12	-	-
Crospovidone	10	150	0.270	-	3.10	1.31
Crospovidone	10	250	0.392	1.96	-	-
Crospovidone	10	350	0.238	0.58	-	-



Material	Mass flow rate (kg/hr)	Impeller speed (rpm)	Holdup (g)	Number of tanks (n)	Delay Time (sec)	RT per Tank (sec)	Blender MRT (sec)
Metformin	20	150	3080	2.62	238.0	121.6	318.1
Metformin	20	250	2213	2.18	103.0	134.4	292.6
Metformin	20	350	1629	1.93	137.4	213.6	413.1
Metformin	40	350	1818	N/A	N/A	N/A	N/A
Metformin	40	250	2499	N/A	N/A	N/A	N/A
Metformin	40	150	4070	N/A	N/A	N/A	N/A
APAP 0081	10	150	Choke	N/A	N/A	N/A	N/A
APAP 0081	10	250	Choke	N/A	N/A	N/A	N/A
APAP 0081	10	350	475	1.76	24.0	55.3	97.6
APAP 0081	10	400	327	1.72	72.4	93.5	160.9
APAP 0081	18	150	Choke	N/A	N/A	N/A	N/A
APAP 0081	18	250	Choke	N/A	N/A	N/A	N/A
APAP 0081	18	350	661	2.46	55.4	57.0	140.0
APAP 0081	18	400	427	2.07	32.5	38.0	78.6
SolkaFloc	20	150	795	3.08	92.2	44.1	135.6
SolkaFloc	20	250	686	1.61	45.1	44.0	71.1
SolkaFloc	20	350	514	1.37	26.9	50.2	68.7
SolkaFloc	10	350	385	1.36	153.2	104.4	141.5
SolkaFloc	10	250	576	4.66	60.6	47.0	218.7
SolkaFloc	10	150	679	3.92	6.2	72.5	284.3
Crospovidone	10	150	273	1.87	64.8	83.4	155.7
Crospovidone	10	250	391	1.64	126.0	342.7	561.6
Crospovidone	10	350	236	1.39	63.4	96.7	134.0
Crospovidone	20	350	370	1.24	56.2	70.5	87.2
Crospovidone	20	250	583	1.61	85.1	145.8	234.5
Crospovidone	20	150	397	1.74	40.3	45.1	78.4

CONCLUSIONS AND FUTURE WORK

- Dynamic houldup experiments were performed at 54 processing conditions and data was fitted to suitable models
- Experiments were performed to determine RTD of the blender at 54 processing conditions. The RTDs were fitted to a tank-in-series model and the model parameters were regressed.
- These model parameters will be correlated to processing conditions and material properties
- Models will be verified by performing additional validation experiments

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