Modelling spray drying of fine particles using gSOLIDS

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Acknowledgements:

- gSOLIDS model development: Mark Pinto (PSE)
- CFD/experiments: Ariane Bisten, Peter Clements (GSK)
- Analytical results: Mark Bloxham, Natalie Fa (GSK)

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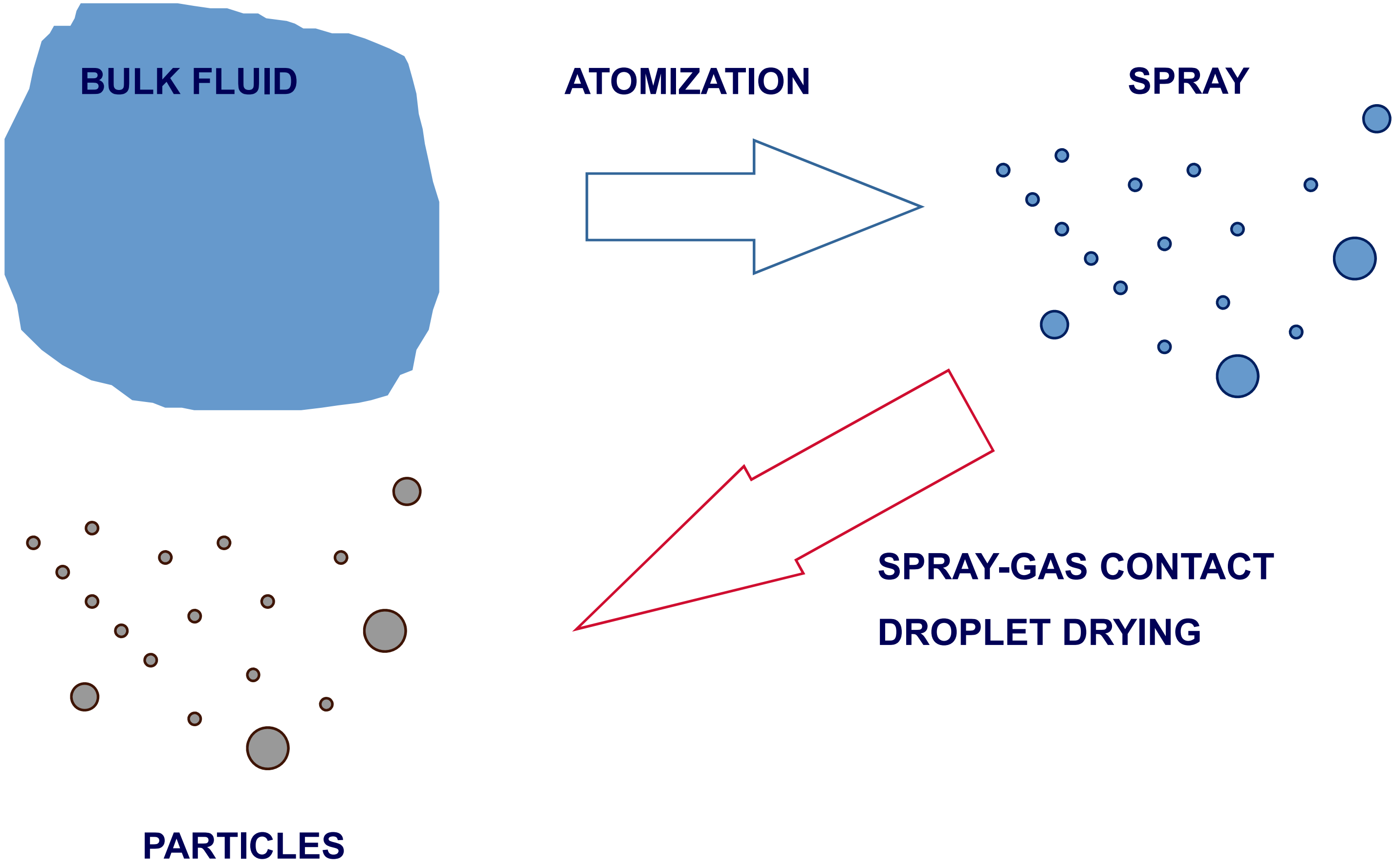
Contents

What is Spray Drying?

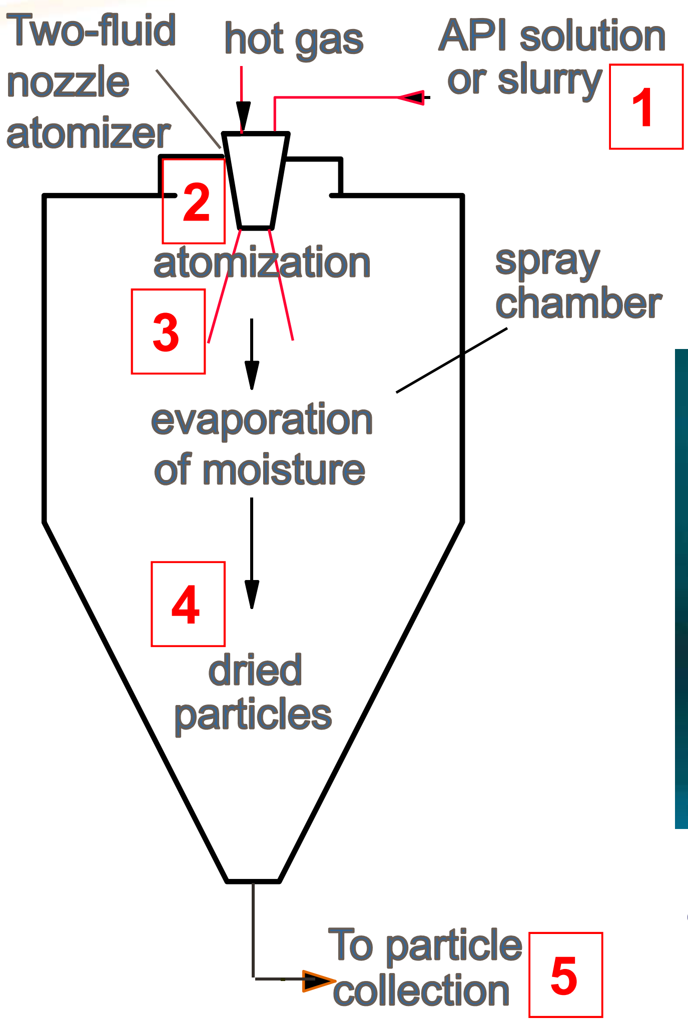
- Spray drying is evaporation of a liquid from a solution or suspension to give a dry powder product, by forming fine droplets and drying with hot gas
- It involves three key steps:
  - Atomisation
  - Droplet drying and particle formation
  - Particle collection

Spray drying – fundamental process



- Atomisation is required to make the droplets small enough to dry rapidly and to produce the required size range for the powder product

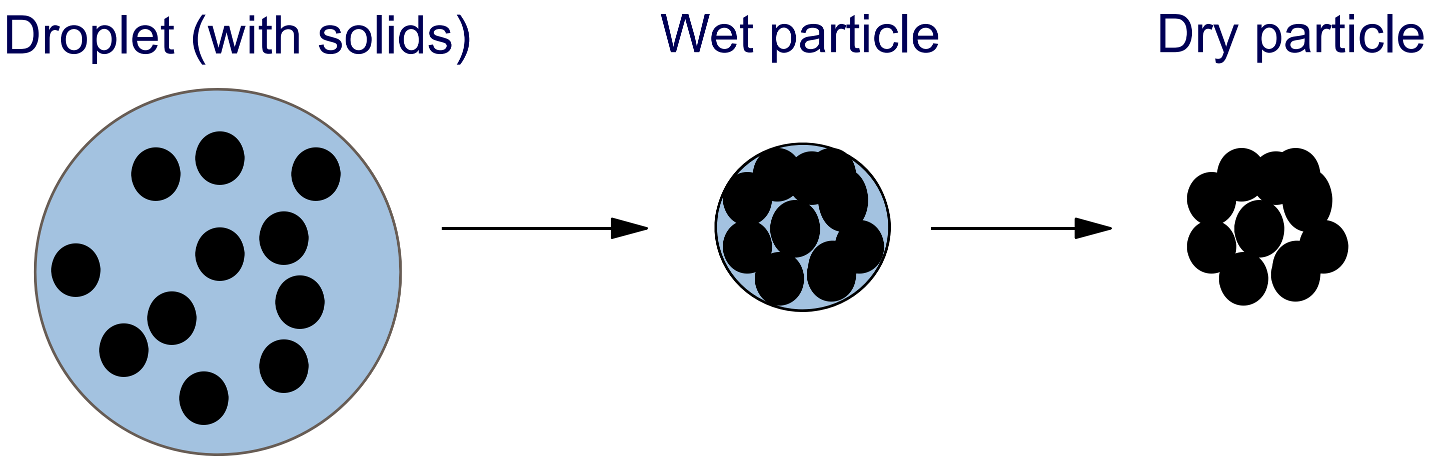
Spray dryers



Buchi 290 laboratory spray dryer (GSK Stevenage)

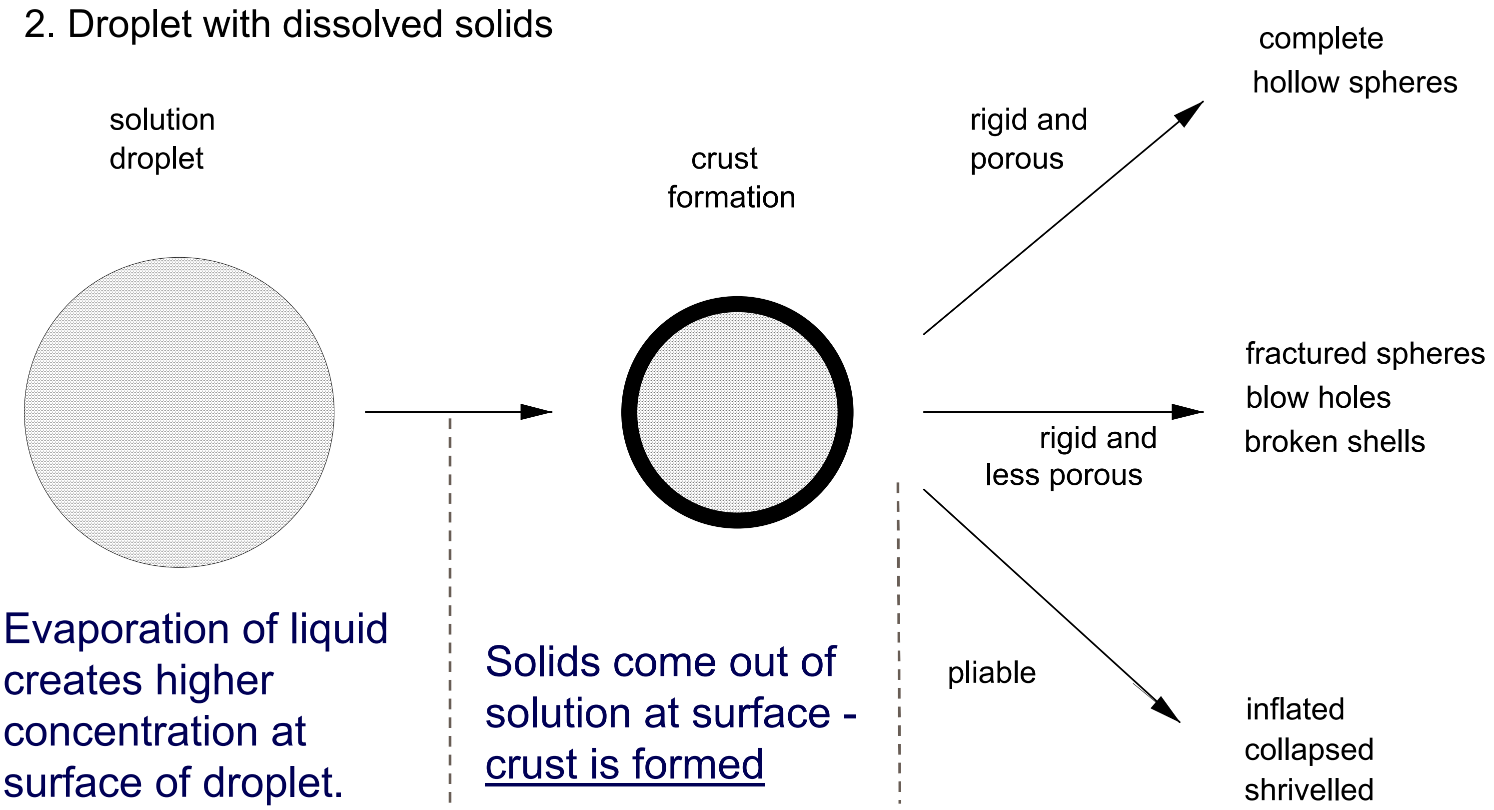
Typical GEA-Niro commercial spray dryer

Spray drying fundamentals - droplet drying



- Removal of bulk liquid; droplet shrinks
- Solids become continuous phase
- Removal of interparticle liquid
- Removal of surface moisture from particles
- Removal of internal moisture from particles

Droplet size changes
with dissolved solids (solution drying)



Evaporation of liquid creates higher concentration at surface of droplet.

Solids come out of solution at surface - crust is formed

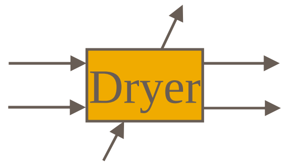
Can also occur to suspensions of insoluble solids if “particle tangling” occurs at surface or if significant soluble material is present

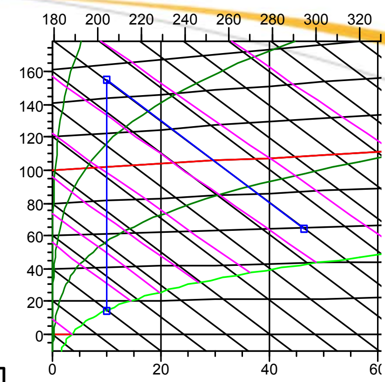
Theoretical steps

- Constant rate drying
  - Droplet surface fully wetted
  - Drying rate is controlled by external heat and mass transfer
  - Not actually constant rate in a cocurrent dryer because temperature driving force is falling continuously
- Falling rate drying
  - Outer surface partially or fully dry
  - Drying rate is controlled by internal mass transfer within the droplet or dry particle

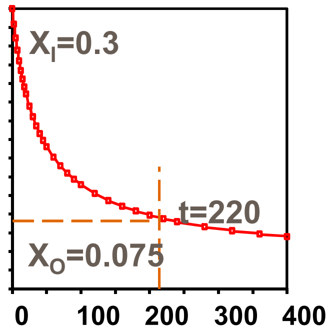
Levels of design models in drying

Macro scale



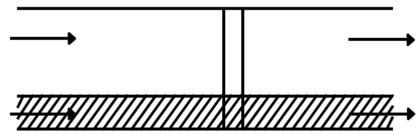


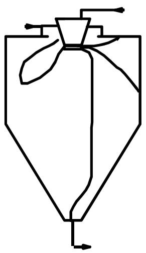
- 1. Heat and mass balance
- 2. Scoping (approximate) design
  - Psychrometric charts for hot air flow rates
- 3. Scaling methods (integral model)
  - Based on experimental batch drying curves



Micro/meso scale

- 4. Particle tracking - 1D incremental models
  - Stepwise integration, assumes plug flow
- 5. Particle tracking – 3D, e.g. CFD
  - Complex or swirling gas flow patterns

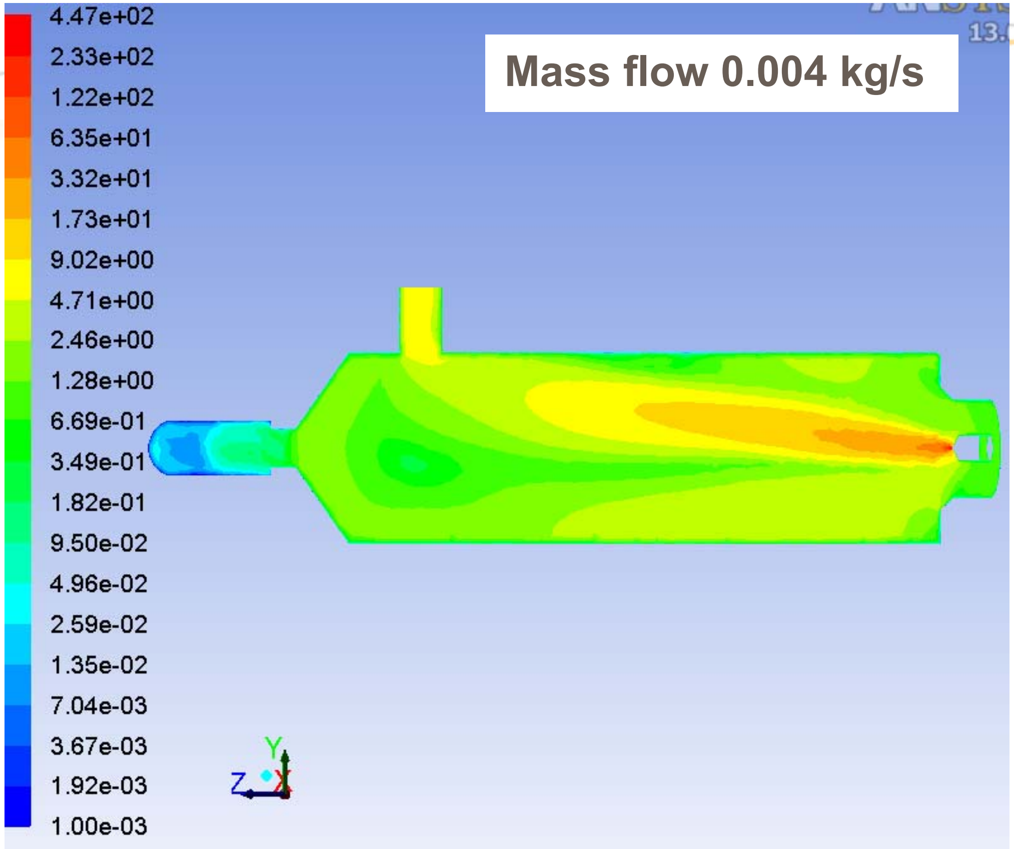


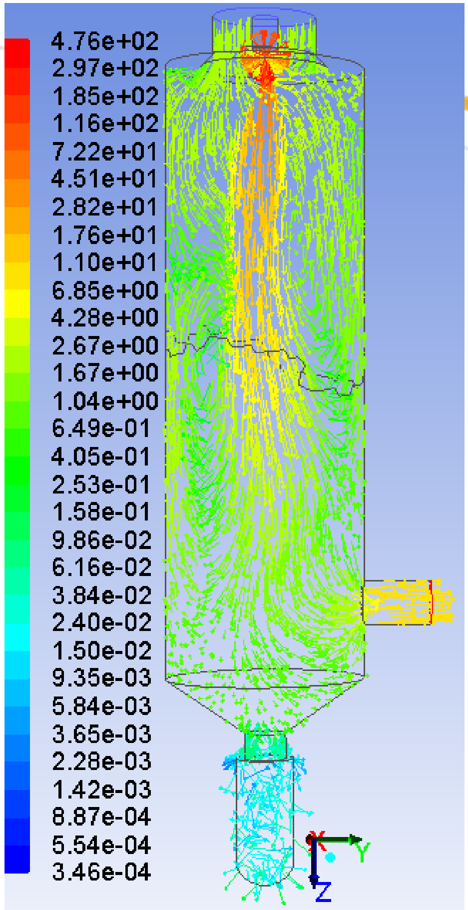


Strategy for spray dryer modelling

- Heat and mass balances (Levels 1 and 2) used for scale-up and production rate calculations
- Simple droplet models (Level 2) show basic relationship of final particle size to initial droplet size and solids concentration
- CFD modelling with FLUENT™ (Level 5) demonstrates flow patterns
  - Cool fast-flowing core, hot central annulus, cool stagnant outer layer
  - Variability in droplet/particle residence time

CFD simulation for Buchi 290 laboratory spray dryer





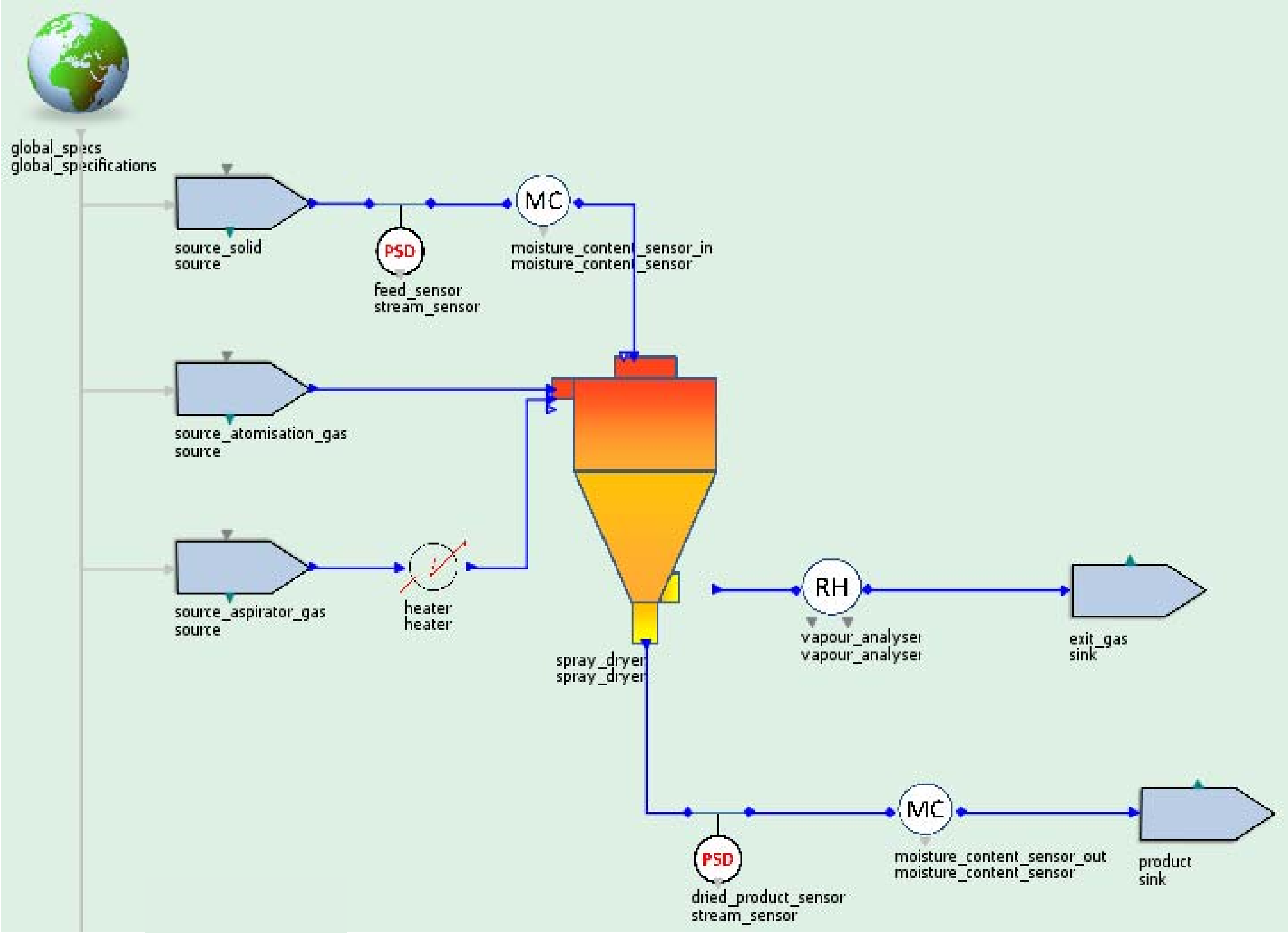
- Particle tracking results for mass flow 0.006 kg/s:
- Average Residence Time (CFD): 0.2 - 0.35 sec
- Minimum Residence Time (CFD): 0.05 - 0.08 sec
- Average Residence Time (Plug Flow or CSTR): 1.5 sec

- Mass Flow: 0.006 kg/s
- Gas Flow in centre, recirculation zones along the walls

Strategy for spray dryer modelling

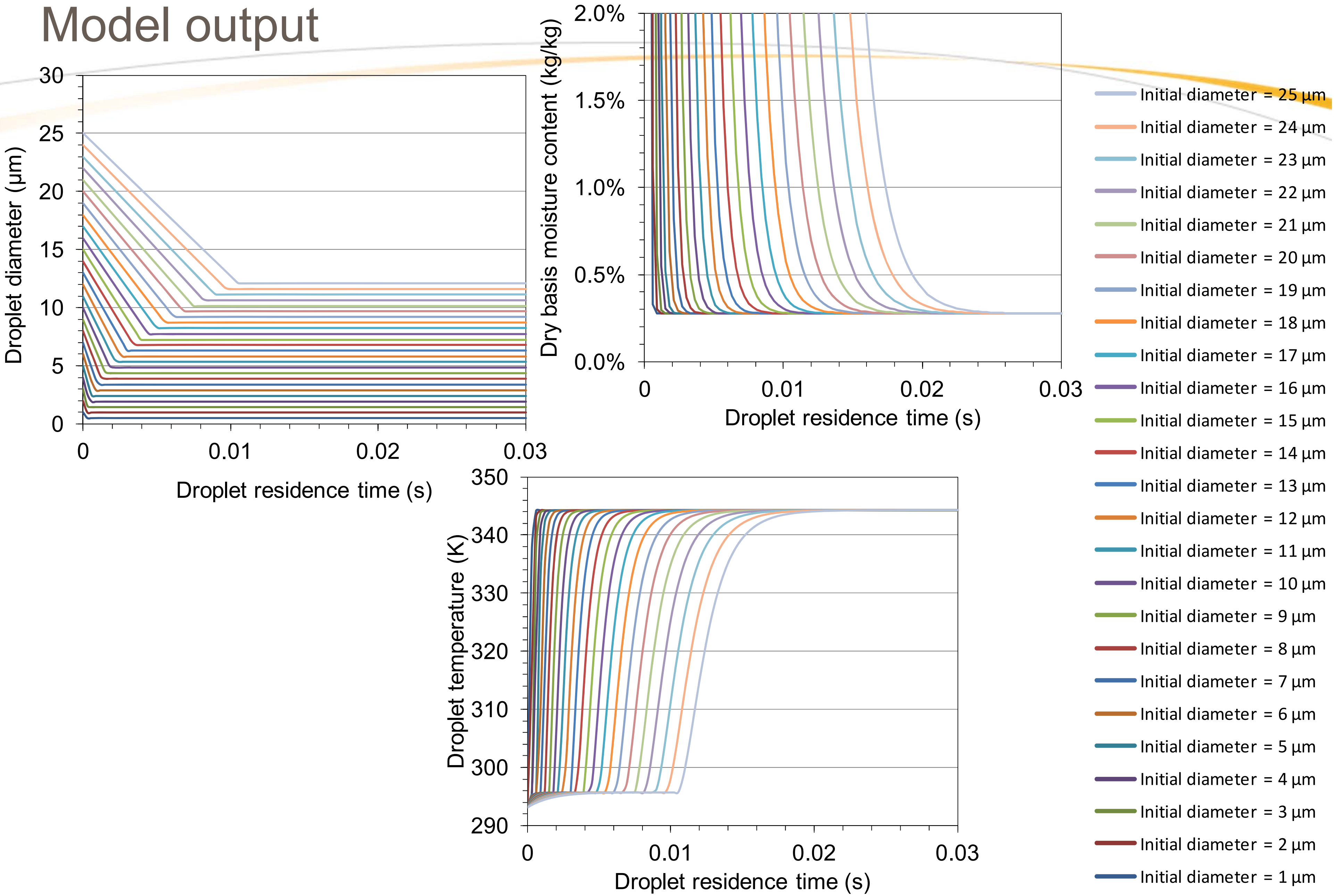
- Heat and mass balances (Levels 1 and 2) used for scale-up and production rate calculations
- Simple droplet models (Level 2) show basic relationship of final particle size to initial droplet size and solids concentration
- CFD modelling with FLUENT™ (Level 5) demonstrates flow patterns; cool fast-flowing core, hot central annulus, cool stagnant outer layer
- PSE gSOLIDS model is a one-dimensional Level 4 incremental model giving droplet and particle tracking through the spray dryer
  - Can incorporate CFD insights on multiple zones rather than assuming plug flow or CSTR
  - Much faster than CFD for "what-if" calculations to show trends and gain process understanding
  - More flexibility than CFD to vary the drying model and allow for crust formation

Modelling Approach in gSOLIDS
User Interface



Modelling Approach in gSOLIDS

Model output



Modelling Approach in gSOLIDS
General method

- Assume a known droplet size distribution from the atomiser
  - Back-calculated from measured particle size distribution; x_{90} ~5μm → d_{90}~10 μm
- Track each individual droplet through the spray dryer
- Calculate local gas temperature and humidity and heat transfer rate
- Calculate local drying rate and change in moisture content
- Calculate shrinkage and new droplet diameter based on mass evaporated
- At a given point, assume crust formation and constant to falling rate transition
- Calculate falling rate drying assuming first-order kinetics

Modelling Approach in gSOLIDS

IPO (current state)

Experimental Database
Process conditions,
Equipment (scale/type),
compounds, solvents
Heat Loss (from outlet temp)
Residence time distribution
(from CFD)

gSOLIDS model includes:

Spray chamber

Input Attributes	Process Parameters	Model Output
Suspension (or solution) attributes Solid Particle Size Solvent properties Gas properties Sorption Isotherm **Inlet droplet size distribution** (back calculated)	Atomisation Flowrate Inlet flow rates (Liq,Gas) Inlet temperatures Spray chamber geometry	temperature history (vs BP, stability, glass transition) **ex spray chamber:** - Yield - Moisture content (dry basis) - Particle Size

Modelling Approach in gSOLIDS

IPO (future state including atomisation, classification & CFD)

Experimental Database
Process conditions,
Equipment (scale/type),
compounds, solvents

CFD model

gSOLIDS model includes:
Atomisation
Spray chamber
Classification, breakage

Input Attributes	Process Parameters	Model Output
Suspension (or solution) attributes	**Atomisation Flowrate**	temperature history
Solid Particle Size	Inlet flow rates (Liq,Gas)	(vs BP, stability, glass transition)
Solvent properties	Inlet temperatures	**ex collection pot:**
Gas properties	**Nozzle type / geometry**	- Yield
Sorption Isotherm	Spray chamber geometry	- Moisture content (dry basis)
	Cyclone geometry	- Particle Size

Modelling Approach in gSOLIDS

Ultimate aim

- Include a range of droplet and particle size distributions
- Include a range of particle residence times
- Determine product moisture content for the full range (e.g. display via a 3-D plot)
- Link to CFD

Results

Experimental Data

- 17 spray drying batches using suspensions of **Lactose/MgStearate in Ethyl Acetate**
- Equipment used: Buchi B-290 small scale spray dryer, using a 2-Fluid nozzle
- Varied control parameters:

  - Aspiration flowrate (main gas flowrate) (10-20m^3/h)

  - Inlet Temperature (100-200 C) → Outlet temperature (60-90 C)

  - Atomisation gas flowrate (0.3, 0.5 g/s)

  - Liquid feedrate (5, 15, 25 mL/min)

  - Solid concentration (2.5, 5, 10 w/w%)
- Measured output attributes:

  - **Particle Size** (x10, x50, x90) → **measured 0.7-13μm**

  - **Moisture content** (Ethyl Acetate) by NMR → **measured 0.3-0.9w/w%**
- Also available: Sorption isotherm (gravimetric vapour sorption), Construct density (particle strength testing), Residence time (CFD modelling)

Results
Sensitivity Study

- Assess impact of process parameters on output attributes
  (no / low ↑ / medium ↑ / high impact ↑) (black: model, red: experiment)
- Increase input parameters 10% from base case → study impact on output attributes

	Control parameters						
	Aspiration flowrate	Inlet temperature	Atomisation gas flowrate	Liquid feedrate	Solids conc	Inlet droplet size	Heat loss
Particle size			↓	↑	↑ ↑	↑	
Solvent content	↓ ↓	↓ ↓		↑ ↑	↓ ↓	↑	↑

- Inlet temperature ↑ → Heat Loss ↑
- Atomisation flowrate ↓, liquid feedrate ↑ → Inlet droplet size ↑

gSOLIDS model agrees qualitatively with experimental findings

gSOLIDS model currently models heat balance but not atomisation process

Process parameters

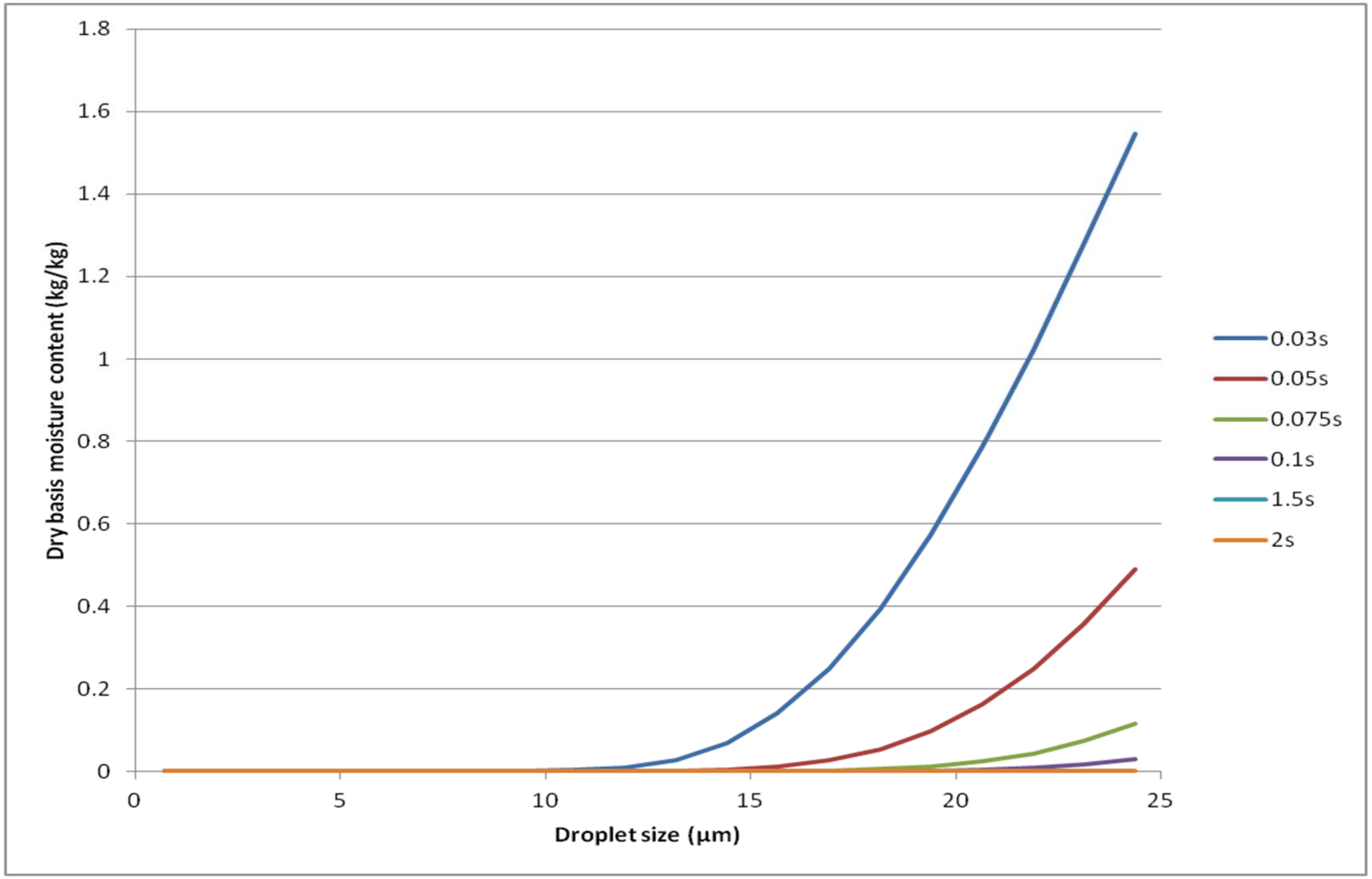
Parameter / Dependance	Aspirator ↑	Humidity drying gas ↑	Inlet temperture ↑	Spray gas flow ↑	Feed rate ↑	Solid concentration ↑	Organic solvent instead of water ↑
Outlet temperature	↑	↑	↑	↓	↓	↑	↑
Particle size	—	—	—	↓	↑	↑	↓
Humidity in final product	↓	↑	↓	—	↑	↓	↓
Yield	↑	↓	↑	—	↓ ↑	↑	↑

Legend:		
	⇧ High influence	Increasing parameter
	↑ Moderate influence	Increasing variable
	↑ Minor influence	Decreasing variable
	— No influence	

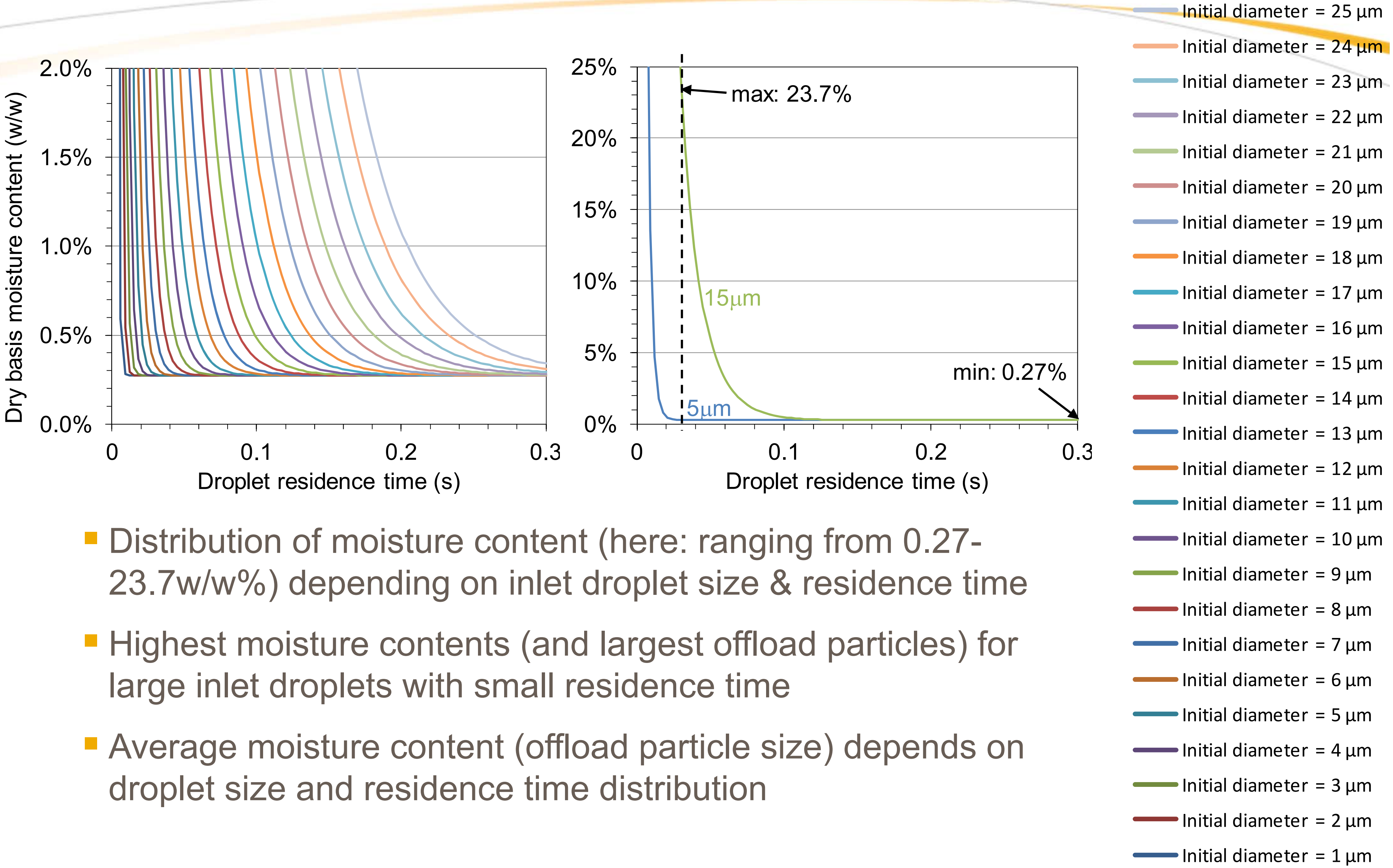
Courtesy Buchi AG, Switzerland

Results
Final moisture content for different droplet sizes

- Minimum residence time to give complete drying for a given droplet size
- Demonstrates importance of effective atomisation



Results
Moisture content for different residence times



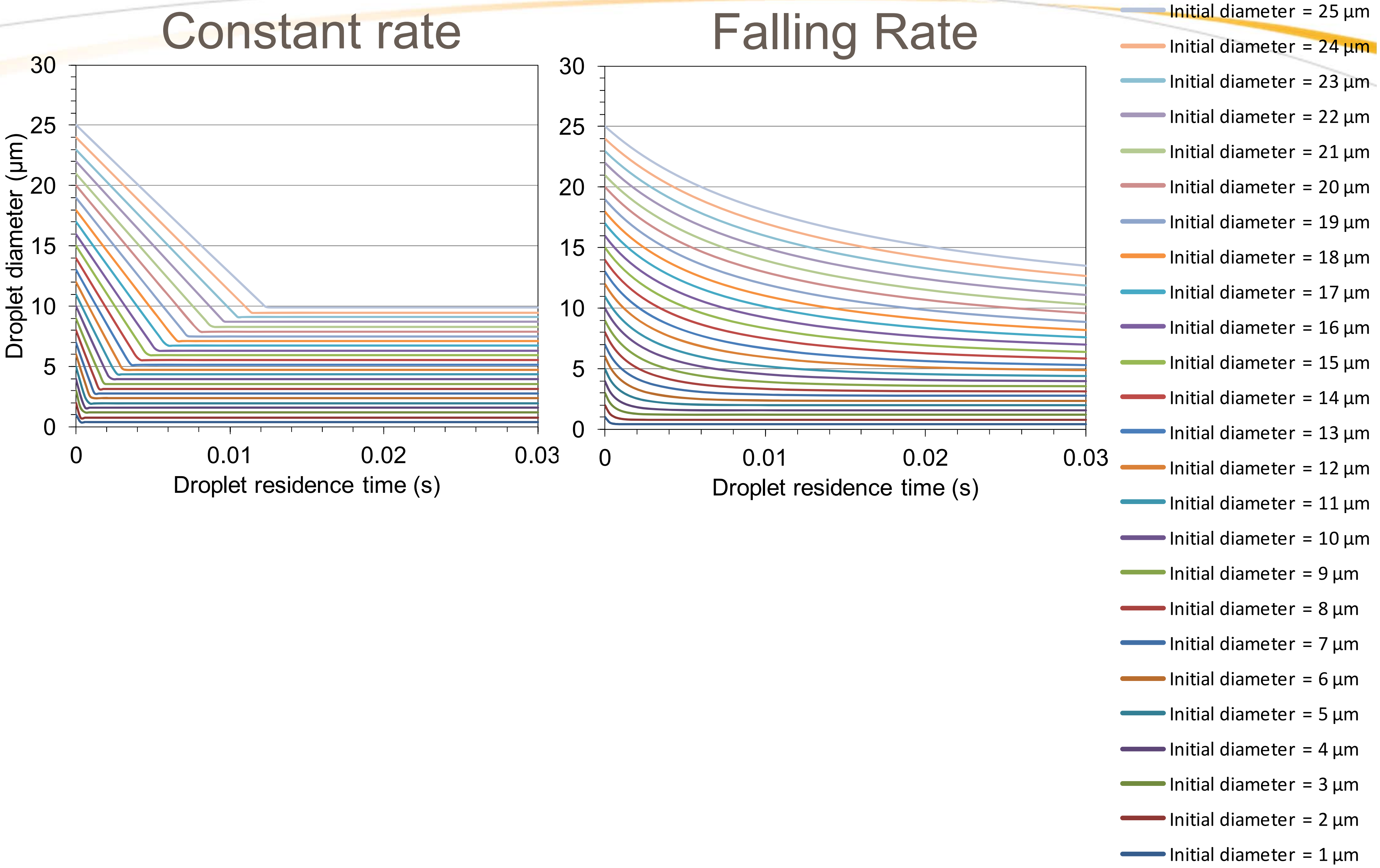
- Distribution of moisture content (here: ranging from 0.27-23.7w/w%) depending on inlet droplet size & residence time
- Highest moisture contents (and largest offload particles) for large inlet droplets with small residence time
- Average moisture content (offload particle size) depends on droplet size and residence time distribution

Results
Alternative scenarios

- Model different cases to give boundary values for the drying achieved
- 1) Falling rate drying throughout, with no shrinkage
  - Instant formation of a rigid crust
- 2) Falling rate drying throughout, with shrinkage
  - Instant formation of a pliable skin
- 3) Constant rate drying throughout, with shrinkage
  - No crust formation
- 4) Constant rate drying throughout, with no shrinkage (physically unlikely)
- 5) Constant rate with shrinkage, followed by falling rate drying with no shrinkage
  - The most physically likely scenario; crust formation at a given surface concentration
  - Should give results intermediate between pure constant and falling rate

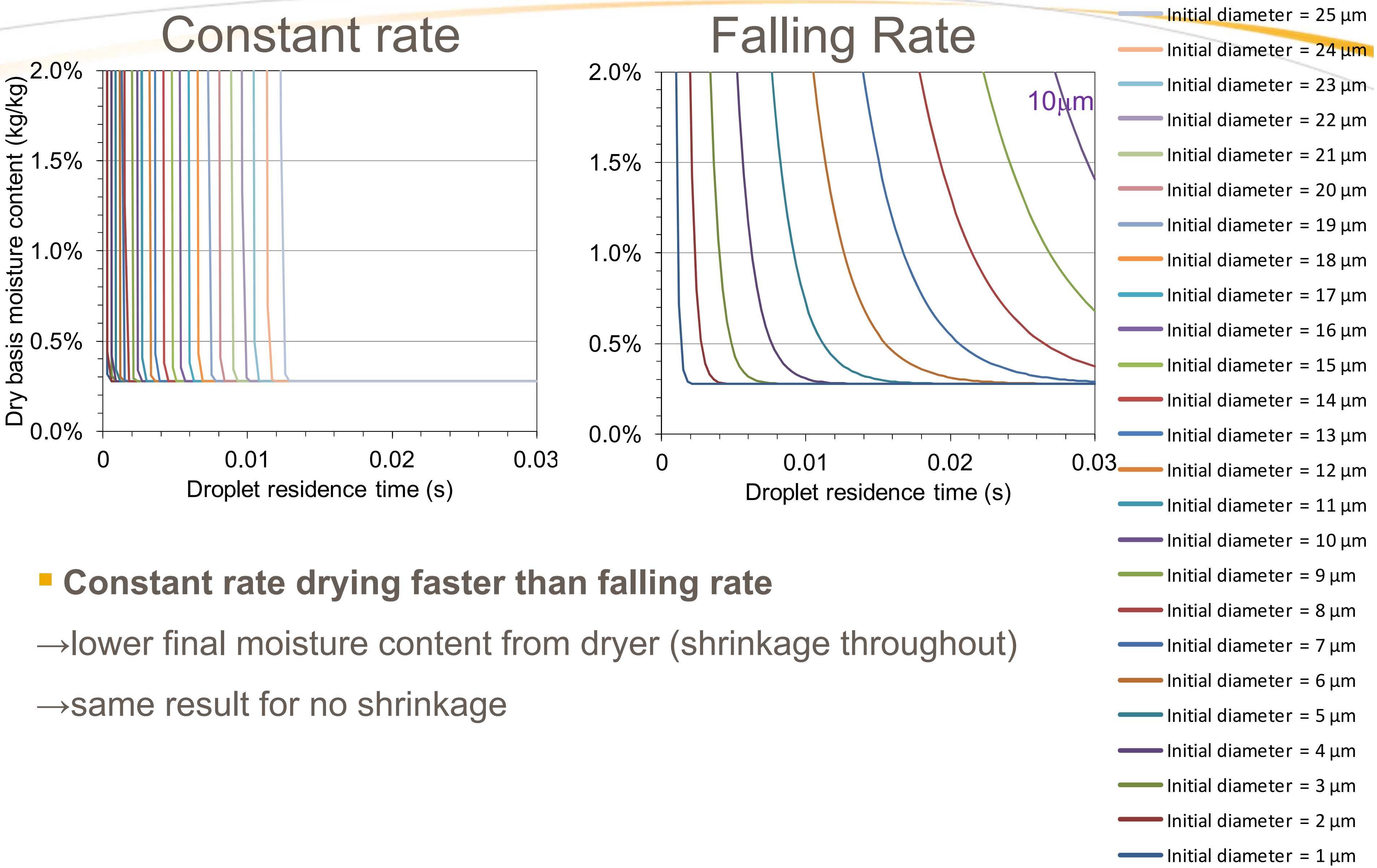
Results – Effect of drying regime

Shrinkage



Results – Effect of drying regime

Shrinkage



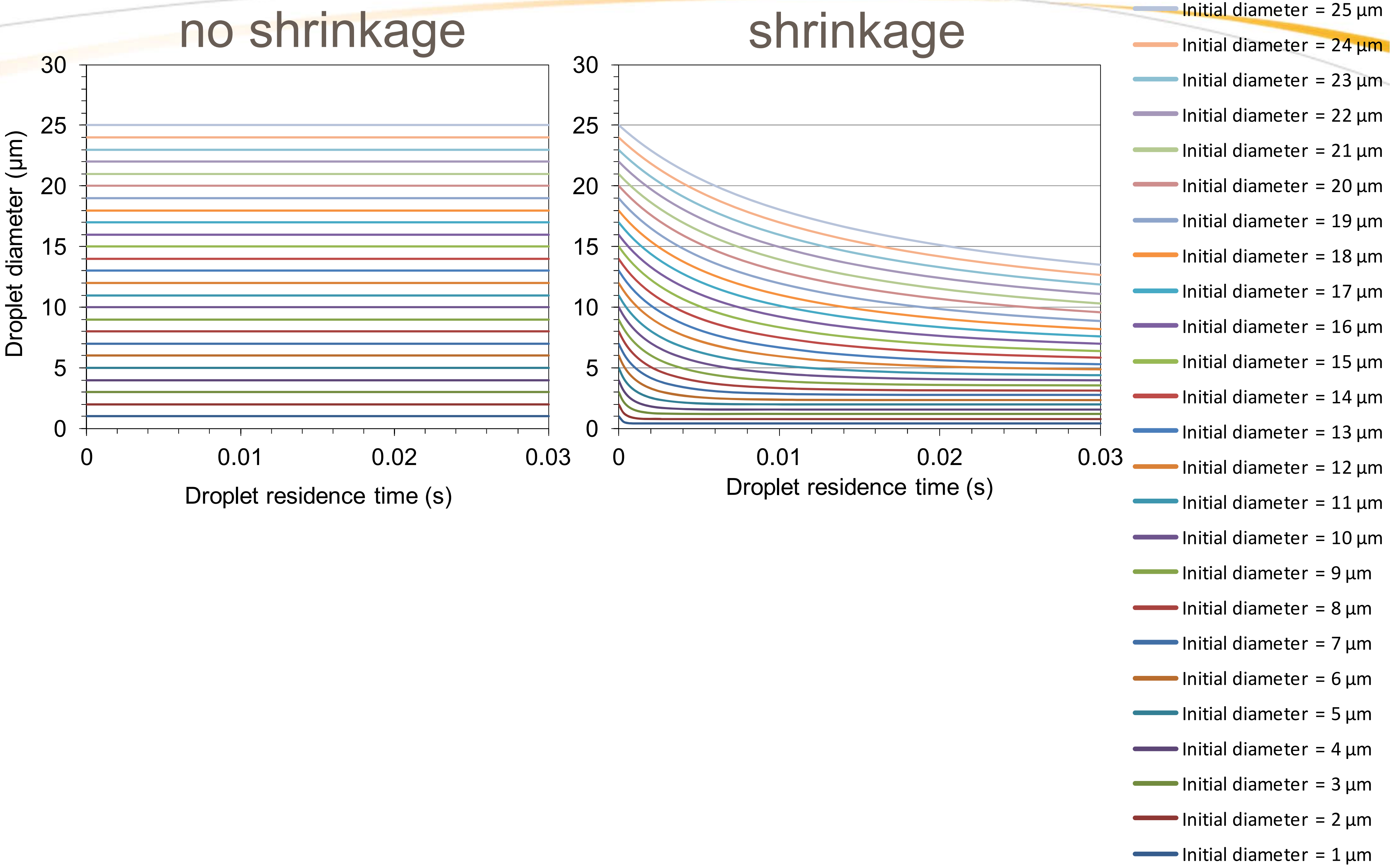
- **Constant rate drying faster than falling rate**

→lower final moisture content from dryer (shrinkage throughout)

→same result for no shrinkage

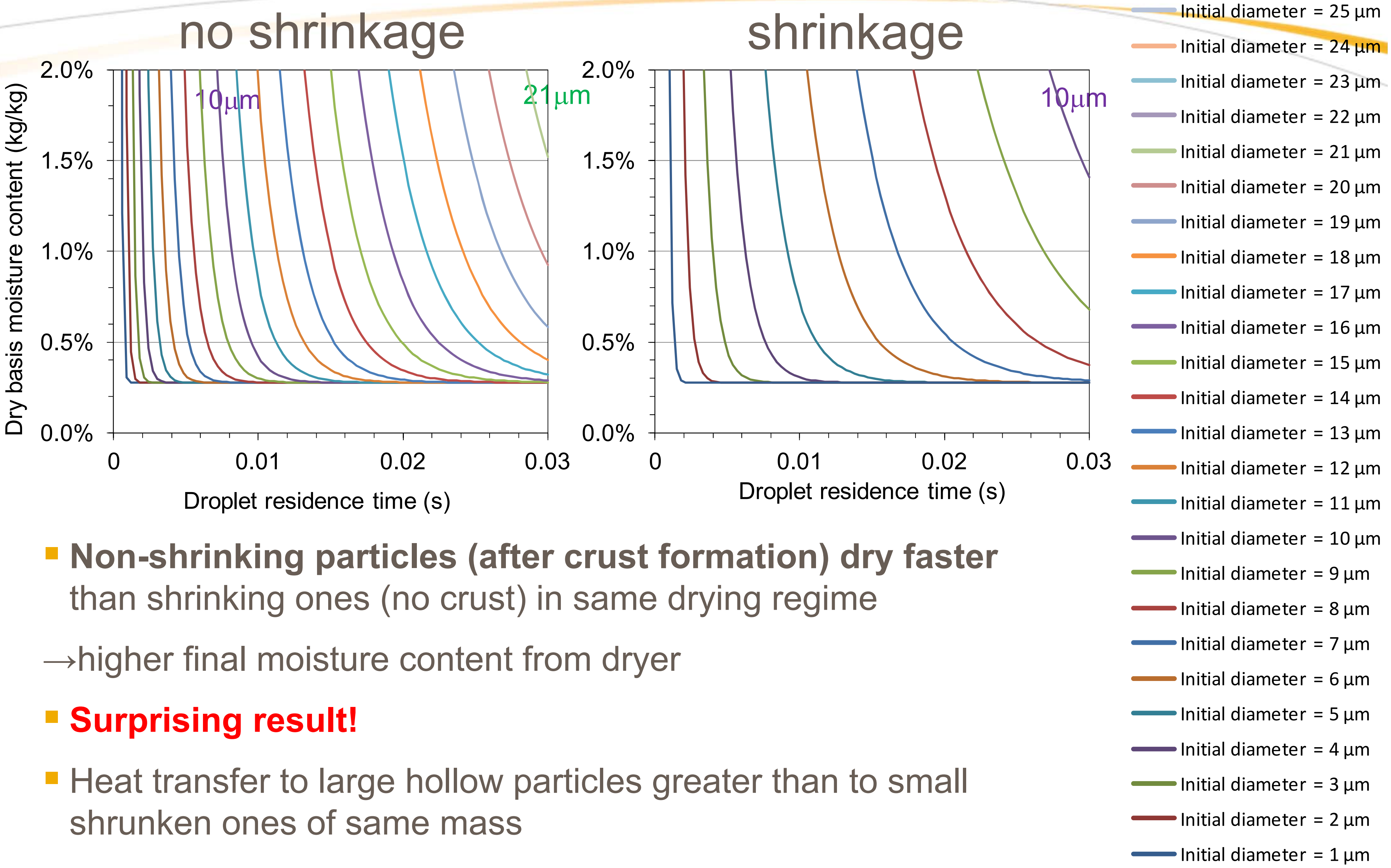
Results – Effect of crust formation

Falling rate drying



Results – Effect of crust formation

Falling rate drying

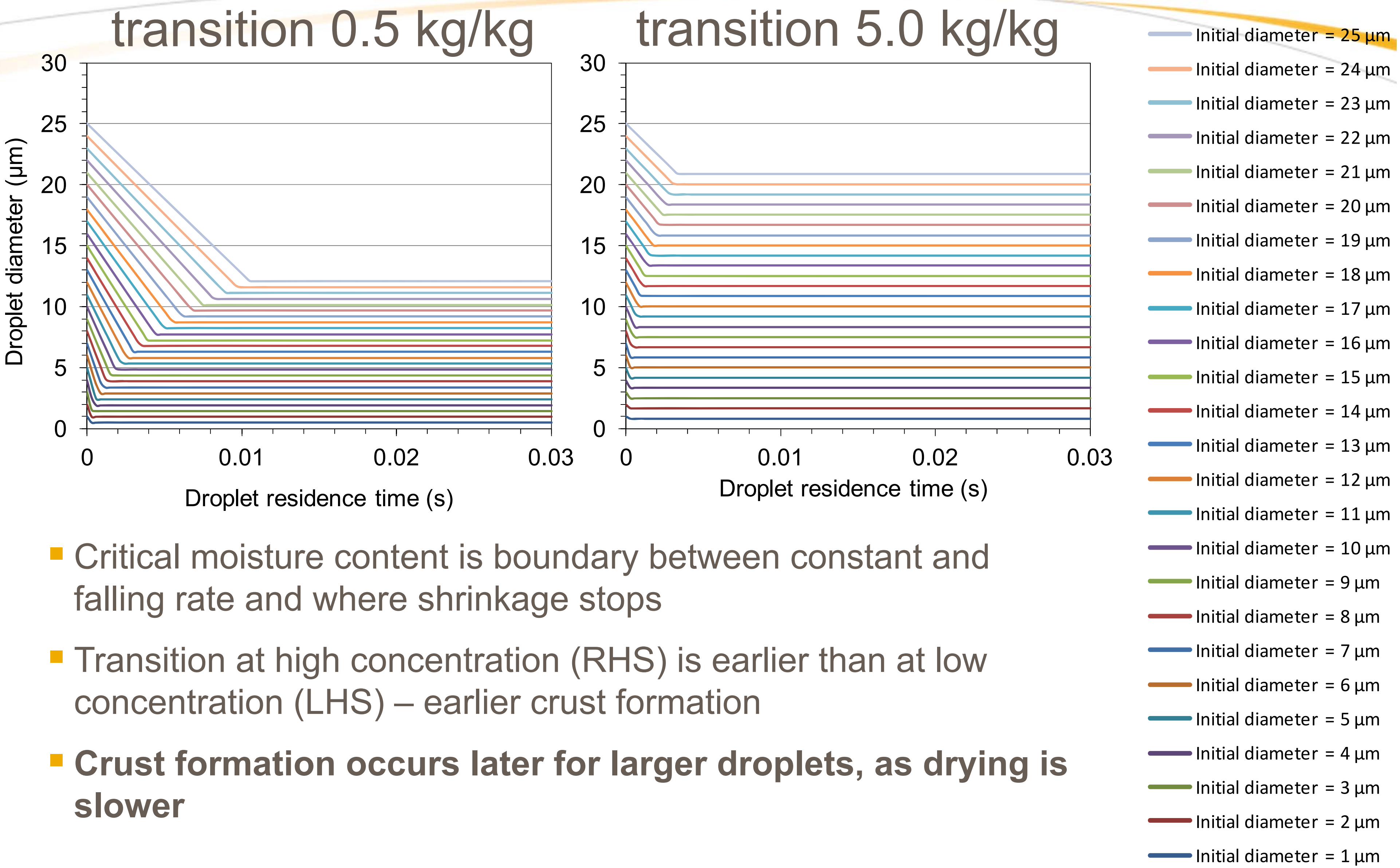


- **Non-shrinking particles (after crust formation) dry faster** than shrinking ones (no crust) in same drying regime

→higher final moisture content from dryer

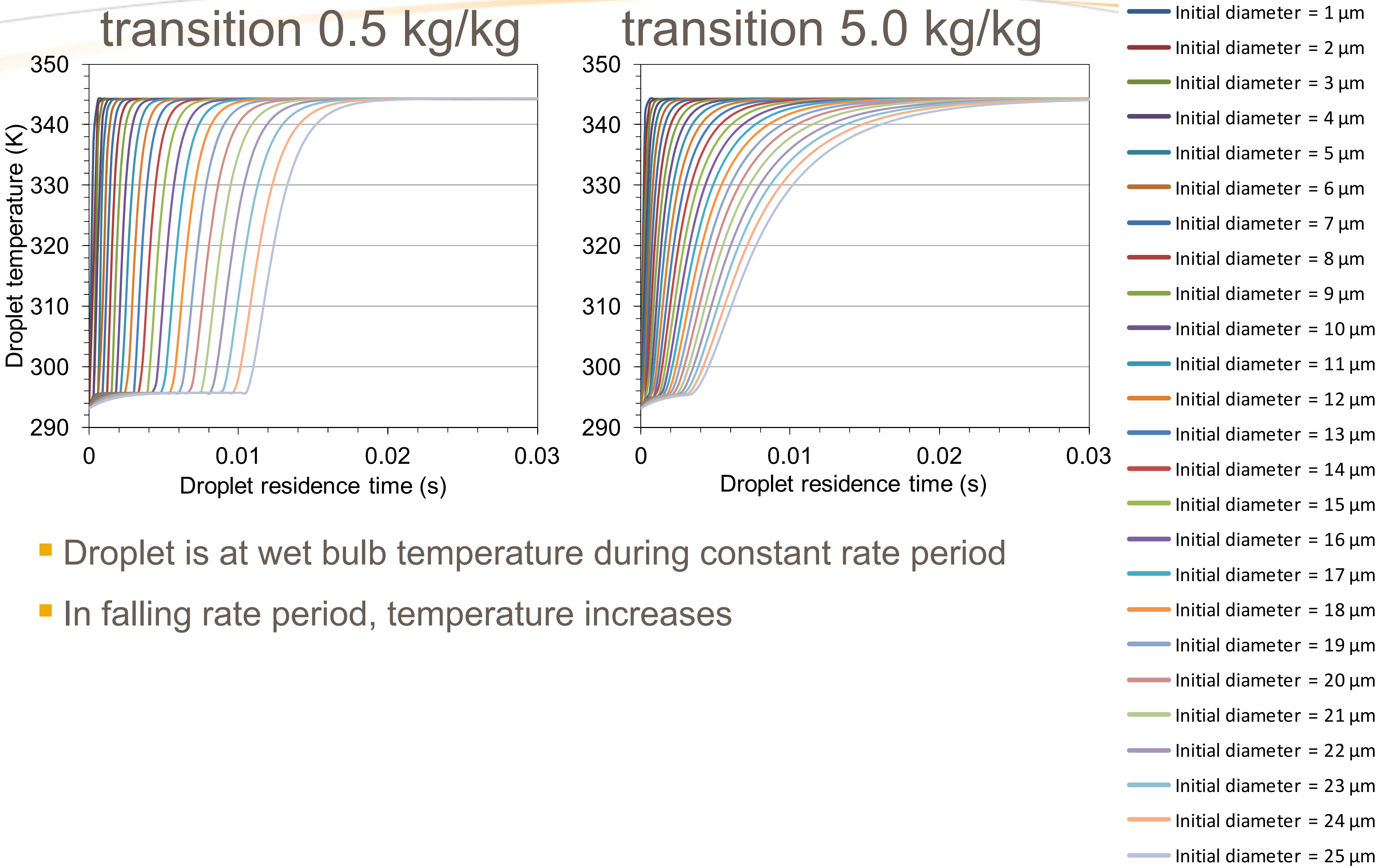
- **Surprising result!**
- Heat transfer to large hollow particles greater than to small shrunken ones of same mass

Constant rate with shrinkage, followed by falling rate drying with no shrinkage



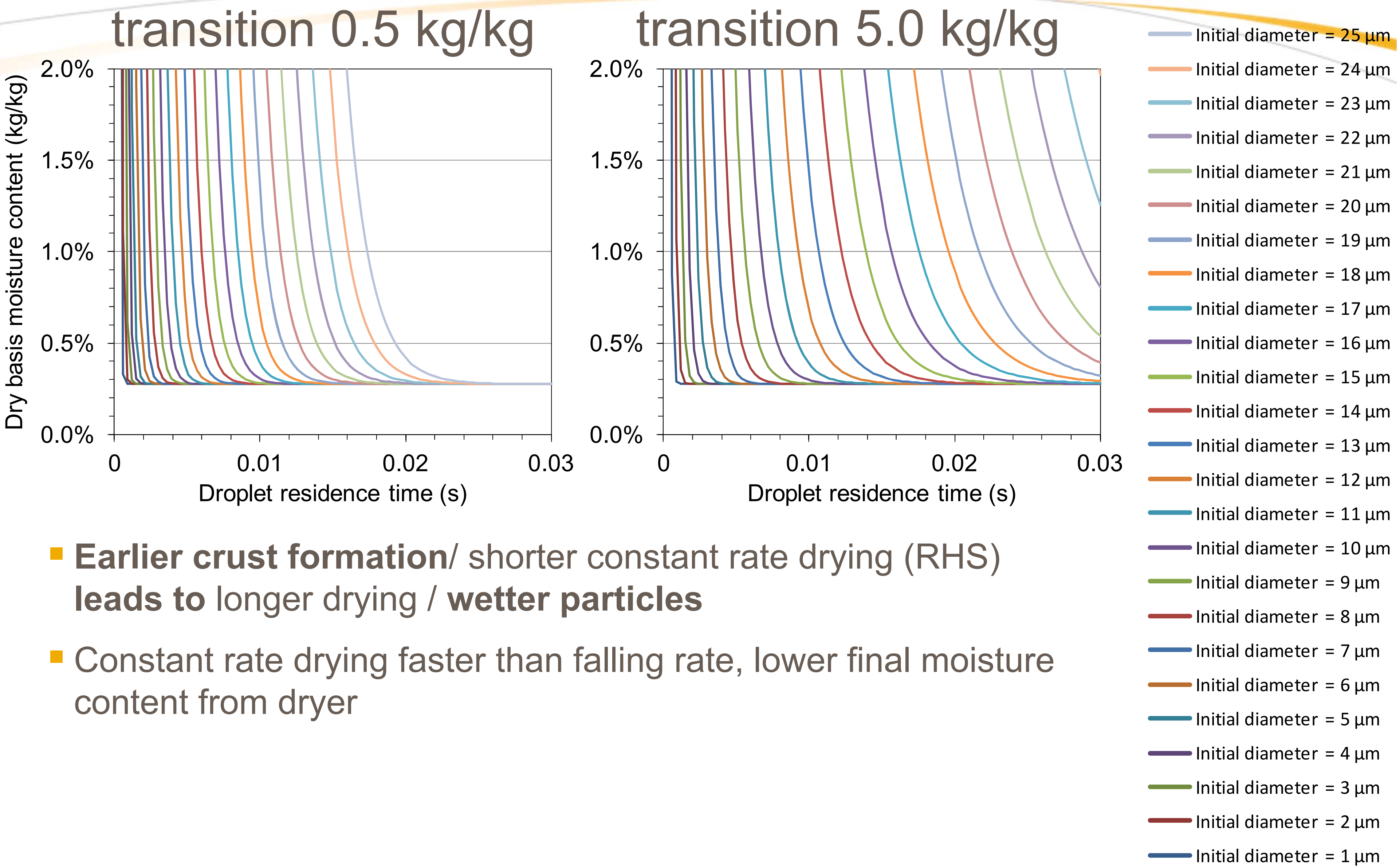
- Critical moisture content is boundary between constant and falling rate and where shrinkage stops
- Transition at high concentration (RHS) is earlier than at low concentration (LHS) – earlier crust formation
- **Crust formation occurs later for larger droplets, as drying is slower**

Constant rate with shrinkage, followed by falling rate drying with no shrinkage



- Droplet is at wet bulb temperature during constant rate period
- In falling rate period, temperature increases

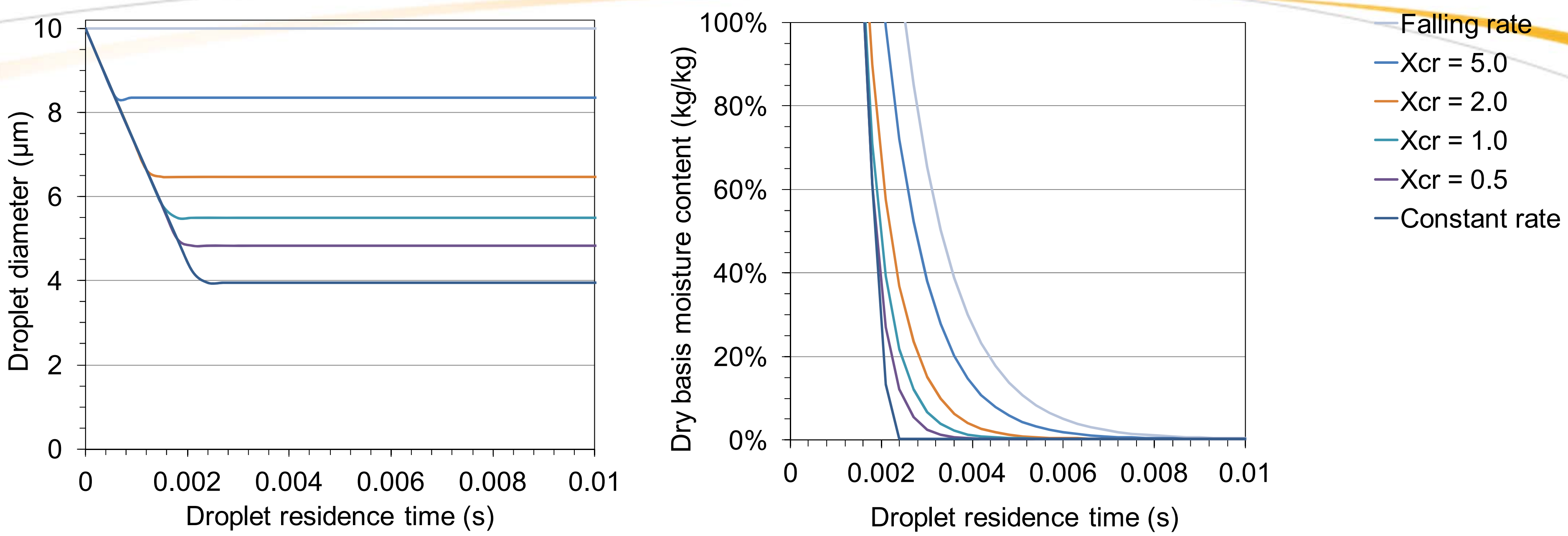
Constant rate with shrinkage, followed by falling rate drying with no shrinkage



- **Earlier crust formation**/ shorter constant rate drying (RHS) **leads to** longer drying / **wetter particles**
- Constant rate drying faster than falling rate, lower final moisture content from dryer

Results – Effect of drying regime

Falling vs constant vs mixed regime (10μm droplets)



- **Earlier crust formation**/ shorter constant rate drying **leads to** longer drying / **wetter particles**
- 10μm droplets reach equilibrium moisture content of 0.27w/w% at 0.01s (minimum residence time is 0.03s) regardless of chosen scenario – offload shows moisture content of 0.3-0.9w/w%

→ **current model is overpredicting drying rates (falling rate period)**

Results
Effect of crust formation and drying regime

Expected from theory, confirmed by model:

- **Constant rate drying faster than falling rate**, lower final moisture content from dryer
- **Constant rate drying with shrinkage is faster than falling rate drying without shrinkage**

New prediction from model, retrospectively confirmed by theoretical analysis:

- **Non-shrinking particles (after crust formation) dry faster than shrinking ones (no crust) in same drying regime**, higher final moisture content from dryer

Results
Alternative scenarios

- Model different cases to give boundary values for the drying achieved
- 1) Falling rate drying throughout, with no shrinkage
  - Would correspond to instant formation of a rigid crust at the outset
- **2) Falling rate drying throughout, with shrinkage**
  - Less likely; instant formation of a pliable crust which shrinks as moisture is lost to give a shrivelled "raisin/currant"; not the expected drying mechanism for lactose
- 3) Constant rate drying throughout, with shrinkage
  - No crust formation; would correspond to pure liquid droplets, very low solids concentration or highly soluble solids
- 4) Constant rate drying throughout, with no shrinkage
  - Instant formation of a rigid but highly porous crust, liquid transport from centre fast enough to keep surface fully wetted throughout; unlikely
- **5) Constant rate with shrinkage, followed by falling rate drying with no shrinkage**
  - The most physically likely scenario; crust formation at a given surface concentration
  - Tricky to model as the crust formation point must be estimated
  - Should give results intermediate between pure constant and falling rate

Closest match of experimental results

Physically most likely scenario

gSOLIDS Spray Drying model
Summary & Conclusion

- Sensitivity Analysis: gSOLIDS Model predicts qualitatively correct the impact of critical process parameters on output attributes
- Different scenarios studied (shrinkage vs no shrinkage, constant vs falling rate) and results compared to experimental data
- Model assists process understanding of droplet drying
- Constant rate drying with shrinkage followed by falling rate drying without shrinkage gives consistent results
- **Predicted outlet moisture content is always very low (close to equilibrium moisture content) and below some experimentally observed values**
- **Suggests that model is overpredicting drying rates in falling rate period**
- Model uses a simple linear falling-rate method (first-order kinetics); appears to be insufficient for porous spray dried particles
- First-order kinetics works well for dryers with minutes/hours residence time, but diffusion rate in crust is probably limiting for residence times << 1 second
- Observed final particle sizes and densities are more consistent with late crust formation (< 1 kg/kg)

gSOLIDS Spray Drying model
Improvements / Developments since 2012

Experimental (GSK)

- Build experimental datasets / generate suitable datasets tailored for modelling

→ DoEs with suspensions of Lactose/MgStearate in Ethyl Acetate on small & large scale

- Determine sorption isotherm, construct density
- CFD modelling → Determine *ranges* of droplet residence times

gSOLIDS model (PSE)

- Overall robustness of the model has been improved considerably
- Link to the DIPPR databank (partly completed)
- Capability for different scenarios: Falling rate vs constant rate drying regime, shrinkage vs no shrinkage

gSOLIDS Spray Drying model

Future Work

Short Term

- Apply gSOLIDS model on large scale spray drying
- Link to the DIPPR databank (solvent properties) complete
- Reformulating the model for multiple zone spray drying

→ Separate model into PFR and CSTR sub-models

Mid term

- Multiple airflow zones near chamber entry (cool core, hot annulus)
- Measure Inlet droplet size, obtain residence time distribution by CFD modelling
- Link gSOLIDS with CFD multizonal modelling

Long term

- Apply gSOLIDS model *predictively* for *scale-up*
- Include *atomisation*, possibly classification and breakage

gSOLIDS Spray Drying model
Acknowledgements

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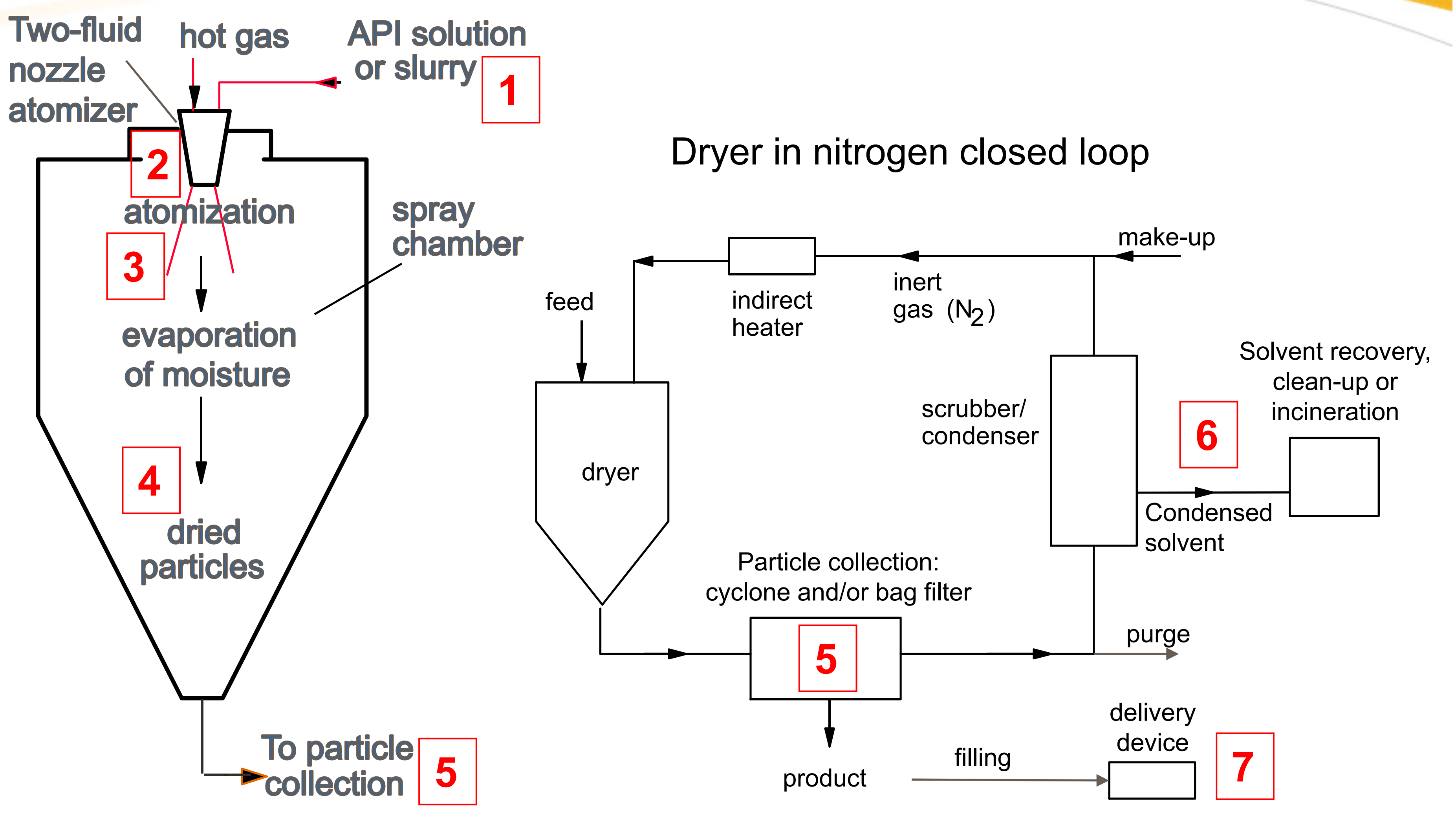
- CFD/experiments: Ariane Bisten, Peter Clements (GSK)
- Analytical results: Mark Bloxham, Natalie Fa, Kim Fordham (GSK)

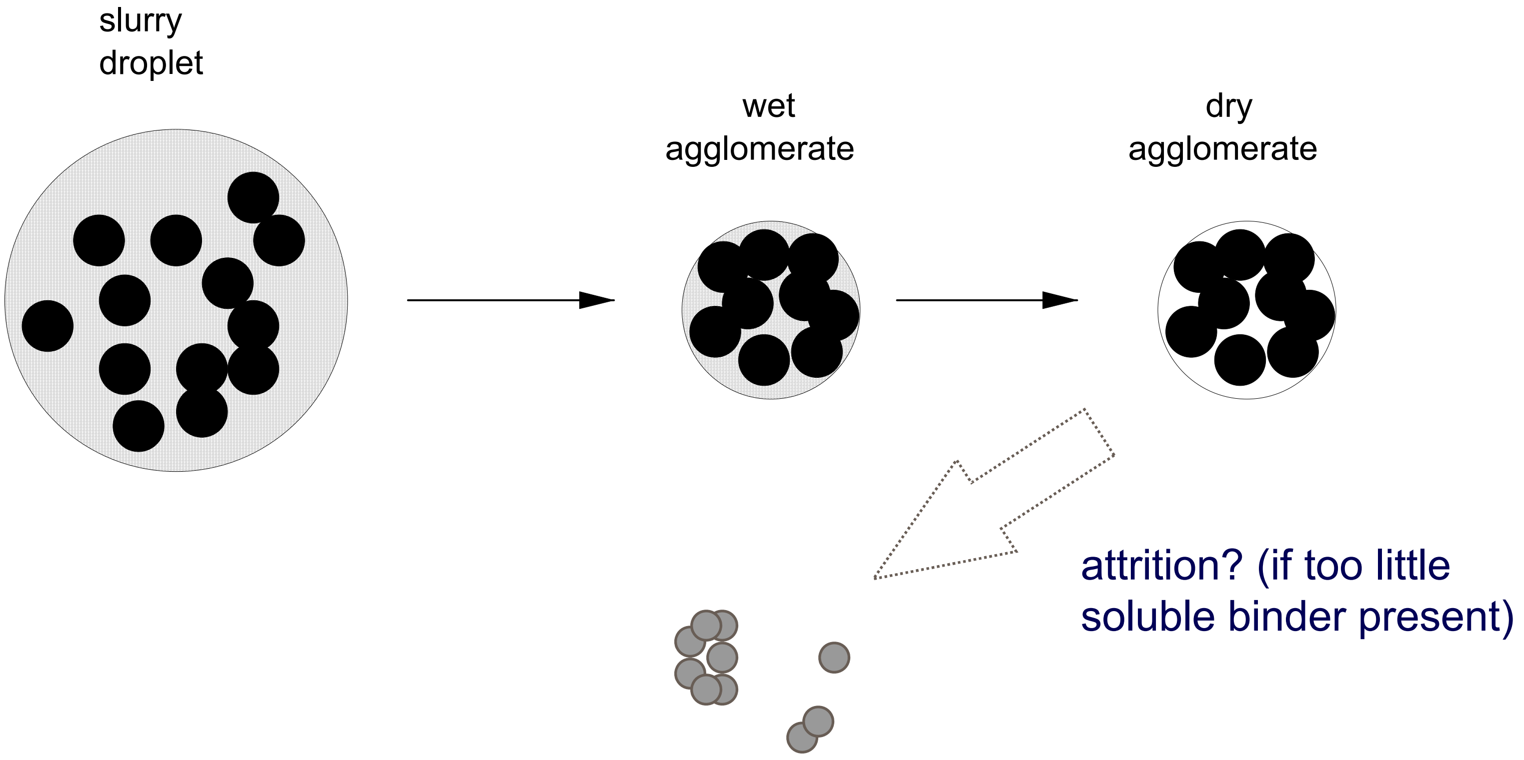
Back-Up

Spray drying – stages for process understanding

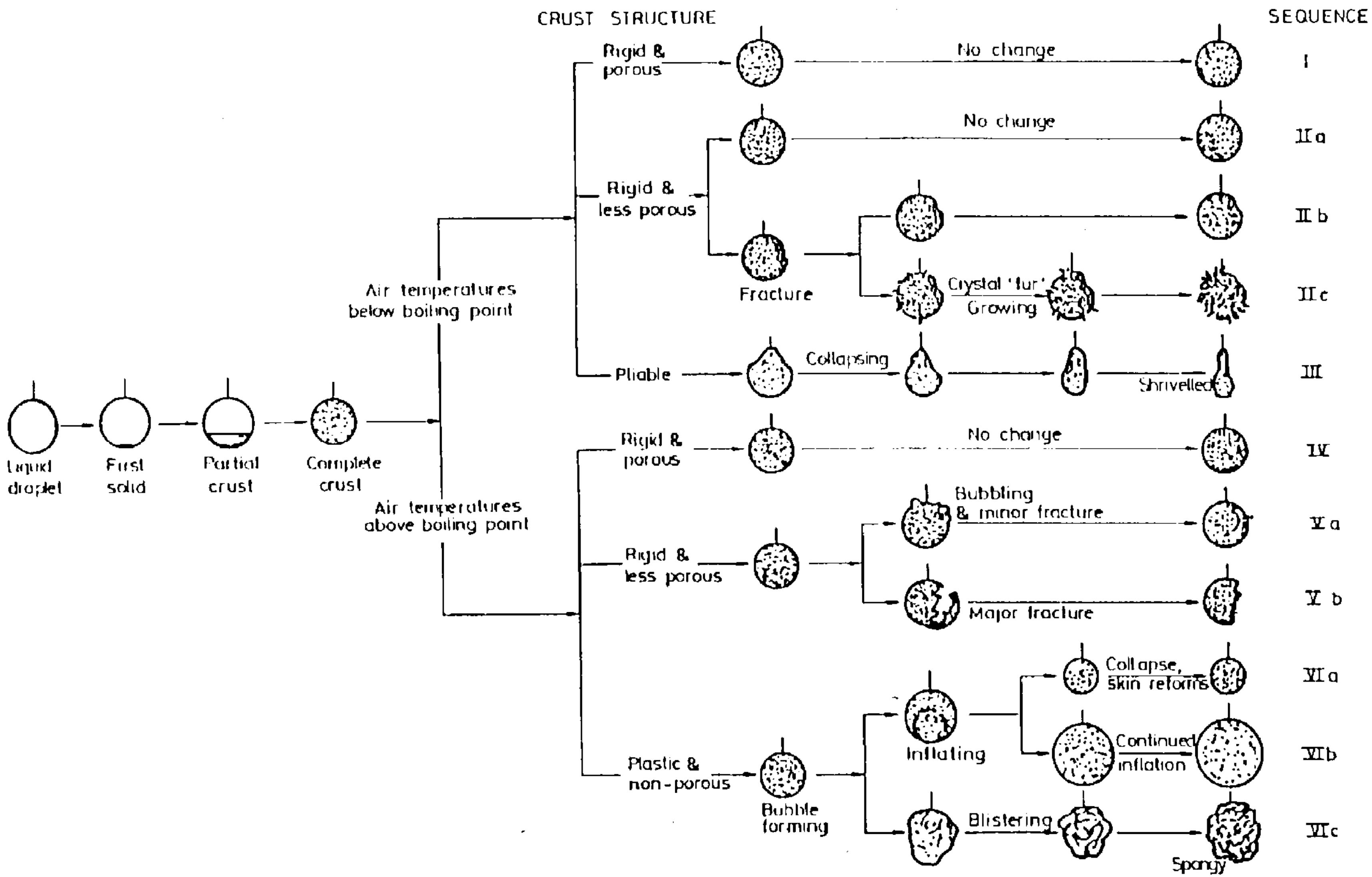


Droplet size changes
with undissolved solids (direct slurry/suspension drying)

1. Droplet with undissolved solids

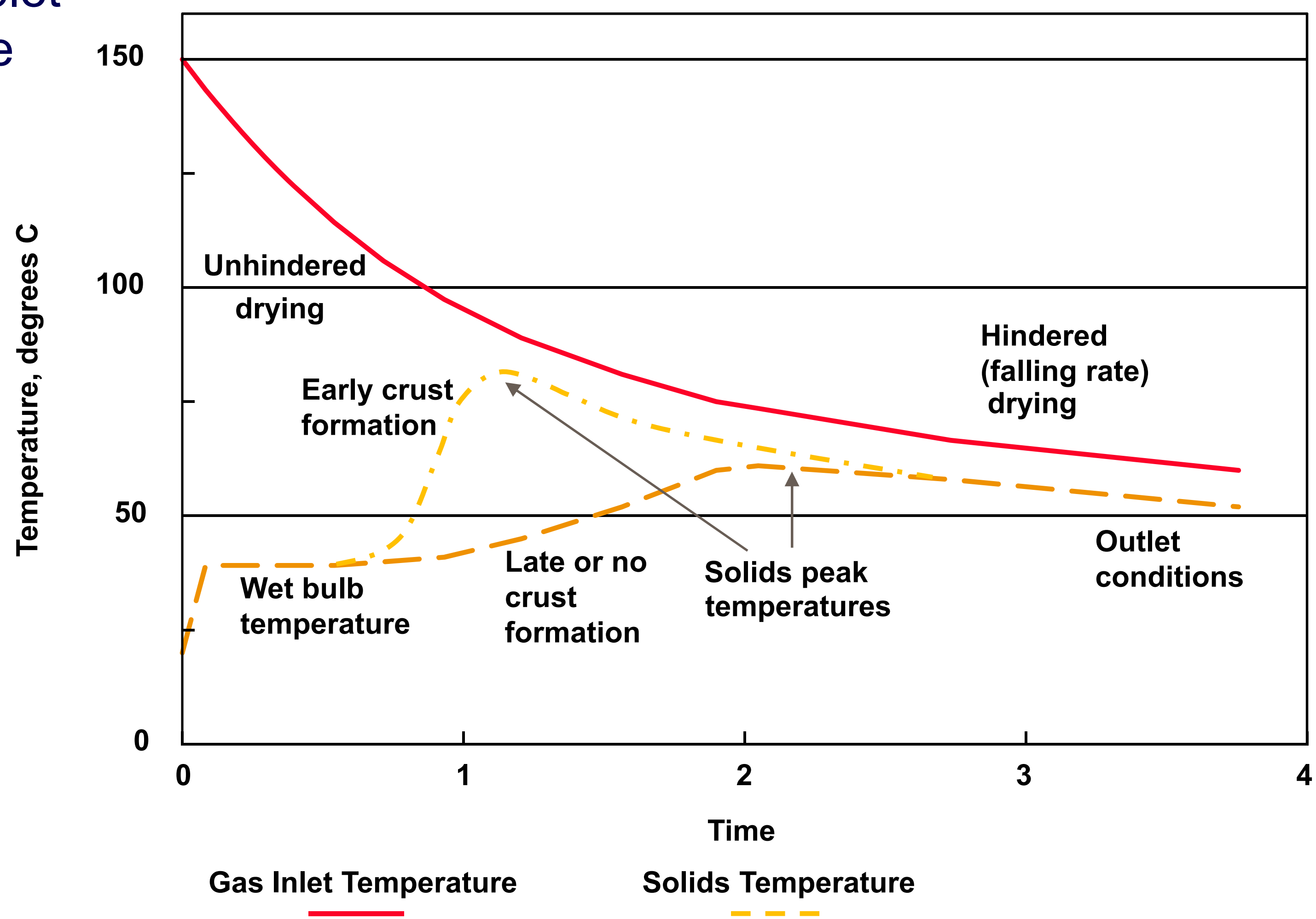


Droplet drying: droplet with dissolved solids
Charlesworth and Marshall, 1960

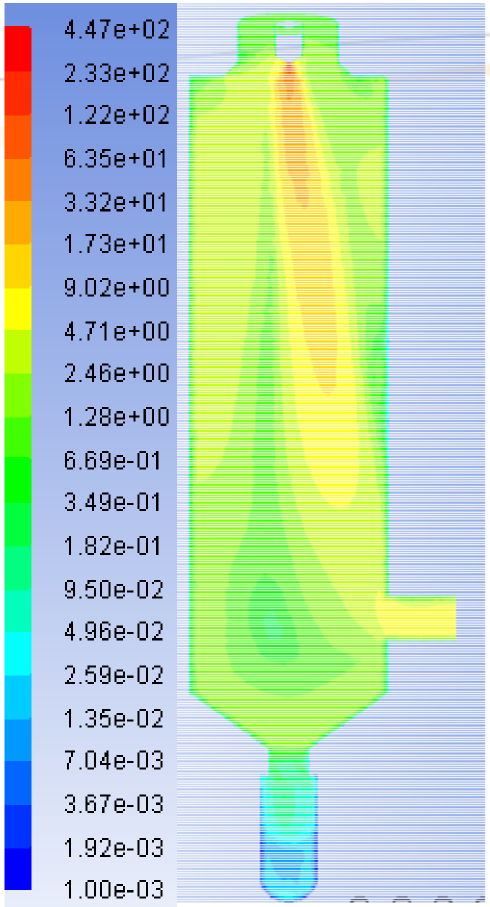


Co-current Spray Dryer: Temperature Profile

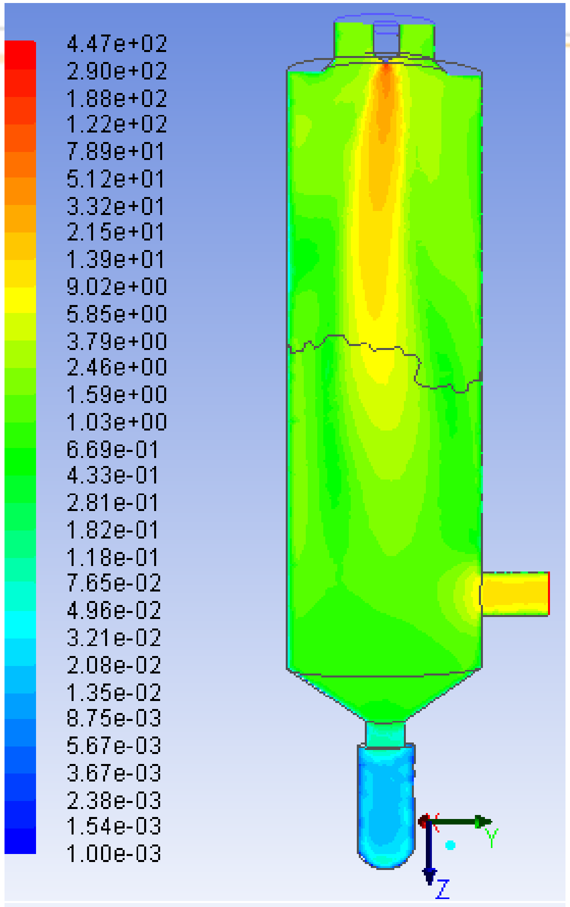
Shows droplet temperature history



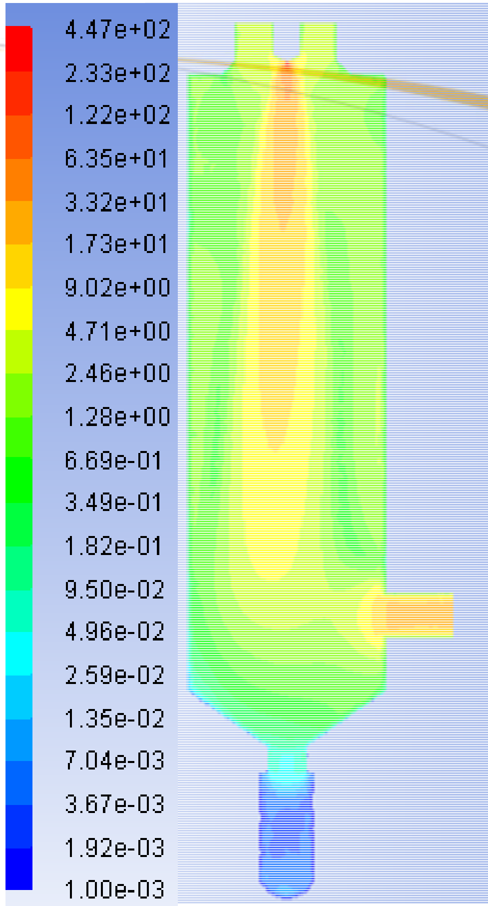
Velocity Profiles for Buchi 290 from CFD simulation



- **Mass Flow: 0.004 kg/s**
- **Volume Flow: ≈ 12.6 m³/h**



- **Mass Flow: 0.006 kg/s**
- **Volume Flow: ≈ 19 m³/h**

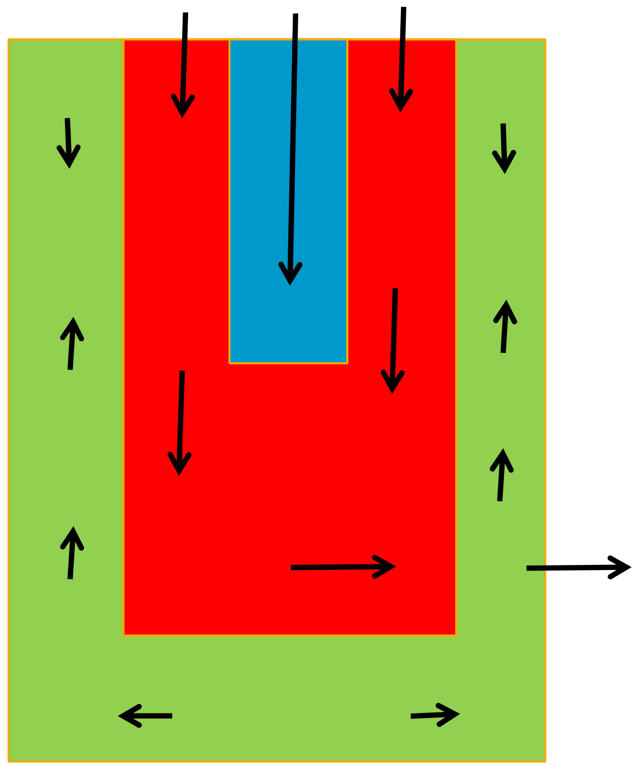


- **Mass Flow: 0.012 kg/s**
- **Volume Flow: ≈ 37 m³/h**

- More direct path at low gas flow; initial high velocity zone similar for all flowrates
- Residence time for gas and particle “core flow” show weaker dependence on gas mass flowrate than proportionality; implies larger recirculation zones at high flows

Multiple zone drying
(future state vision)

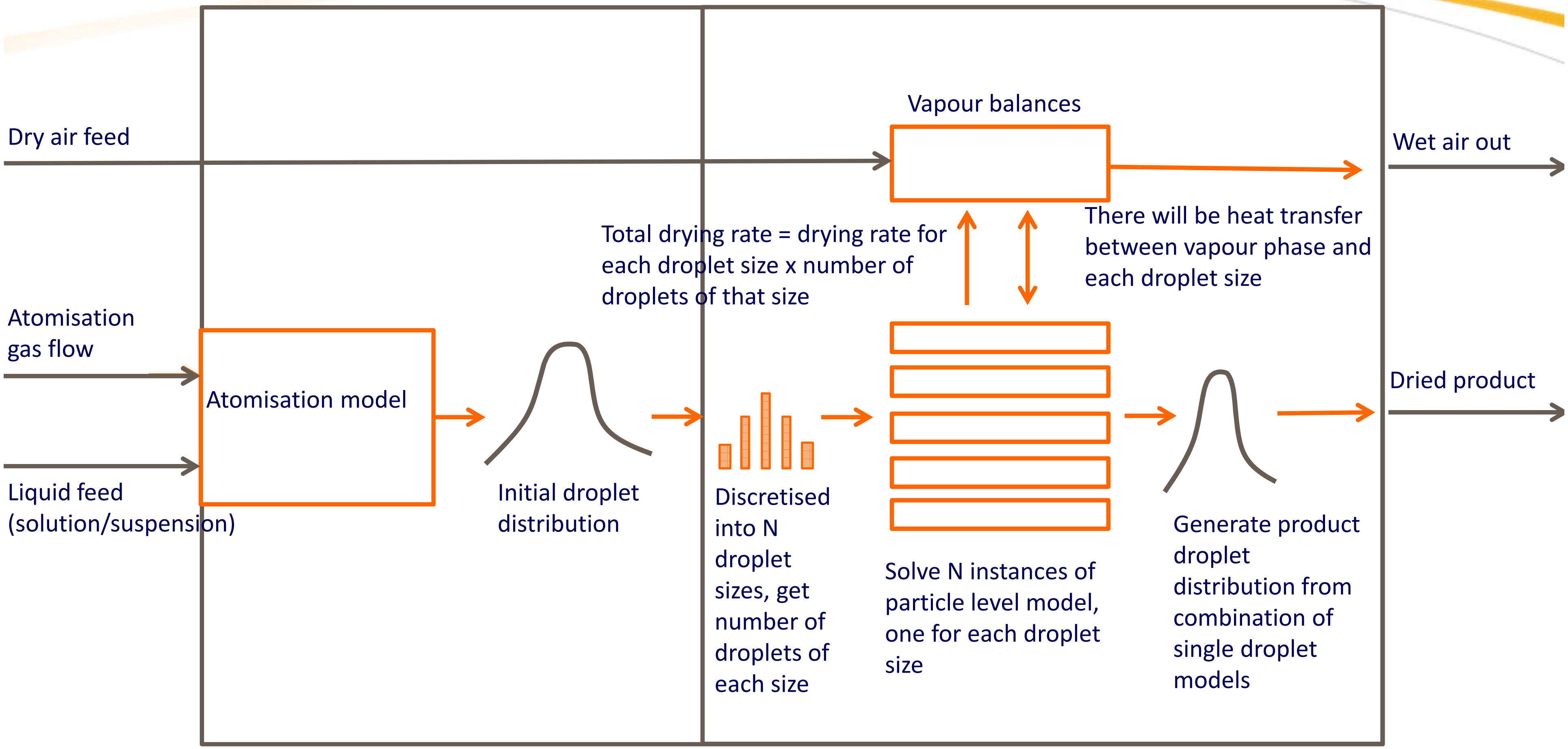
- Minimum and average particle residence times from CFD simulation (0.05-0.35s) are actually much lower than either plug-flow or CSTR values (1.5 s)
- Due to fast moving core flow from atomiser
- Actually three zones within spray dryer:
  - Central core where droplets contact cool fast-moving atomisation gas
  - Annular region where central core mixes with main hot gas flow
  - External recirculation zone where gas moves slowly, recirculates and loses heat to walls
- Need to allow for at least the two inner zones in any spray drying model
- Current model assuming immediate contact with hot gas will tend to overpredict drying
- Plan to incorporate zones in next stage



Results – Effect of crust formation (Falling rate)
Trends and explanation

- Large droplets dry more slowly than small droplets
- Large particles (early crust formation) apparently dry faster than small particles (shrinking) if in same drying regime, e.g. both constant rate
- What is the reason for this paradox?
  - Drying time $t \propto$ mass of liquid to be evaporated / evaporation rate
  - Evaporation rate $\propto$ heat transfer rate $Q = hA\Delta T$
  - Nusselt number $Nu = hd/k$, $h \propto 1/d$; $A \propto d^2$, hence $Q \propto d$ approximately
  - Liquid mass $\propto$ liquid volume $\propto d^3$,
  - Hence for different droplets, drying time t is roughly proportional to d^2
  - Corollary: for same residence time, small droplets will dry further (reaching lower moisture content) than large ones
  - For the same droplet with/without crust formation, the mass of the droplet is fixed
  - Hence drying time t is proportional to (1 / evaporation rate) or $1/d$
  - Corollary: for same residence time, unshrunk larger droplets will dry further (reaching lower moisture content) than small shrunk ones
- However, shrinkage comparison may not be physically realistic because shrinking liquid droplets are in constant rate drying (fast), crusts give falling rate (slow)
  - But could have both shrinking and non-shrinking particles in falling rate

Modelling Approach in gSOLIDS
Overview



Experimental results

OSD batch ID	DoE	univariate	**API concentration** %w/v	Inlet Temp °C	**Outlet Temp** °C	**Aspirator volume flow** m^3/h	**Atomization Gas Flow Rate** g/s	**Product Feed Rate** mL/min	Yield %	x10 µm	x50 µm	x90 µm	% Ethyl Acetate by NMR %w/w
R18041-50-1	Fact		10	152	88	19	0.5	6.5	67	0.8	1.7	3.8	0.3
R18041-50-10	Center		5	174	85	17	0.5	19.4	65	0.7	1.6	4.5	0.7
R18041-50-11	Fact		10	116	62	19	0.5	22.8	47	0.7	1.5	4.7	0.6
R18041-50-12	Fact		10	191	86	17	**0.3**	33	68	0.7	2.2	13.0	0.6
R18041-50-13	Fact		2.5	145	85	18	0.3	6	72	0.7	1.6	4.3	0.9
R18041-50-14		low conc	1.7	105	62	18	0.5	6.3	70	0.7	1.5	3.6	0.9
R18041-50-15		low asp	5		85	10	0.5	19.6	79	0.8	1.8	4.5	
R18041-50-16		open loop	5	180	90	18	0.5	19.3	57	0.8	1.6	3.8	
R18041-50-17	Fact		10	110	67	19	0.3	8	52	0.7	1.7	5.1	
R18041-50-2	Fact		2.5	103	62	19	0.5	6.1	61	0.7	1.5	3.6	0.8
R18041-50-3	Center		5	125	63	19	0.3	19	75	0.7	1.6	7.1	0.8
R18041-50-4	Center		5	154	85	19	0.3	19	82	0.7	1.7	6.8	0.6
R18041-50-5	Center		5	176	89	18	0.5	19.0	71	0.7	1.6	4.0	0.6
R18041-50-6	Center		5	113	62	20	0.5	19.2	72	0.7	1.6	5.1	0.8
R18041-50-7	Fact		2.5	117	**60**	19	**0.3**	35	65	0.7	1.8	9.1	0.9
R18041-50-8	Fact		2.5	197	87	16	0.5	30.9	81	0.7	1.7	5.4	0.5
R18041-50-9		low mass flow	10	117	63	**13**	0.3	6.4	64	0.7	1.9	6.0	0.9

			1.7	103	60	10	0.3	6	47	0.7	1.5	3.6	0.3
			10	197	90	20	0.5	35	82	0.8	2.2	13.0	0.9

Modelling Approach

Atomization Model

input attributes	process	model output
Physical Properties for Feed (solution/suspension) & gas	Atomisation parameters (flow rates) Nozzle orifice diameter	Inlet droplet size (distribution)

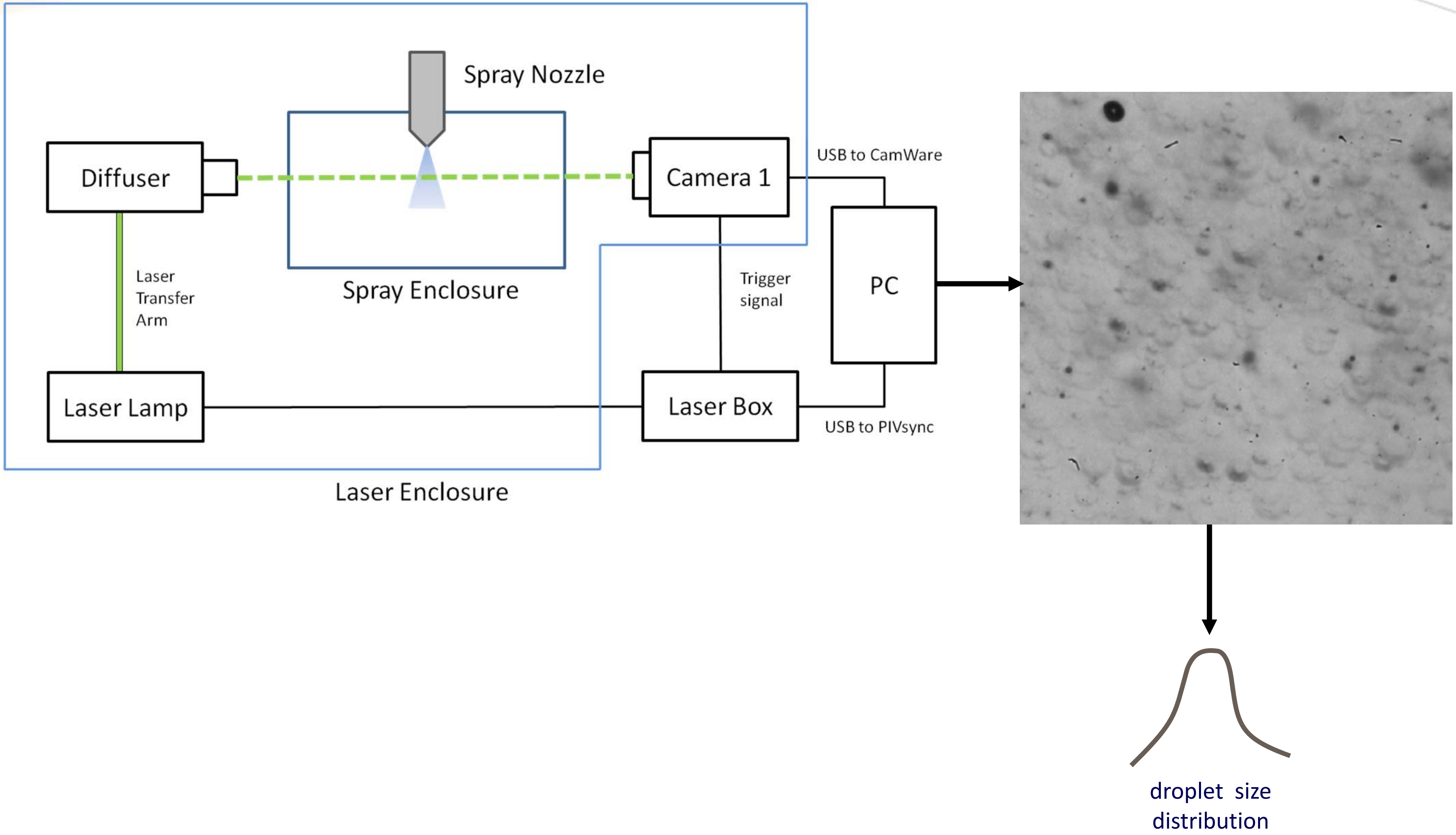
Spray Chamber Model

input attributes	Process	model output
Physical Properties for solvent, solid & gas Solid loading Inlet droplet size distribution	Spray chamber geometry Inlet flow rates Inlet temperatures	PSD ex spray chamber **temperature history** **moisture content**

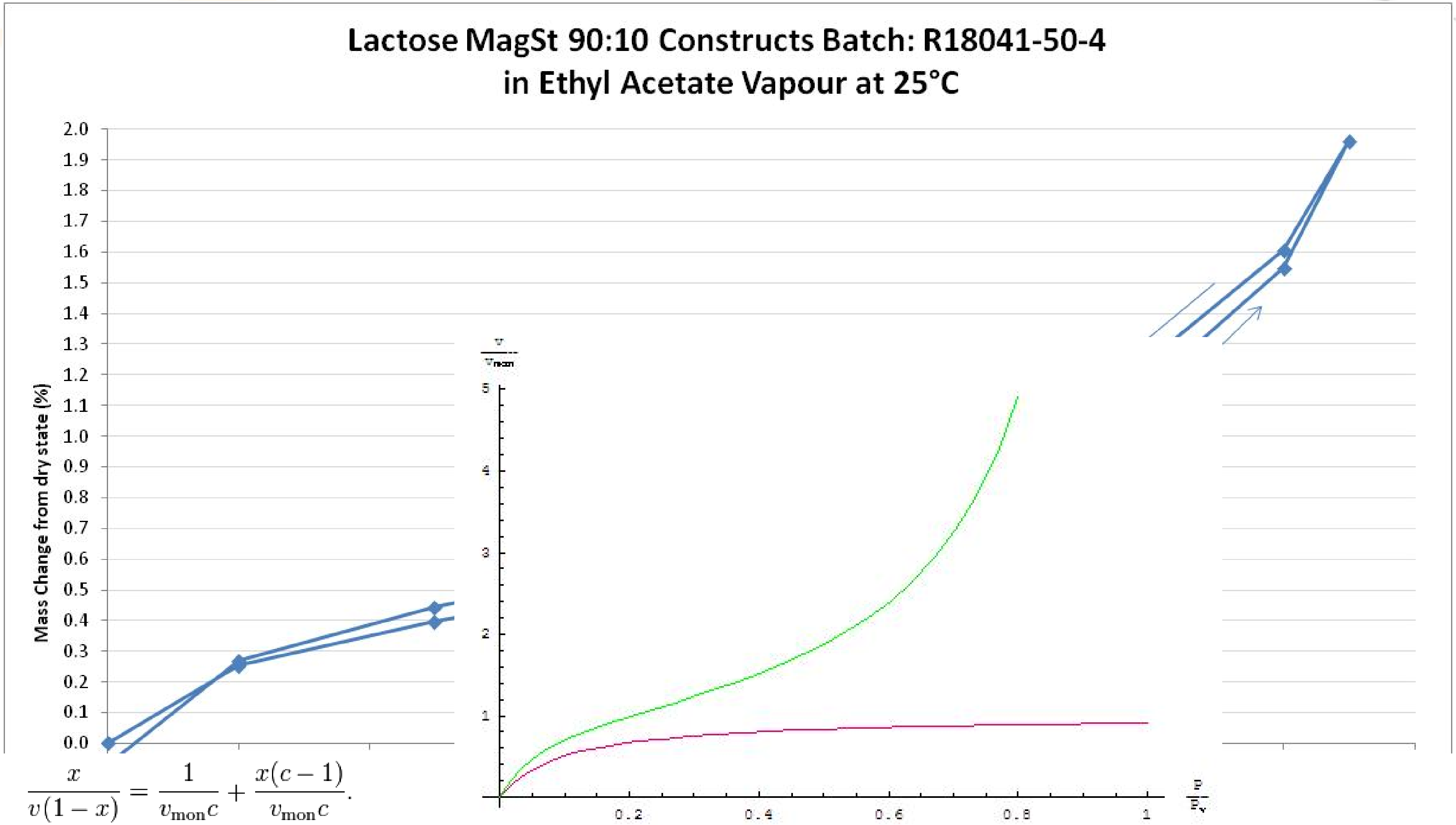
Cyclone Model

input attributes	process	model output
PSD ex spray chamber Solid loading Physical Properties for solid & gas	Cyclone geometry Gas flow rate	**PSD in offload** (collection pot / fines filter) **Yield**

Particle imaging



Sorption Isotherm



$$\frac{x}{v(1-x)} = \frac{1}{v_{\mathrm{mon}}c} + \frac{x(c-1)}{v_{\mathrm{mon}}c}.$$

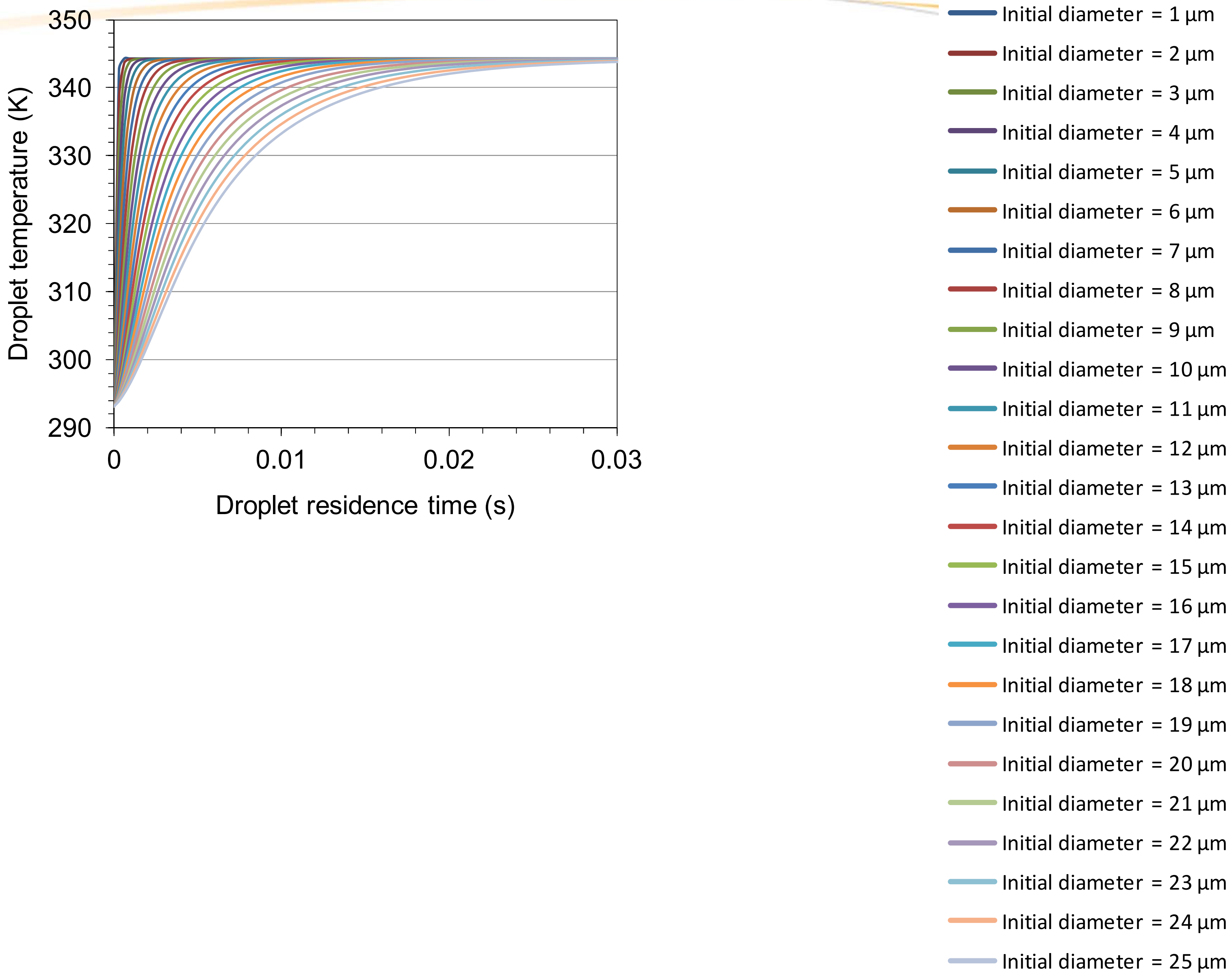
x is the pressure divided by the vapor pressure for the adsorbate at that temperature (usually denoted P/P_0), *v* is the STP volume of adsorbed adsorbate, v_{mon} is the STP volume of the amount of adsorbate required to form a monolayer and *c* is the equilibrium constant *K* we used in Langmuir isotherm multiplied by the vapor pressure of the adsorbate. The key assumption used in deriving the BET equation that the successive heats of adsorption for all layers except the first are equal to the heat of condensation of the adsorbate.

Construct Density

Sample ID	SD conditions	Nozzle type	Equv	solids concentration	Air flow	atomisation pressure	atomisation flow	Liquid flow	inlet temperature	outlet temperature	**Construct Density**	**Porosity**
			nm	w/w%	kg/h	bar	kg/h	kg/h	dC	dC	**g/cm3**	**%**
R18235/90/1	CP1	GEA internal mixing NTF	11	5.0%	1250	16	270	55	130	85	**0.73**	**51**
R18235/90/2	high liquid flow	GEA internal mixing NTF		5.0%	1250	16	270	**95**	150	85	**0.71**	**53**
R18235/90/3	low atomisation	GEA internal mixing NTF		5.0%	1250	**8**	**140**	55	125	85	**0.75**	**50**
R18235/90/4	low atomisation	GEA internal mixing NTF	10	5.0%	1250	**8**	**140**	55	90	60	**0.74**	**51**
R18235/90/5	CP2	GEA internal mixing NTF	9	5.0%	1250	16	270	55	100	60	**0.80**	**47**
R18235/90/6	very low atomisation	GEA internal mixing NTF		5.0%	1250	**4**	**70**	55	130	85		
R18235/90/7	high concentration	GEA internal mixing NTF	12	**10.0%**	1250	16	270	55	140	85		
R18235/90/8	high liquid flow low concentration	GEA internal mixing NTF	13	**2.5%**	1250	16	270	**100**	150	85		
R18235/90/9	CP1	Schick external mixing	5	5.0%	1250	8	270	55	100	60	**0.76**	**49**
R18235/90/10	very low atomisation	Schick external mixing	4	5.0%	1250	**4**	**140**	55	90	60	**0.74**	**51**
R18235/90/11	CP2	Schick external mixing	1	5.0%	1250	8	270	55	140	85	**0.75**	**50**
R18235/90/12	high concentration	Schick external mixing	7	**10.0%**	1250	8	270	55	140	85		
R18235/90/13	low concentation	Schick external mixing	8	**2.5%**	1250	8	270	55	140	85		
R18235/90/14	very low atomisation high liquid flow	Schick external mixing		10.0%	1250	**4**	**140**	**100**	150	85		
										MIN =	0.71	47
										AVERAGE =	0.75	50
										MAX =	0.80	53

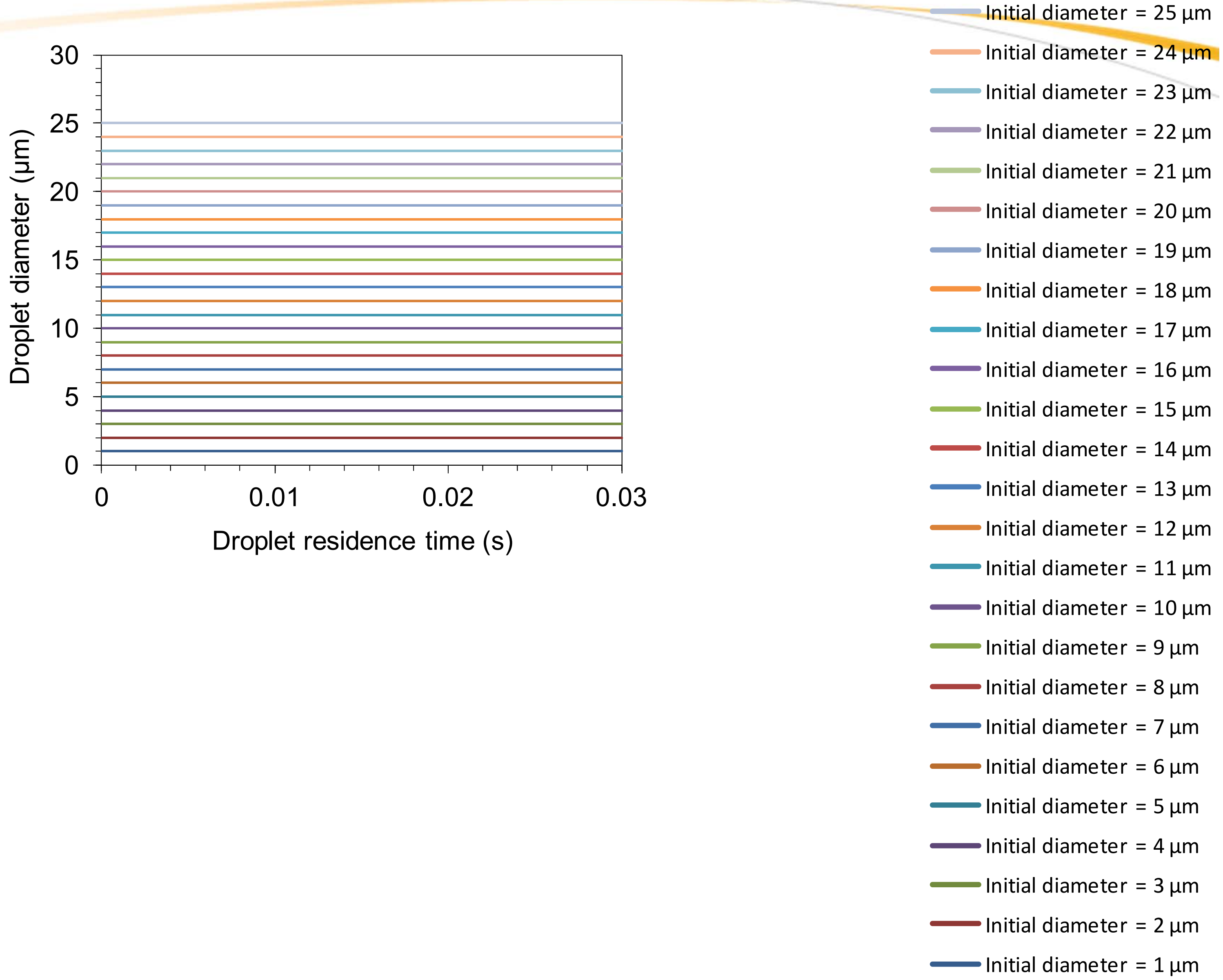
Model Results

1) Falling rate drying throughout, with no shrinkage



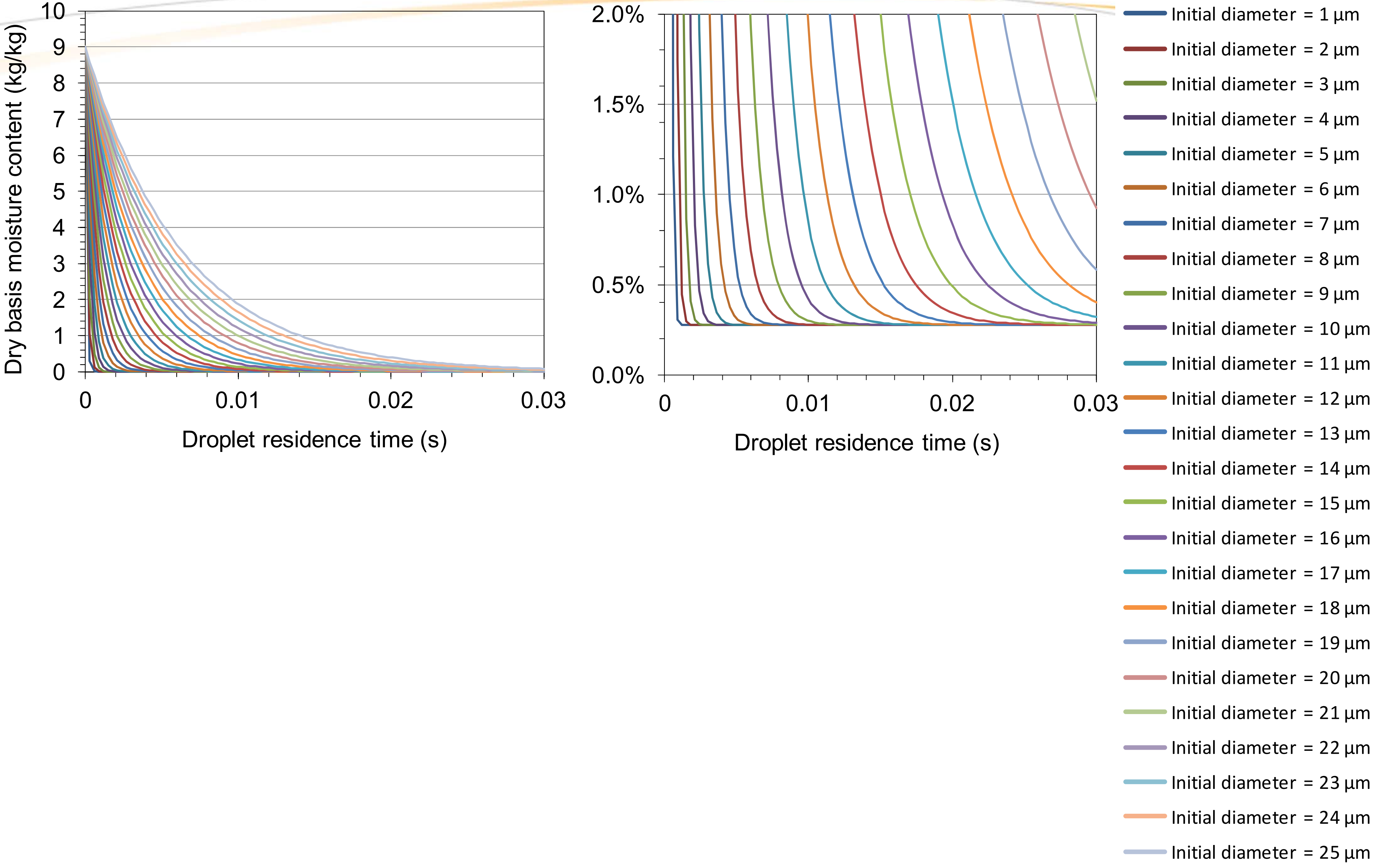
Model Results

1) Falling rate drying throughout, with no shrinkage



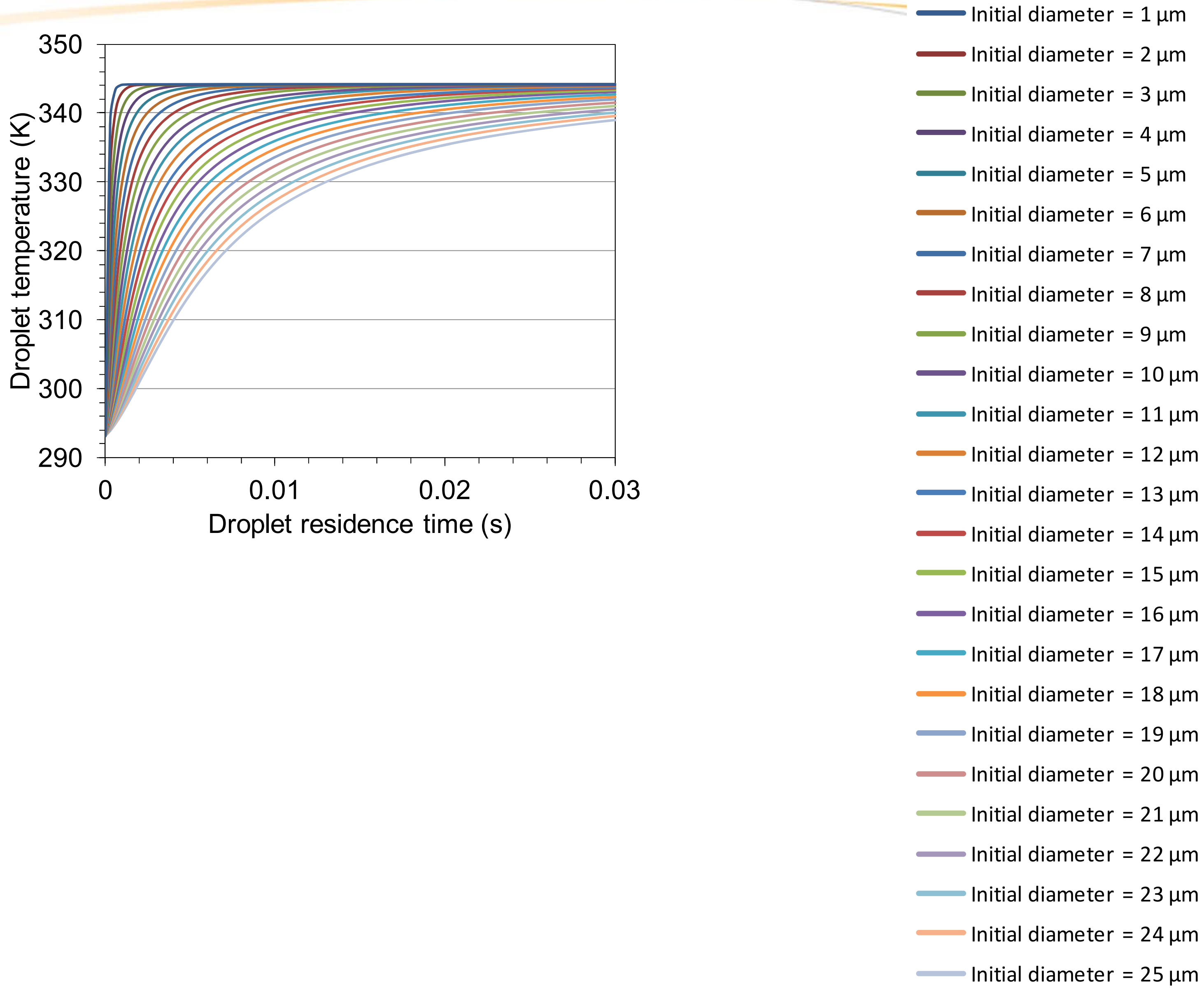
Model Results

1) Falling rate drying throughout, with no shrinkage



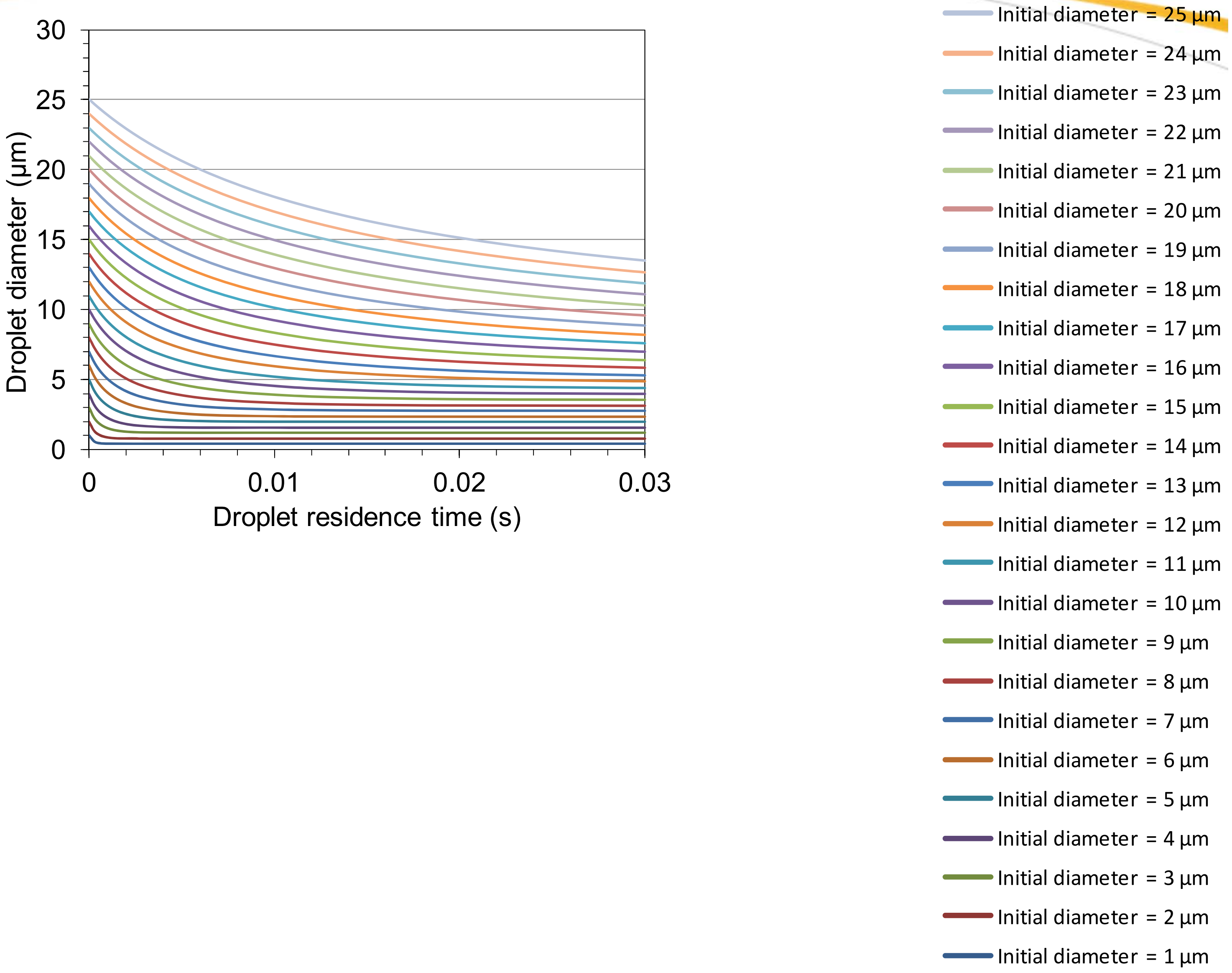
Model Results

2) Falling rate drying throughout, with shrinkage



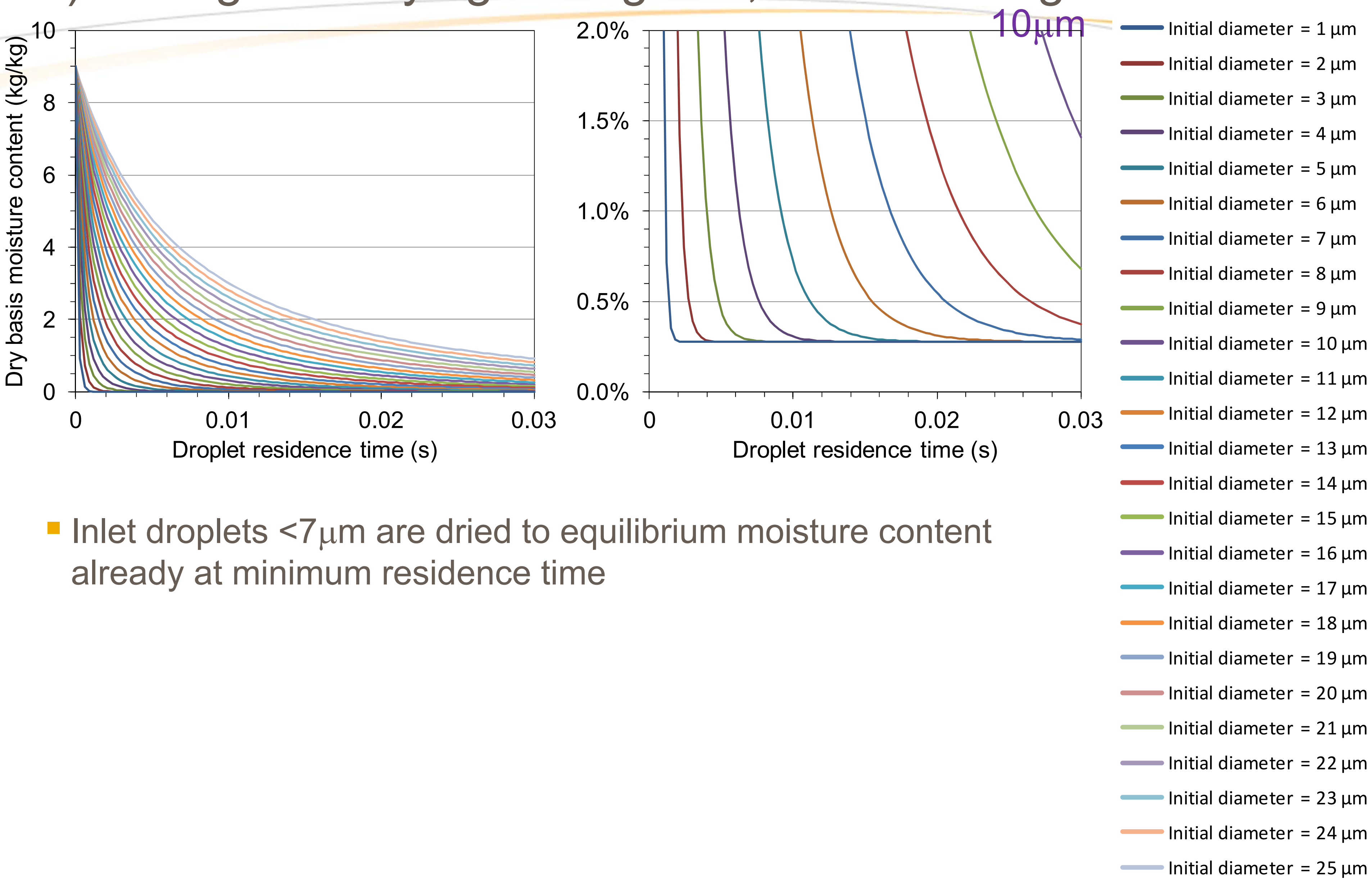
Model Results

2) Falling rate drying throughout, with shrinkage



Model Results

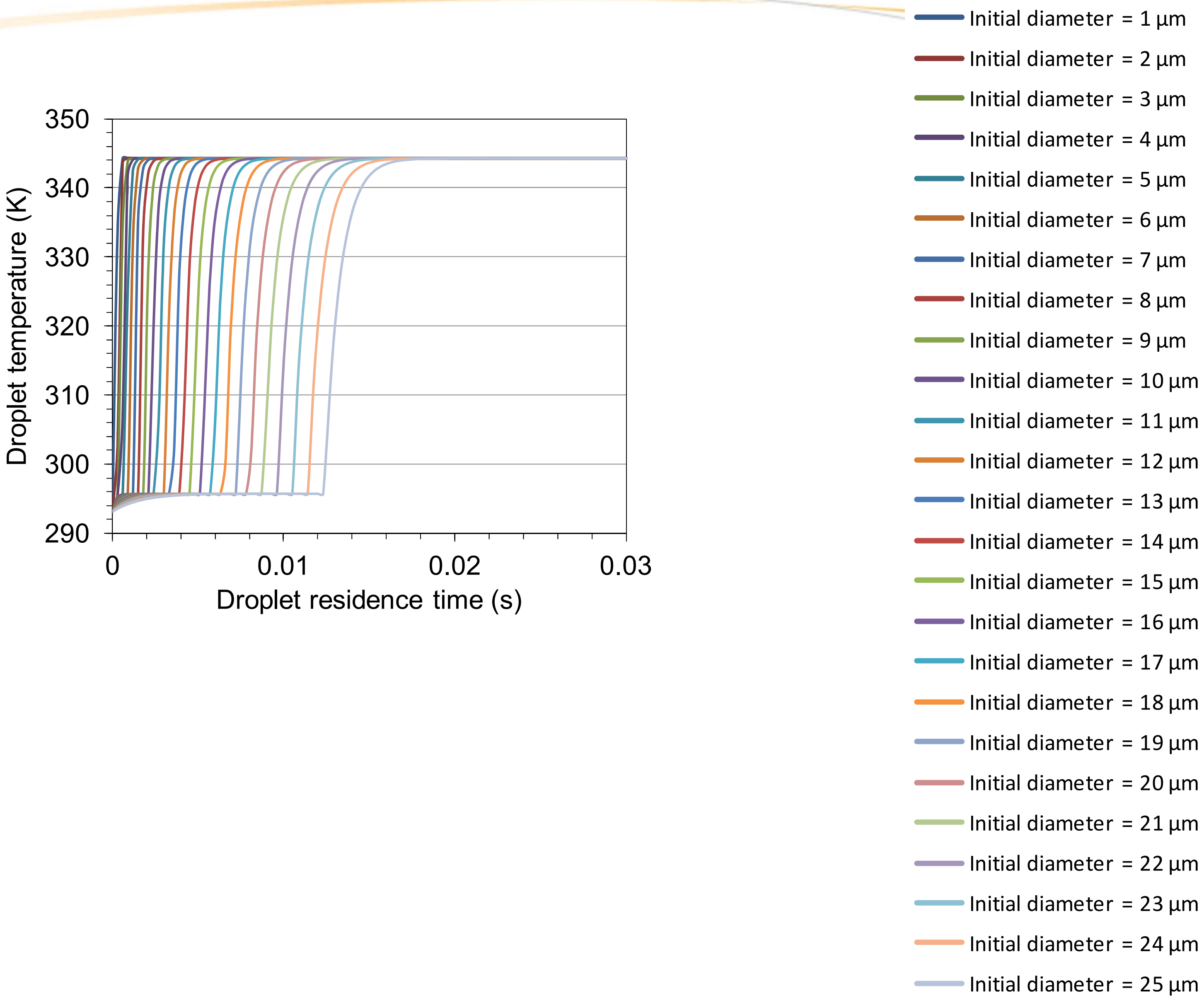
2) Falling rate drying throughout, with shrinkage



- Inlet droplets <7μm are dried to equilibrium moisture content already at minimum residence time

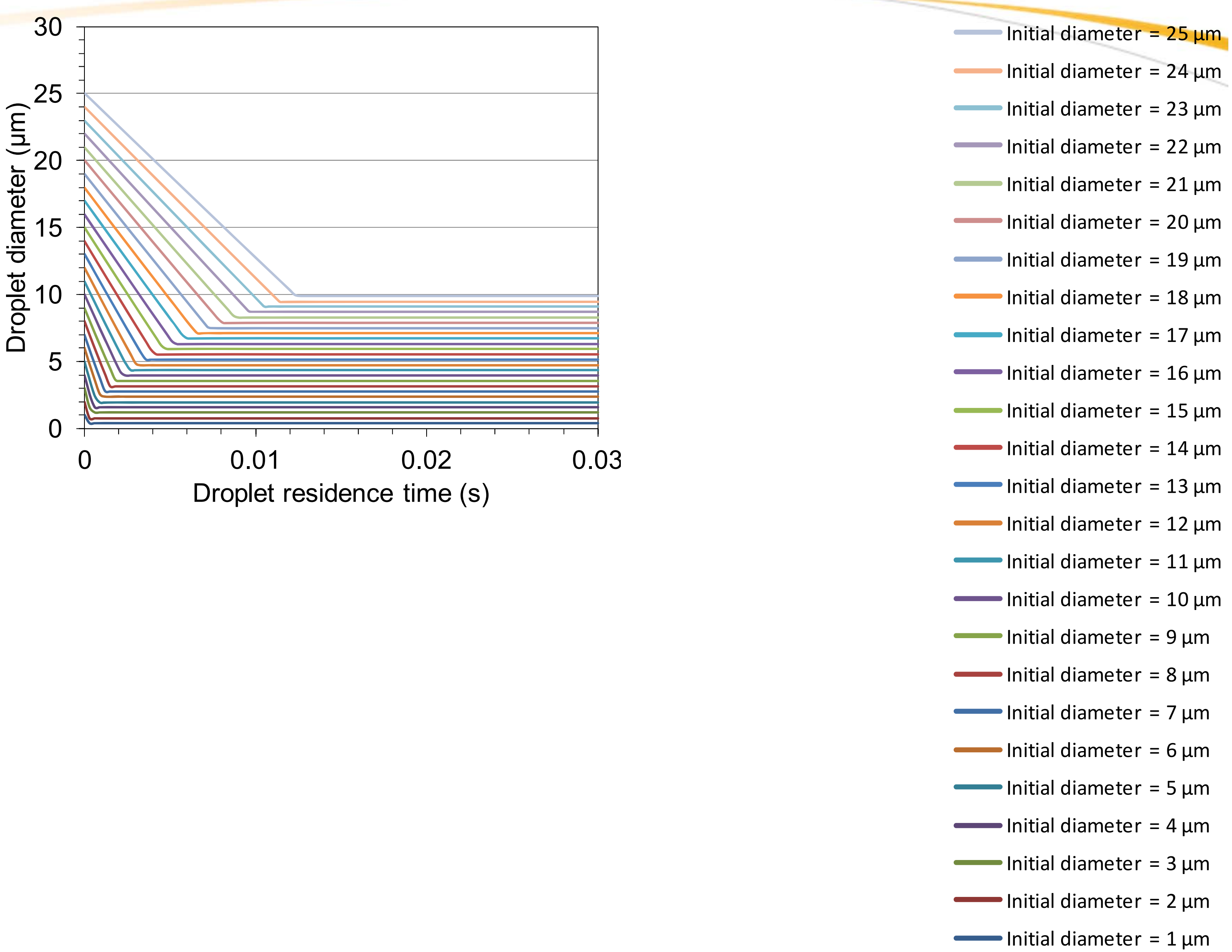
Model Results

3) Constant rate drying throughout, with shrinkage



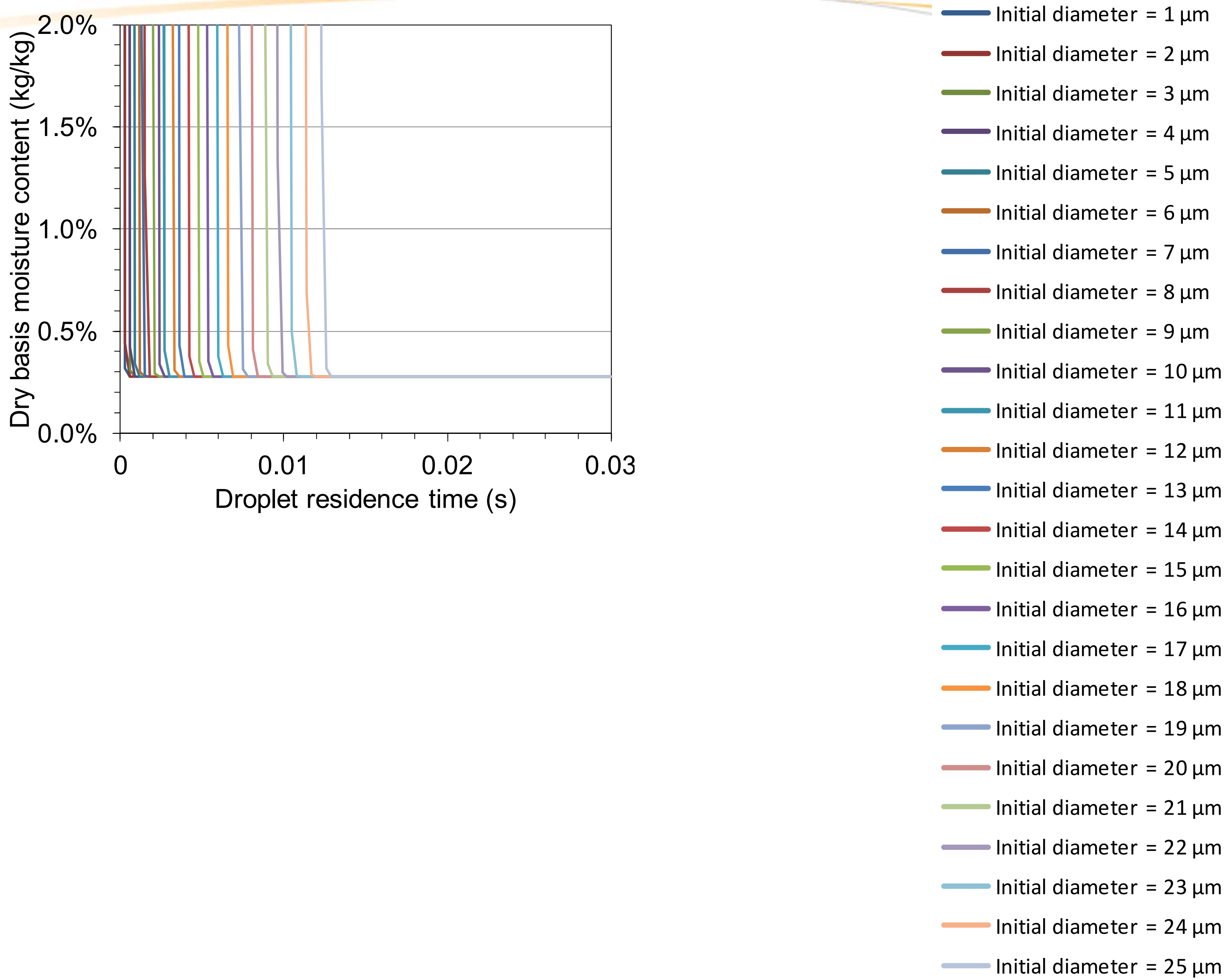
Model Results

3) Constant rate drying throughout, with shrinkage



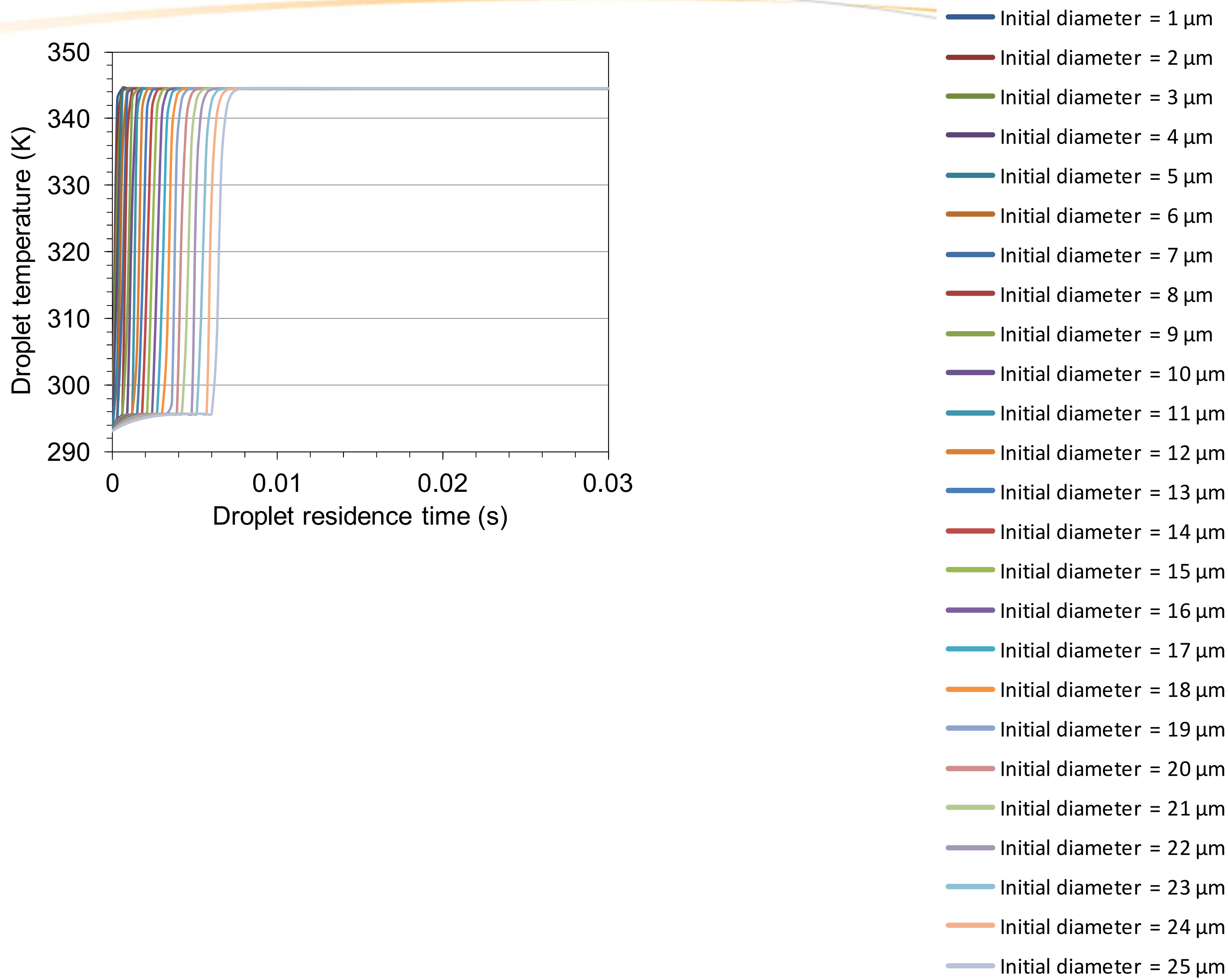
Model Results

3) Constant rate drying throughout, with shrinkage



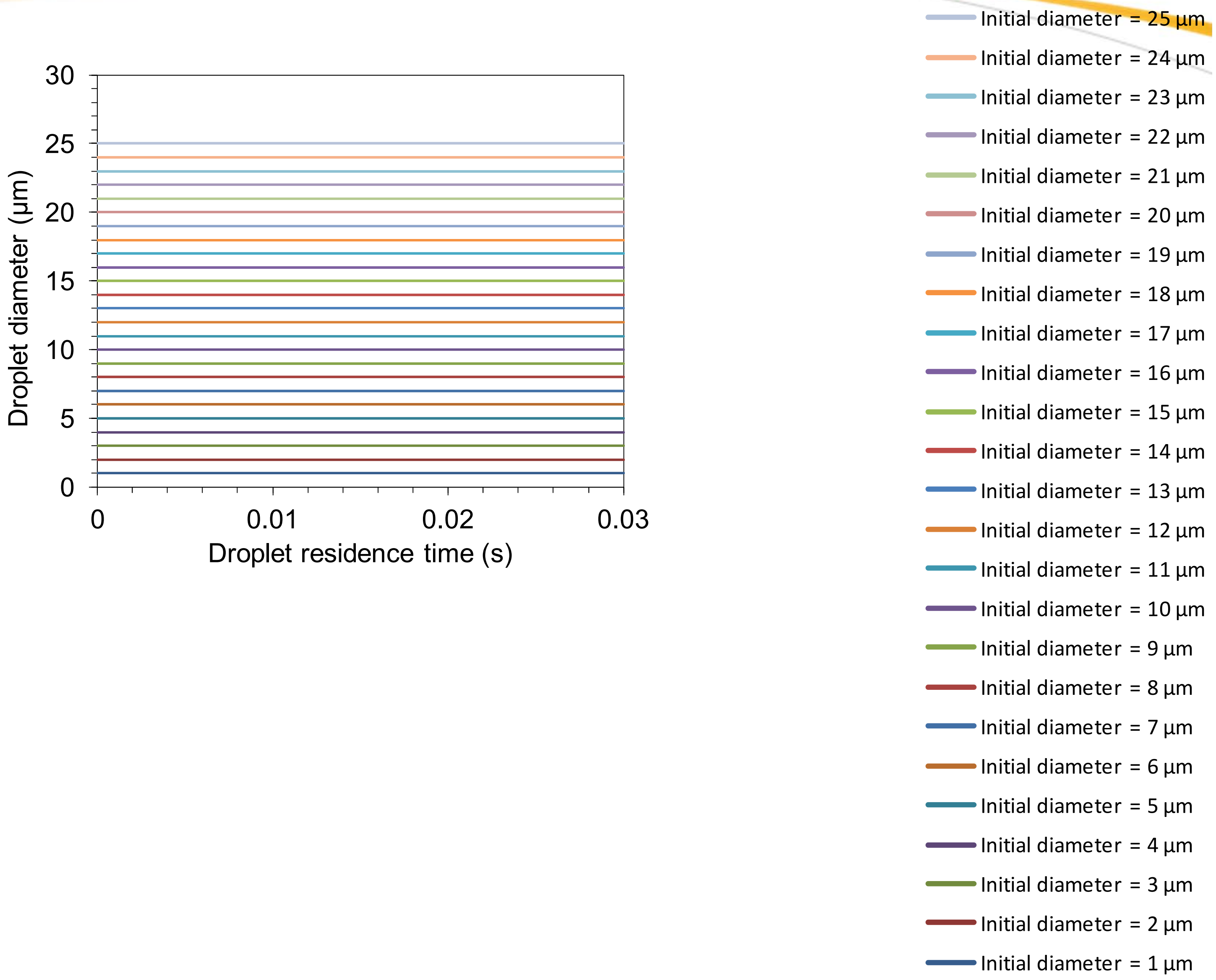
Model Results

4) Constant rate drying throughout, with no shrinkage



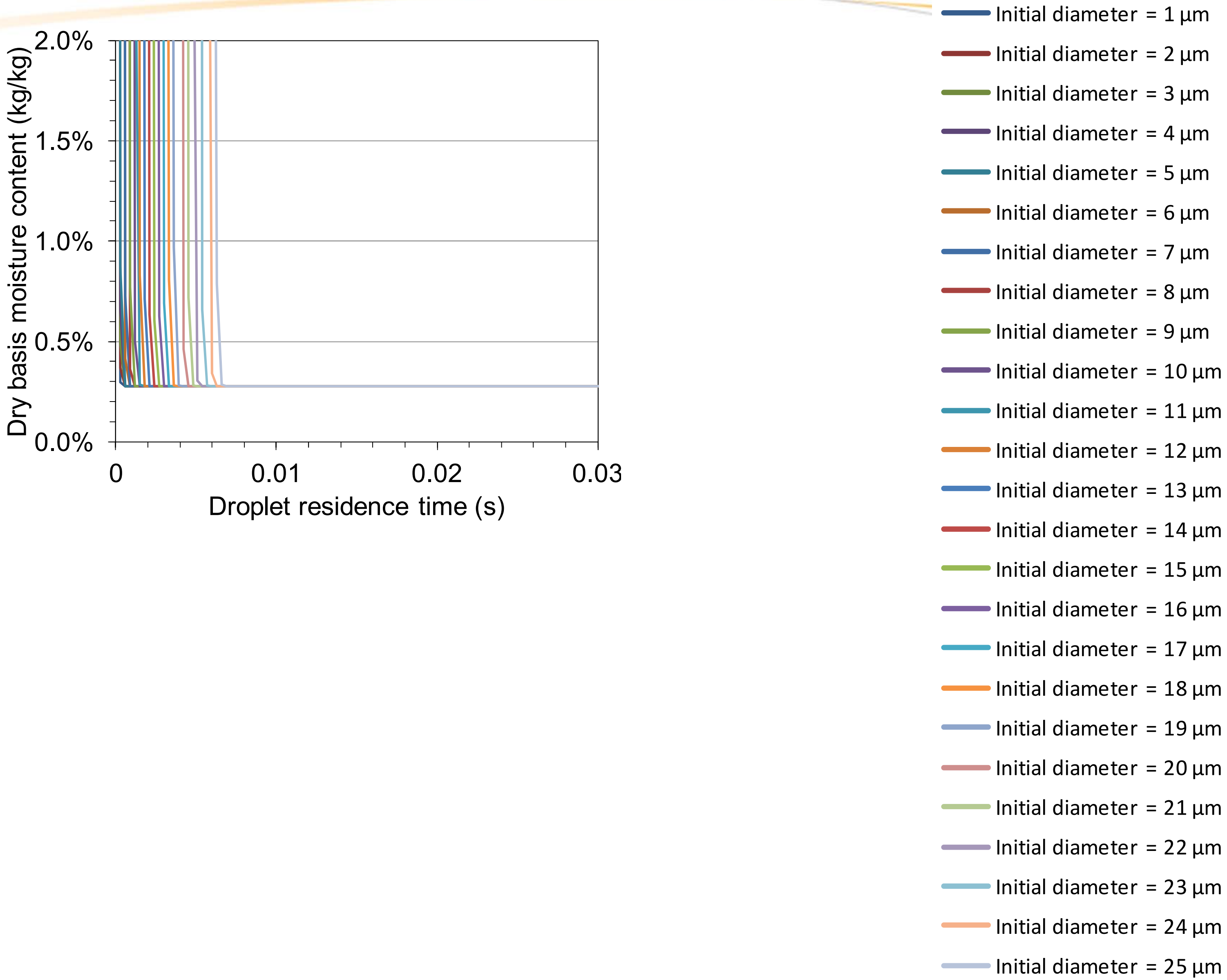
Model Results

4) Constant rate drying throughout, with no shrinkage

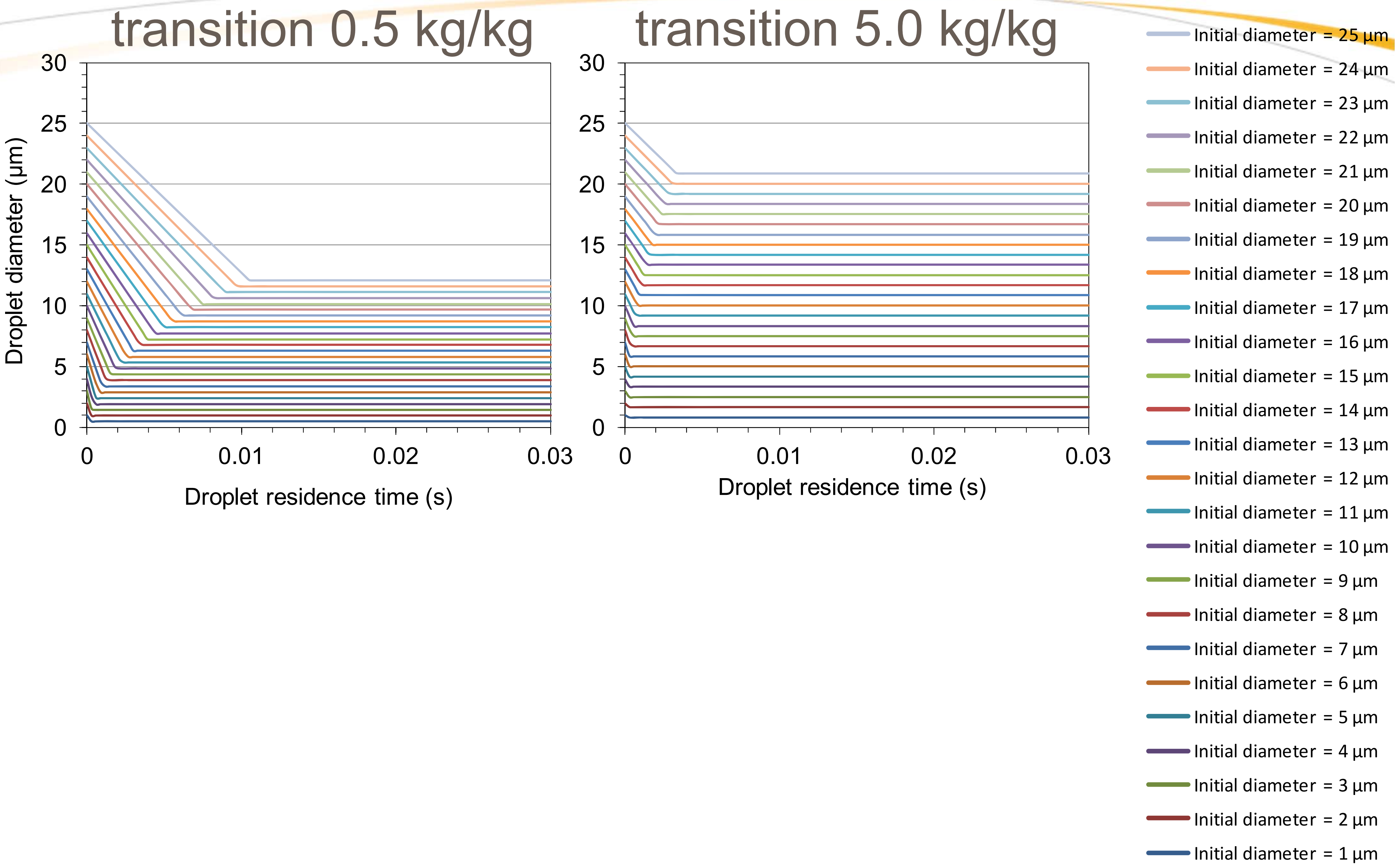


Model Results

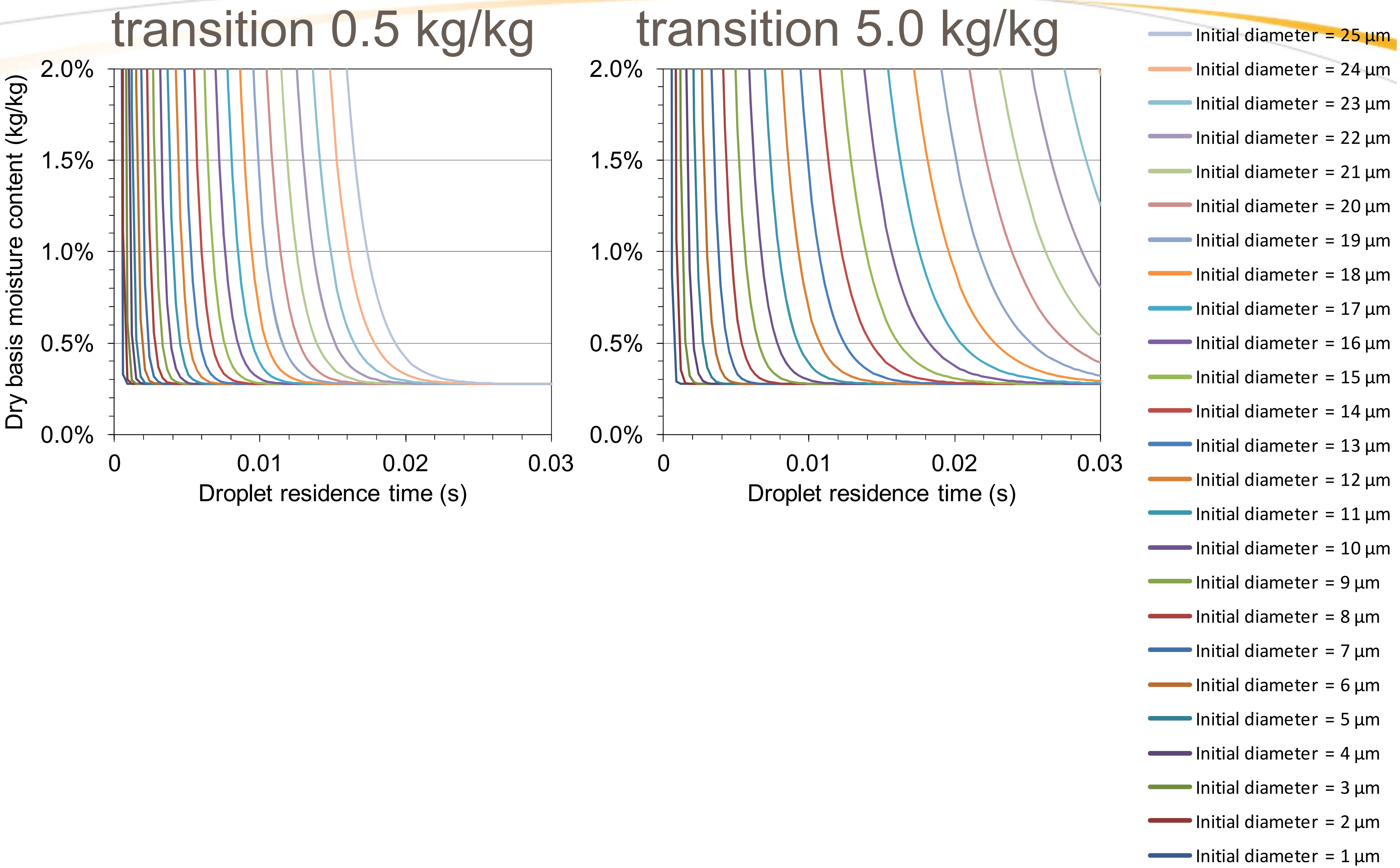
4) Constant rate drying throughout, with no shrinkage



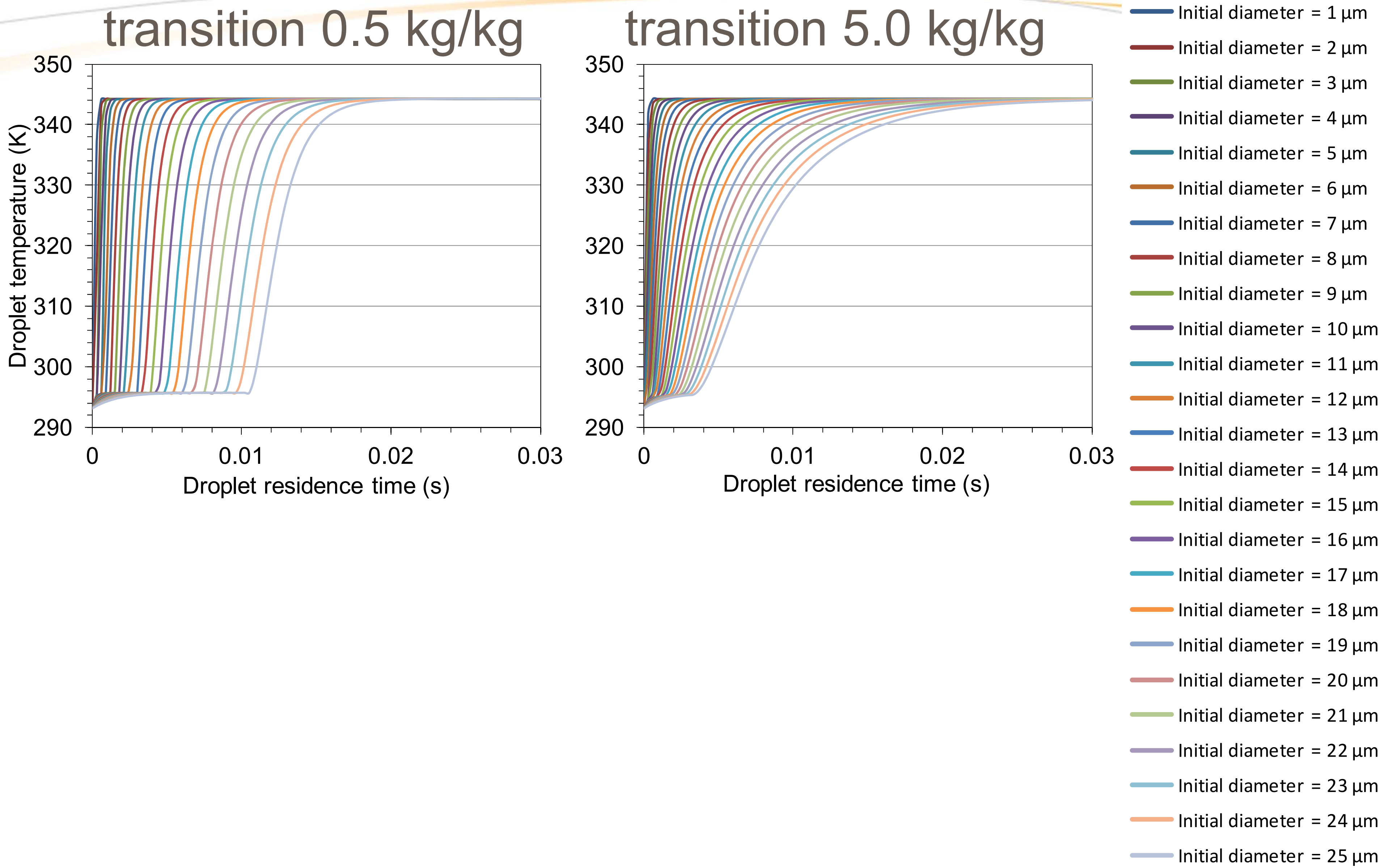
Constant rate with shrinkage, followed by falling rate drying with no shrinkage



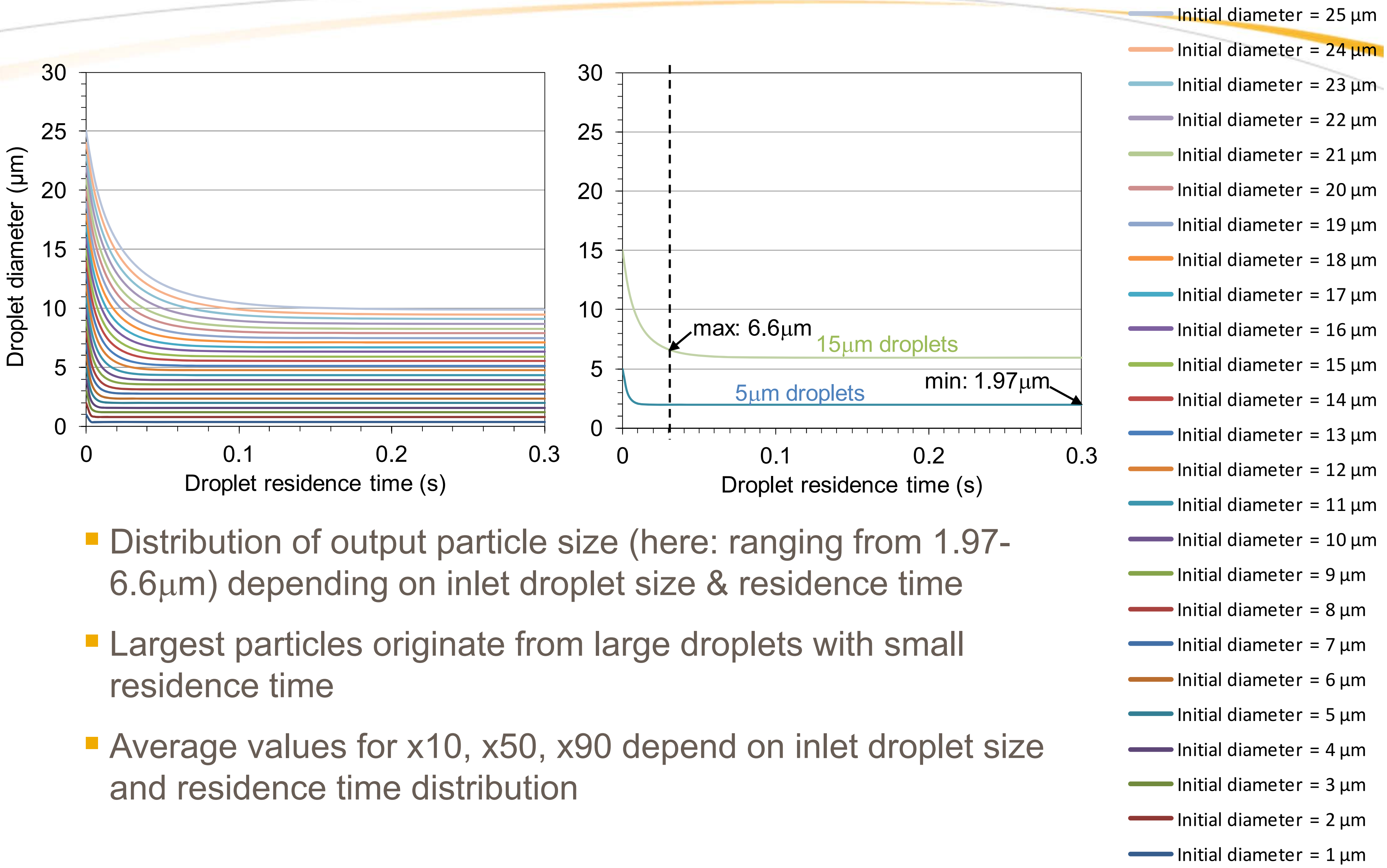
Constant rate with shrinkage, followed by falling rate drying with no shrinkage



Constant rate with shrinkage, followed by falling rate drying with no shrinkage



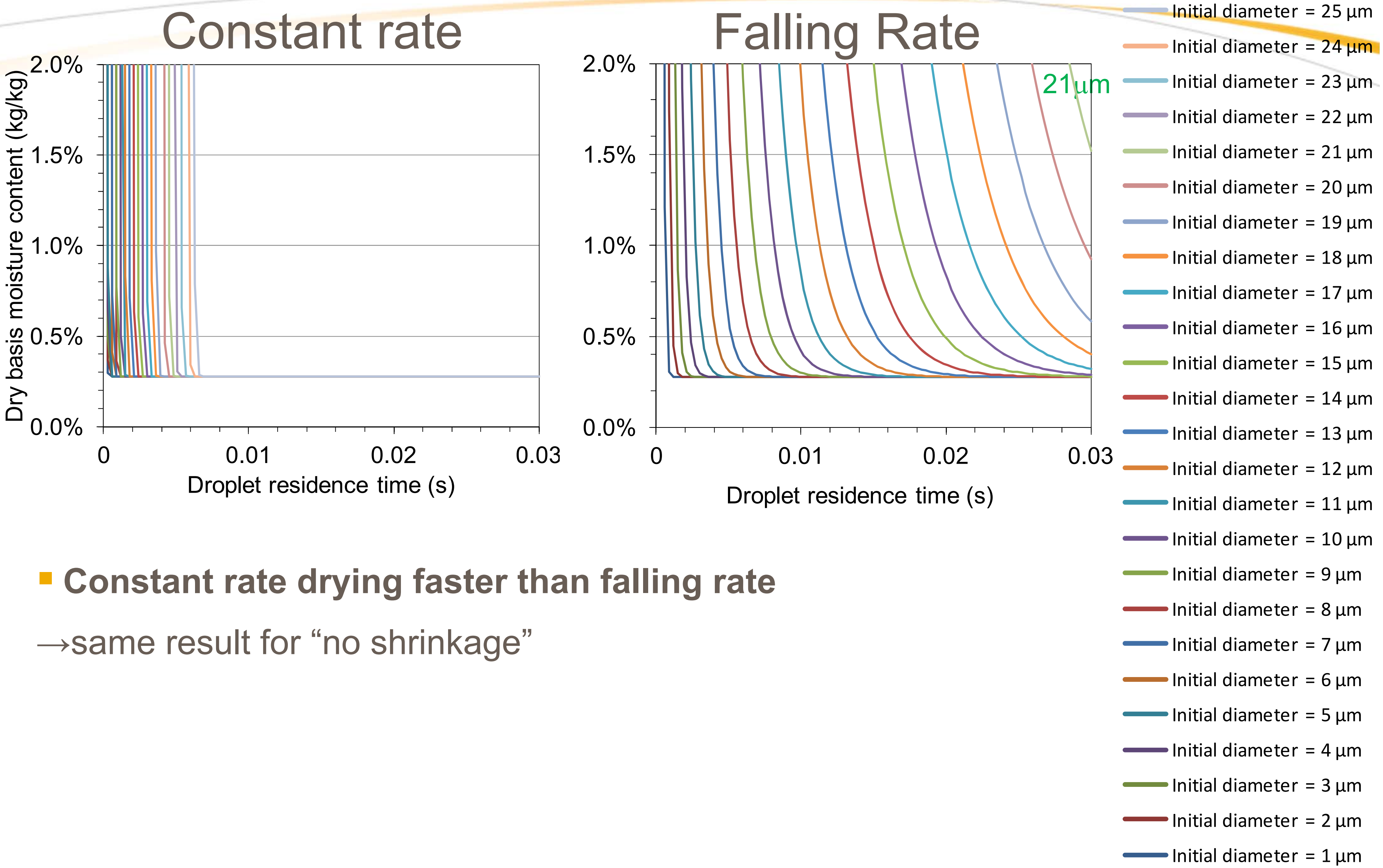
Results
Particle size for different residence times



- Distribution of output particle size (here: ranging from 1.97-6.6µm) depending on inlet droplet size & residence time
- Largest particles originate from large droplets with small residence time
- Average values for x10, x50, x90 depend on inlet droplet size and residence time distribution

Results – Effect of drying regime

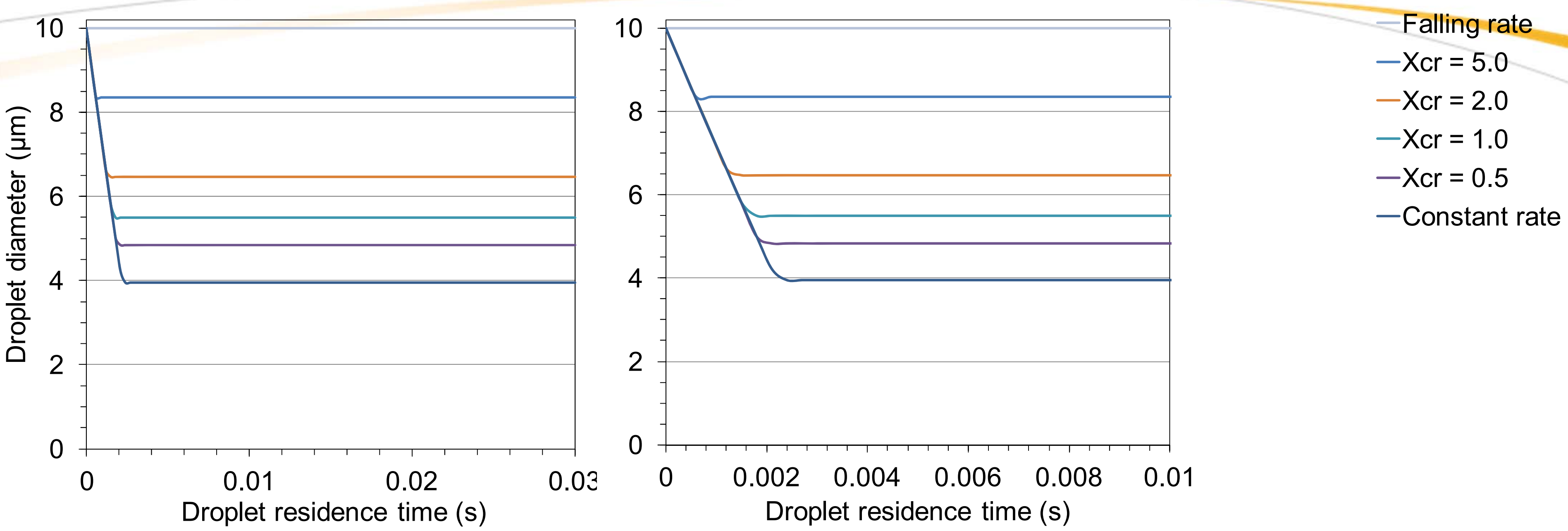
No shrinkage



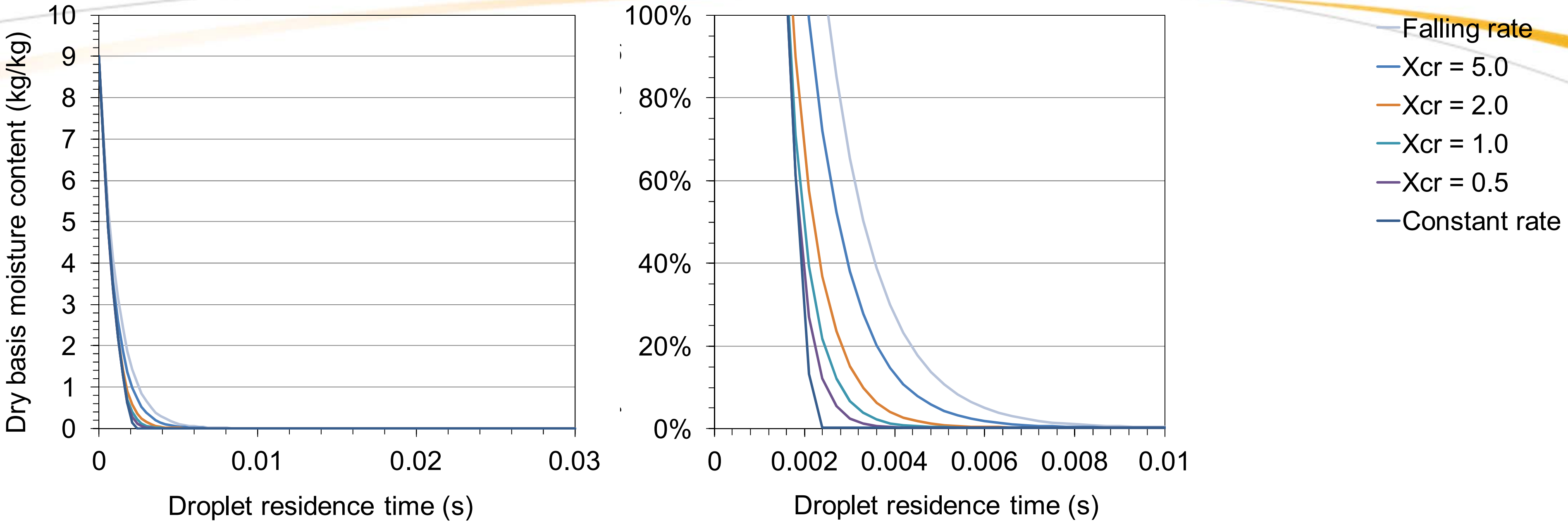
- **Constant rate drying faster than falling rate**

→same result for “no shrinkage”

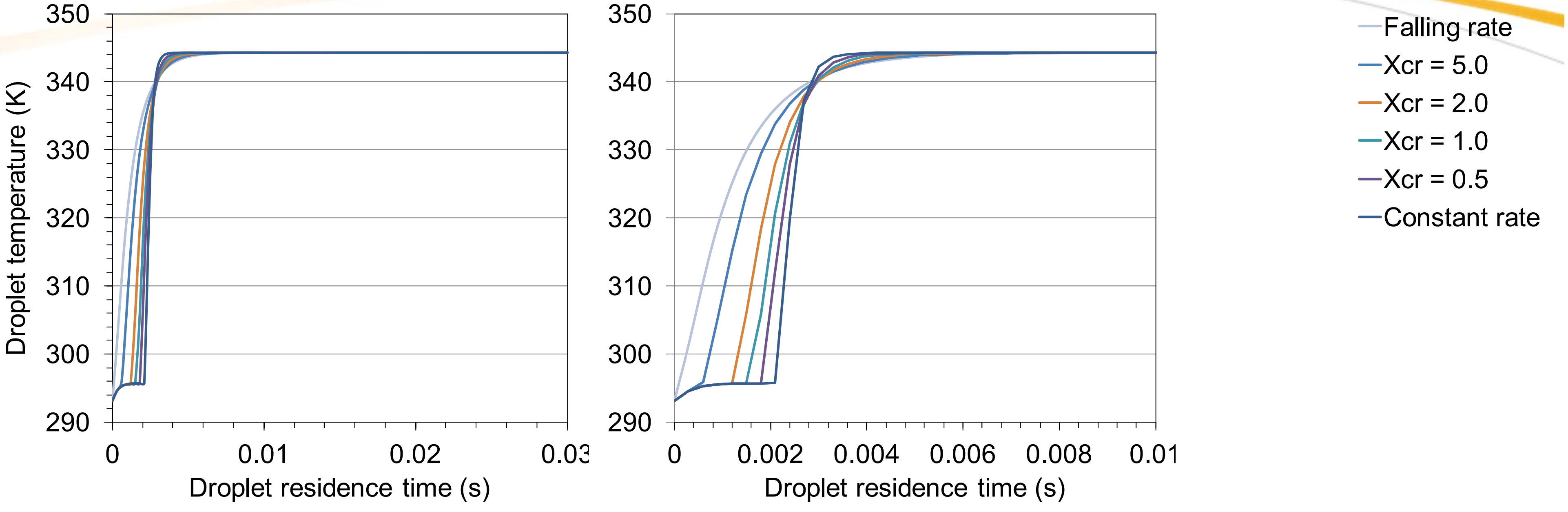
Results – Effect of drying regime



Results – Effect of drying regime



Results – Effect of drying regime



BACKUP: Thoralf's 2012 PSE Forum presentation
Using gSOLIDS to Optimise Spray Drying Operations

Thoralf Hartwig

18 April 2012

Acknowledgements:

- Mark Pinto (PSE)
- Ian Kemp, Yoong See-Toh (GSK)

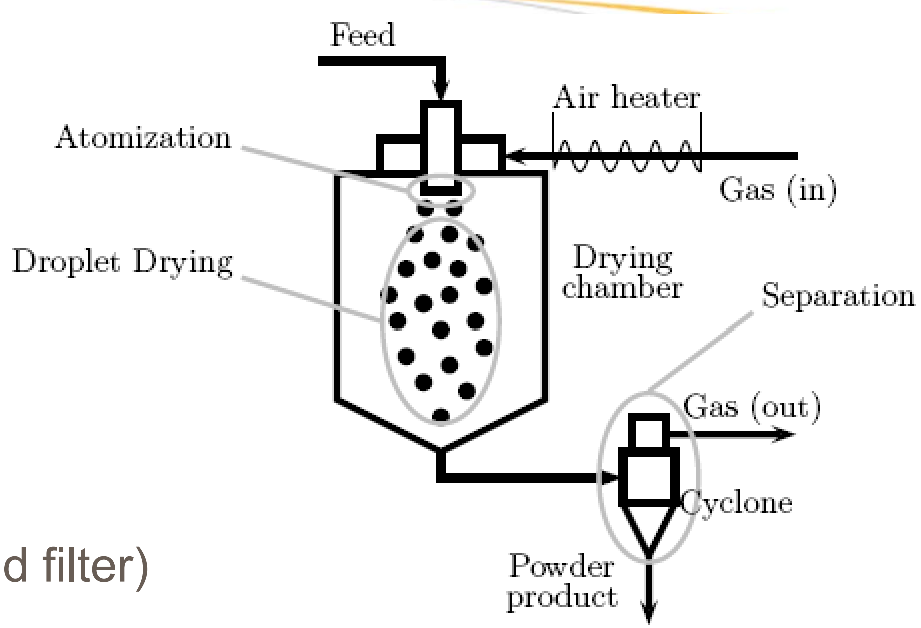
Using gSOLIDS to Optimise Spray Drying Operations

Contents

Introduction

- *Principle*:

  1. Atomisation
  Liquid feed suspension (or solution)
  of solids in water (or organic solvents)
  is atomised through a 1-/2-Fluid nozzle
  2. Droplet Drying
  Droplets evaporate into a stream of
  hot air (or nitrogen)
  3. Gas-Solid Separation
  Solids are collected in cyclone (or a dead-end filter)



- *Applications:*

  - food industry (milk powder, starch)

  - industrial applications (catalysts, enzymes, paint pigments)

  - pharmaceutical industry (antibiotics, proteins)

- *Advantages:*

  - **Unimodal size distribution** → catalysts

  - **Mild drying conditions** → antibiotics, proteins

Introduction
Equipment

Introduction
Why do we need modelling?

- **Making material of desired quality / identification of process parameters**

  (a) Existing knowledge gathered at small scale to make material of desired attributes at large scale. (**Scale-Up/Optimisation**)

  (b) New compound, no process knowledge about this material, but of others at same scale with same desired output attributes. (**Feasibility**)

  Objective: Putting in place a quantitative model (predictive or empirical) that link input attributes & process conditions to outlet attributes

  The identification of process parameters prior to validation experiment will save time and material. (material limitation in early stage development processes)

- **Quality critical attributes in Spray Drying are:**

  Temperature History → crystallinity/ form/ stability limits → function

  Moisture Content → bacterial growth (water), toxicity (organic solvents)

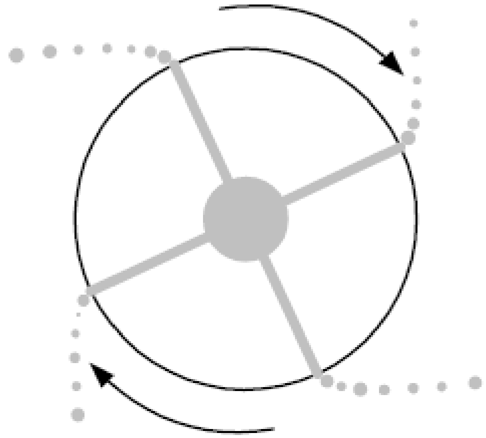
  Particle Size & Shape → blending, dissolution, aerosolisation → bioavailability

- **Manufacturability attributes in Spray Drying that could also be obtained by modelling:**

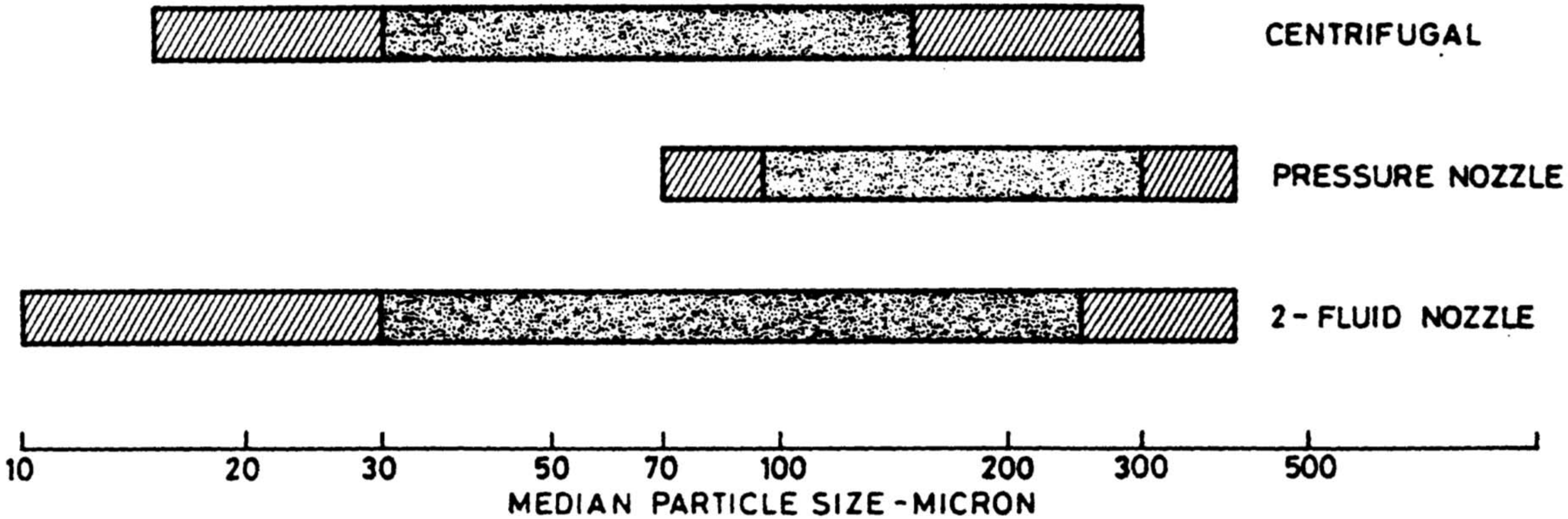
  Yield, Production rate, energy&solvent consumption (→ carbon footprint)

Modelling Approach

1. Atomisation



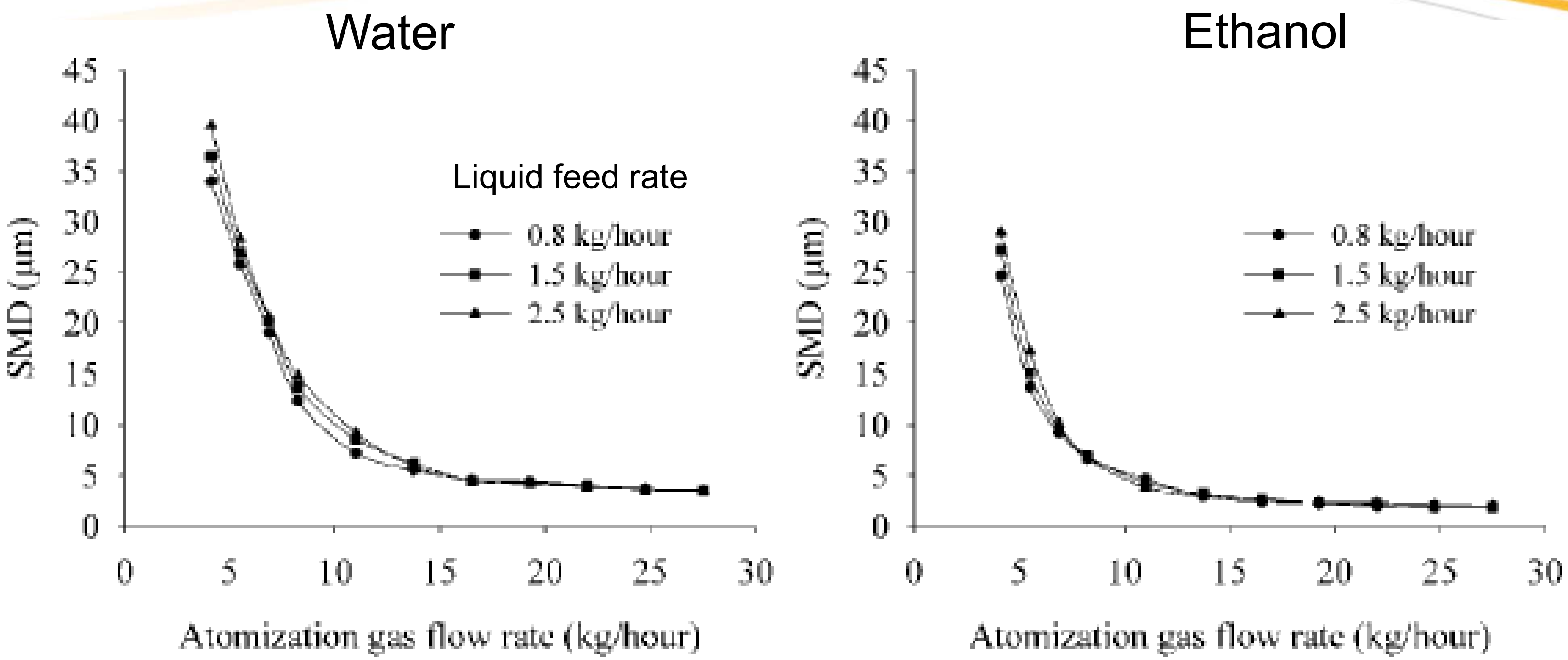
- Standard and extreme ranges as given by Lang (1984)
- For large-scale industrial dryers → 100 kg/h up to 10 t/hr



Modelling Approach
1. Atomisation

- Inlet droplet size depends on:
  - Nozzle type (2-fluid, rotary…) → equipment specific
  - Nozzle orifice diameter(s)
  - Atomisation gas flow rate, liquid flow rate, ALR (gas/liquid ratio) → shear force
  - Surface tension, viscosity & density of liquid phase
- Inlet droplet size could be assessed by:
  - **Direct measurement**: Particle Image Velocimetry (**PIV**) → high speed camera
  - **Indirect measurement**: Back-calculated from offload PSD (via mass balance)
  - **Modelling**: Empirical correlations by Mansour et al. (1995)

Modelling Approach
1. Atomisation



$$\frac{SMD}{d_0} = \left(1 + \frac{M_l}{M_g}\right) \cdot X_2 \cdot \left(\frac{\boldsymbol{Oh}}{We}\right)^{x_1}$$

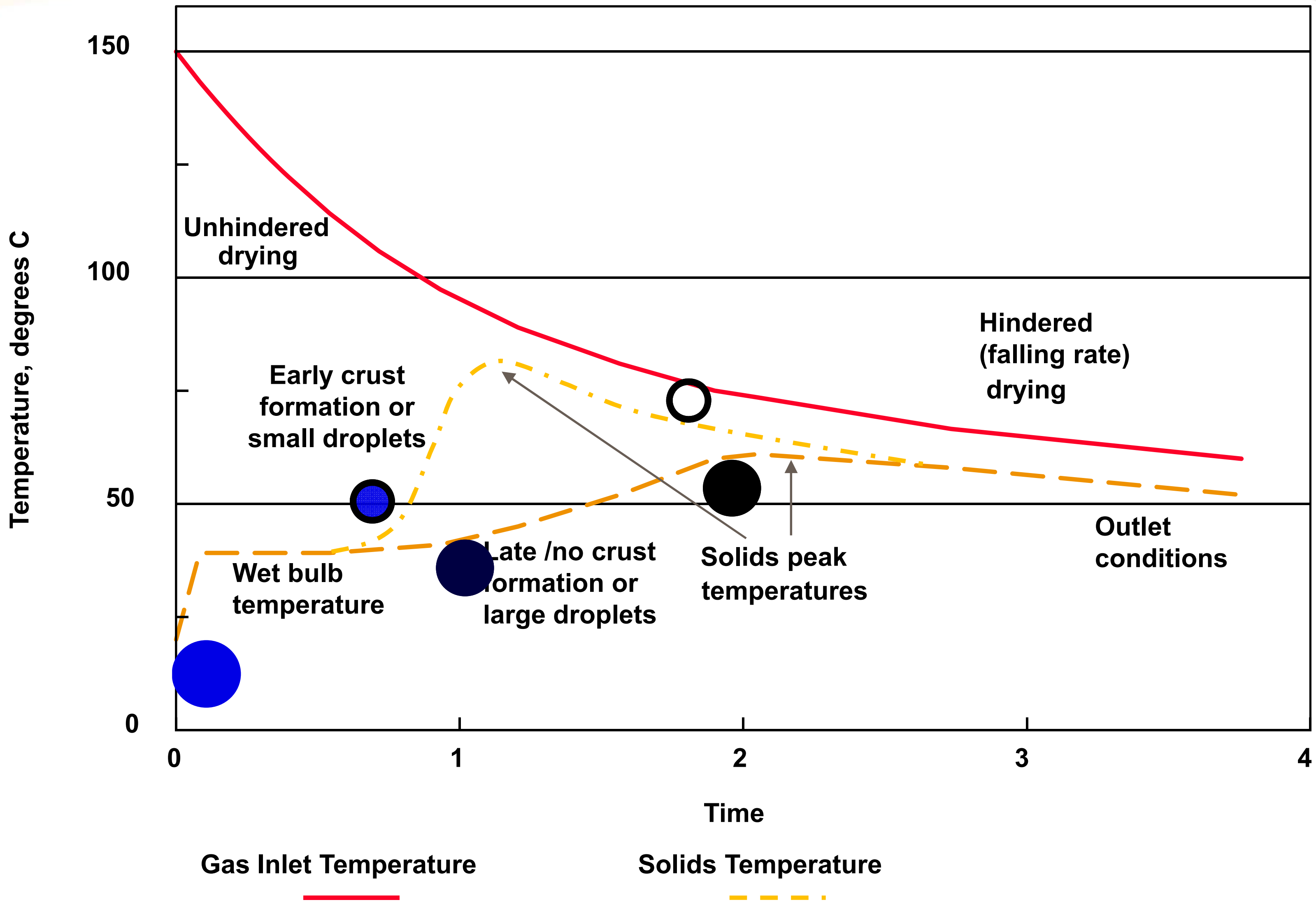
$$\mathrm{Oh} = \frac{\mu}{\sqrt{\rho \sigma L}} = \frac{\sqrt{\mathrm{We}}}{\mathrm{Re}} \sim \frac{\text{viscous forces}}{\sqrt{\text{inertia} \cdot \text{surface tension}}}$$

$$We = \frac{\rho v^2 l}{\sigma}$$

Thybo et al. (2008): Droplet Size Measurements for Spray Dryer Scale-Up. Pharmaceutical Development and Technology vol. 13, pp 93–104.

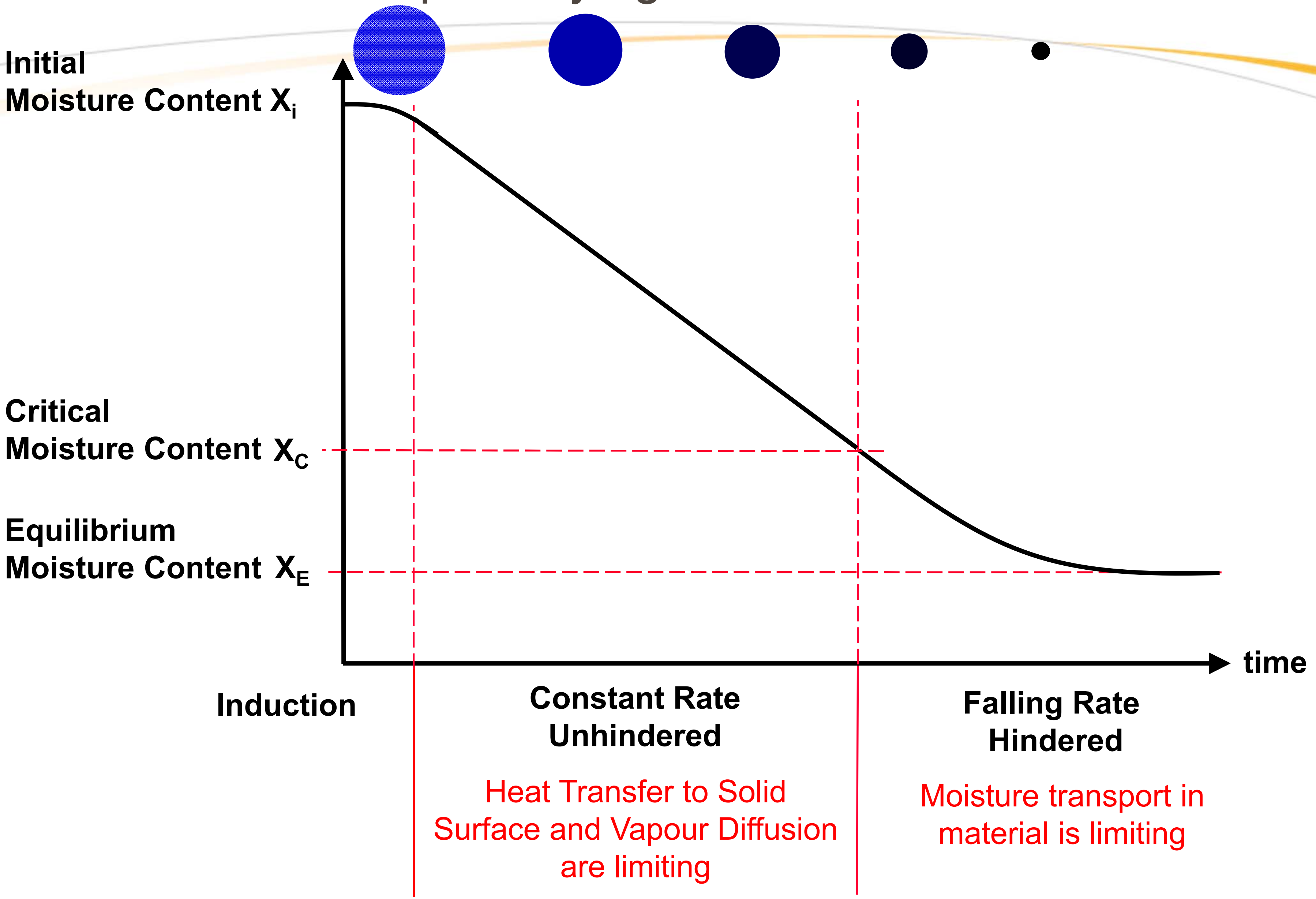
Modelling Approach

2. Droplet Drying – Temperatures (co-current drying)



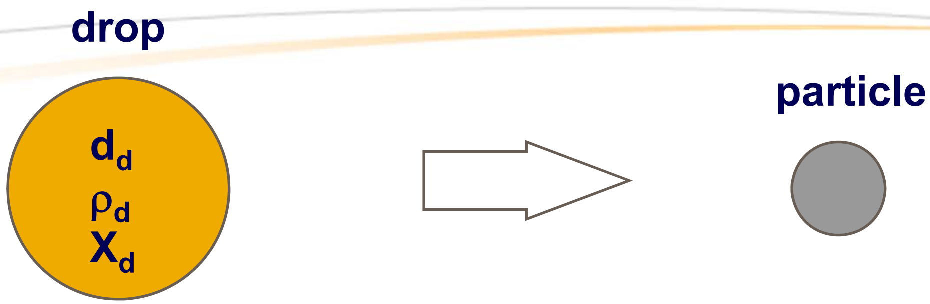
Modelling Approach

2. Droplet Drying – Moisture Content



Modelling Approach

2. Droplet Drying – Droplet Size (Ideal Shrinkage)



m_p = mass (m)
d_p = diameter (m)
ρ_p = particle density (kg/m^3)
X_p= solids content (kg/kg)

- Balancing solids content of droplets and particles:

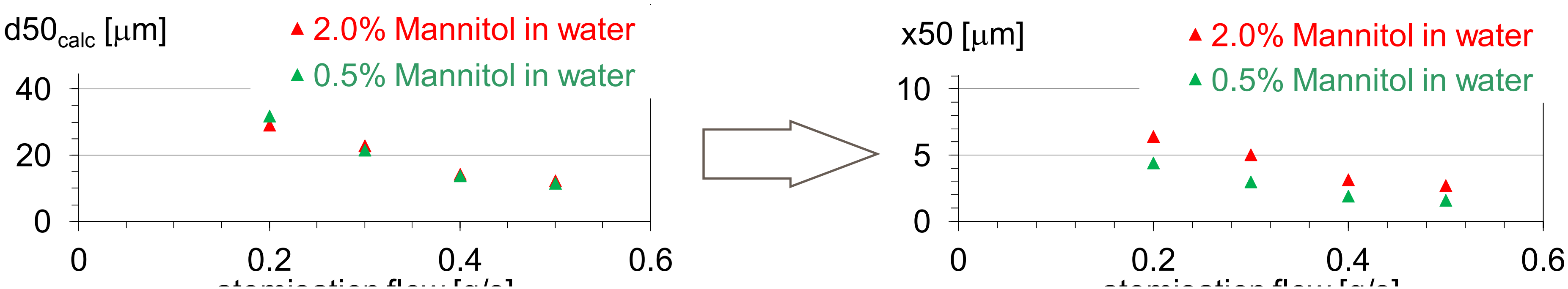
$$m_S = m_d X_d = \frac{\pi}{6} d_d^3 \rho_d X_d = m_p X_p = \frac{\pi}{6} d_p^3 \rho_p X_p$$

$$d_p = d_d \left(\frac{\rho_d X_d}{\rho_p X_p} \right)^{\frac{1}{3}}$$

- Example: 20 μm droplet, X_d=1%, X_p=98%, ρ_d=1000, ρ_p=500

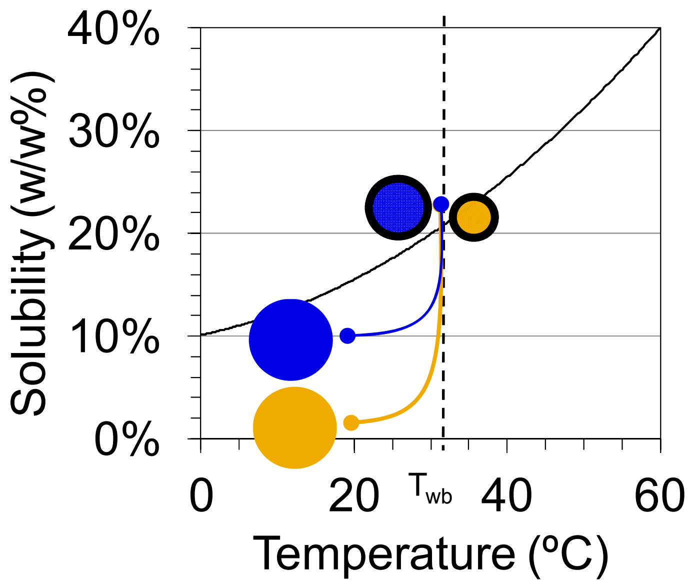
→ Final particle size 5.5 μm (or 6.9 μm with X_d=2%)

system: Mannitol in aqueous solution
equipment: Büchi B-290, 2-fluid nozzle
settings: feed flow 6.2 g/s, T_{in} = 150 C



Modelling Approach

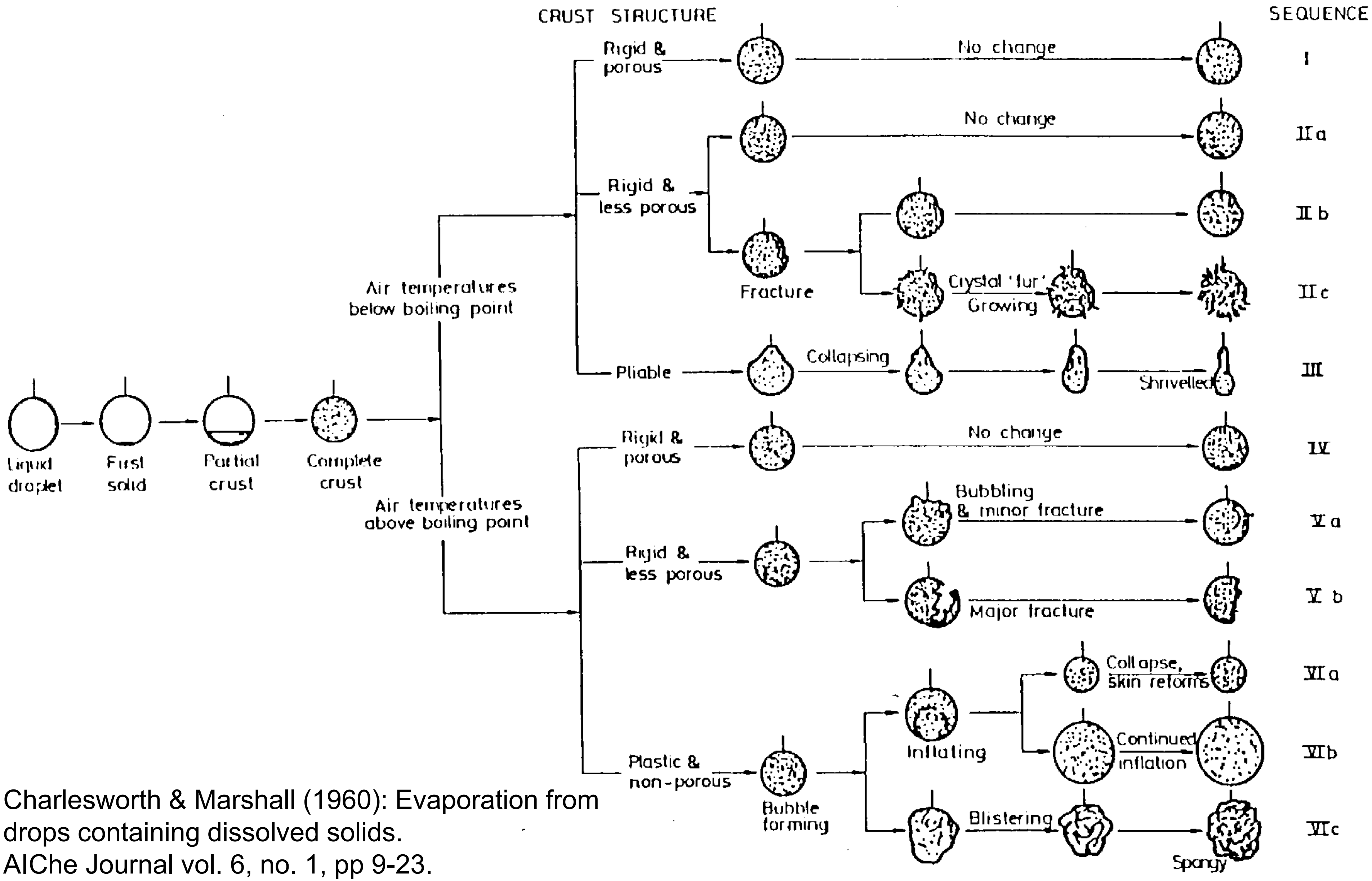
2. Droplet Drying – Droplet Size (solution spray drying)



- Crust formation in solution spray drying occurs at an earlier stage in higher concentrated solutions closer to solubility limit
- Example (Mannitol in Water): solubility 18 w/w% at wet bulb temperature (25ºC), 30 μm droplet inlet size
- 1% Mannitol solution → crust formation at 11μm
- 10% Mannitol solution → crust formation at 23μm

Modelling Approach

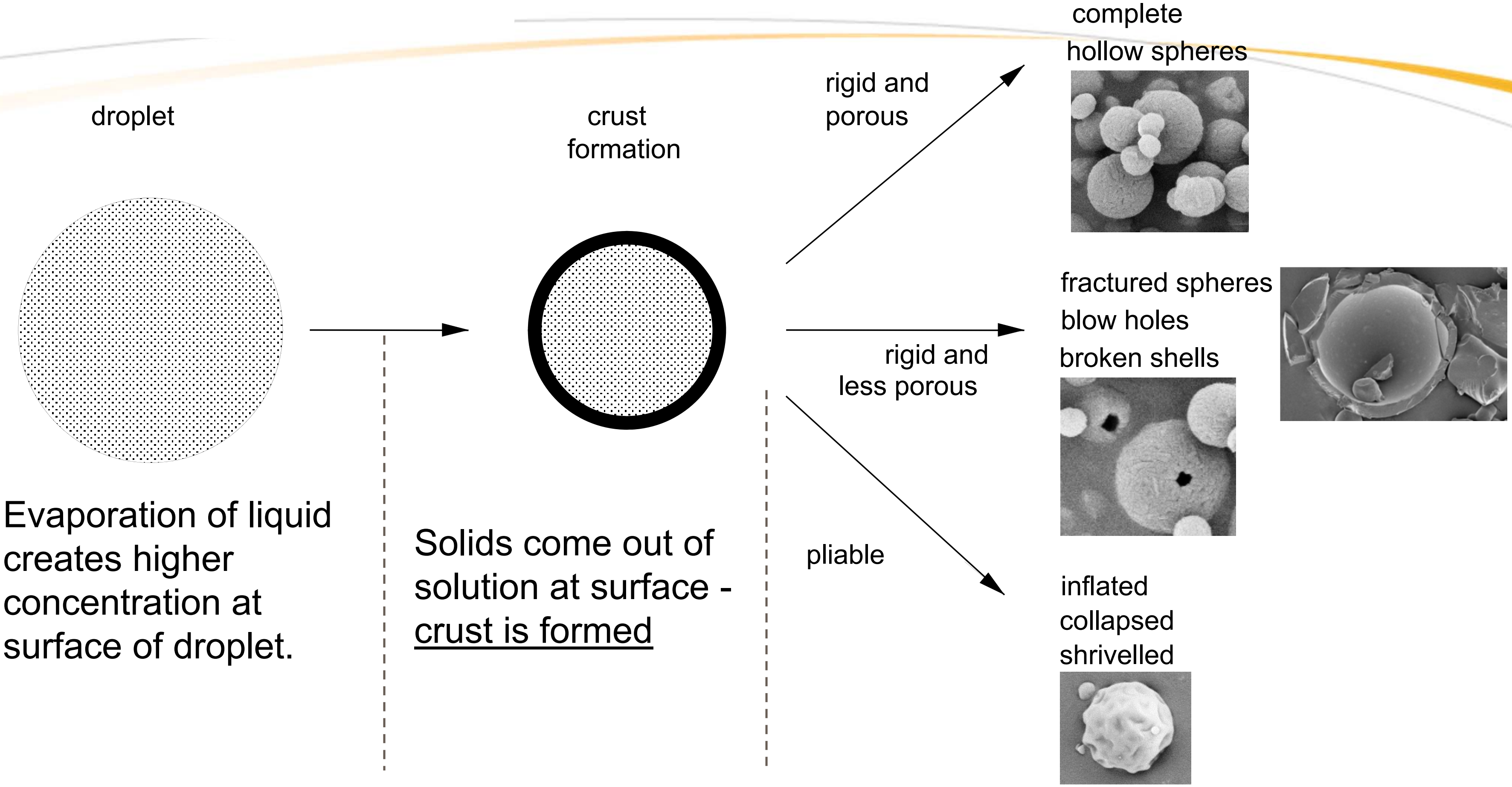
2. Droplet Drying – Droplet Size (Real Effects)



Charlesworth & Marshall (1960): Evaporation from drops containing dissolved solids.
AIChe Journal vol. 6, no. 1, pp 9-23.

Modelling Approach

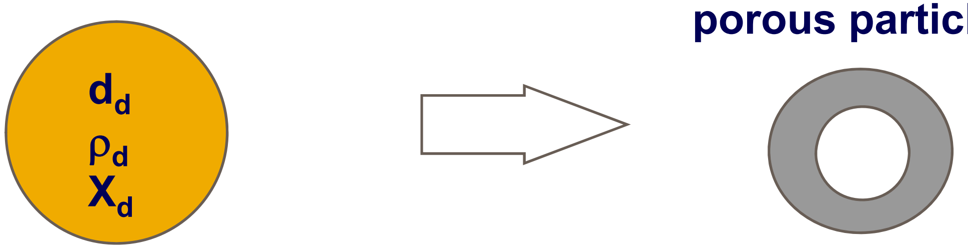
2. Droplet Drying – Droplet Size (Crust Formation)



Modelling Approach
2. Droplet Drying – Droplet Size (Crust Formation)

drop

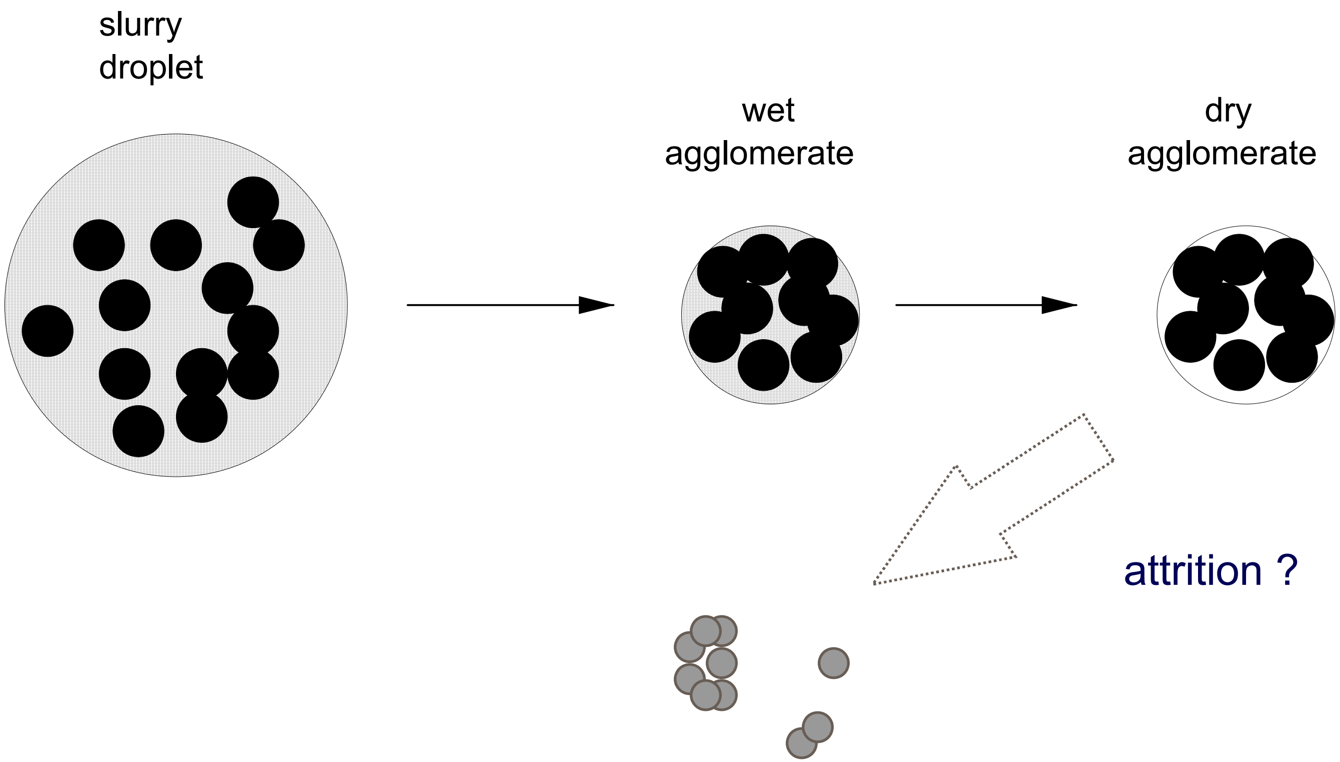
hollow or porous particle



m_p = mass (m)
d_p = diameter (m)
ρ_b = bulk density (kg/m^3)
X_p= solids content (kg/kg)

- Mass Balance remains valid: $$d_p = d_d \left(\frac{\rho_d X_d}{\rho_b X_p} \right)^{\frac{1}{3}}$$
- However bulk densities are smaller compared to massive particles
- Example: 20 μm droplet, 10 μm particle, X_d=1%, X_p=98%, ρ_d=1000
- Particle bulk density 82 kg/m^3 (or 163 kg/m^3 with X_d=2%)

Modelling Approach
2. Droplet Drying – Droplet Size (Attrition)



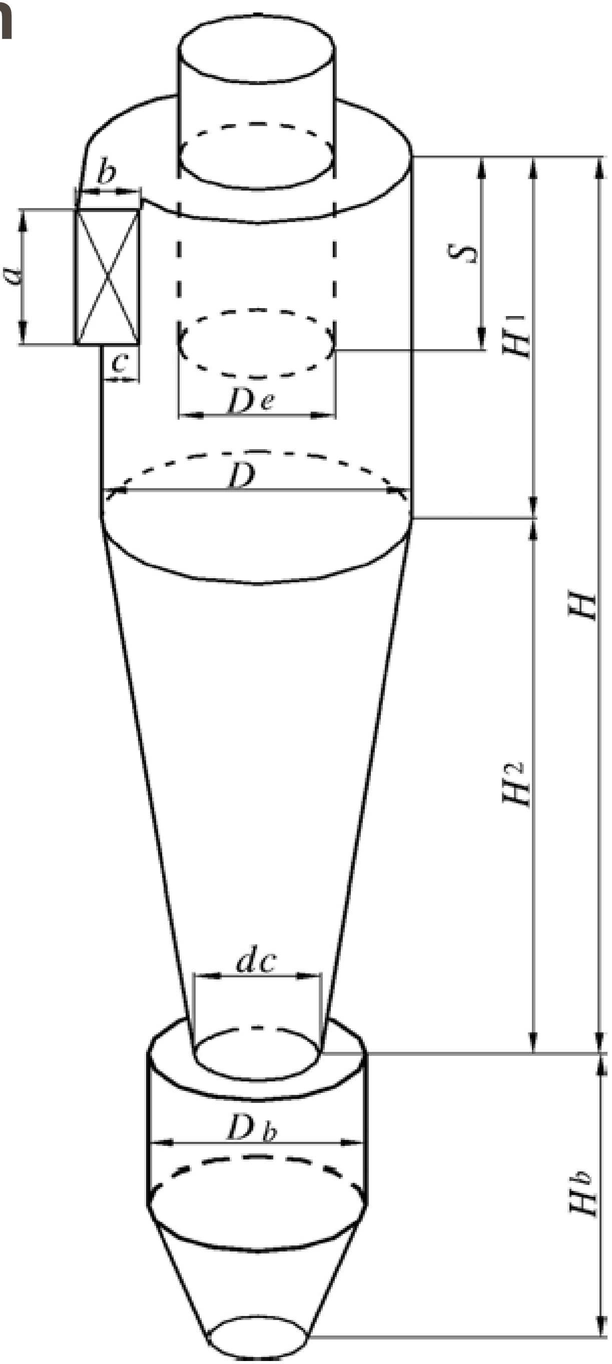
Modelling Approach
3. Cyclone

- Cut size (separation efficiency) depends on:
- Cyclone geometry
- Physical properties of gas & solid (density, viscosity)
- Volume flow, velocity, solid loading

Results for lab driers / lab experiments:

→ Cut size in lower micron / submicron region

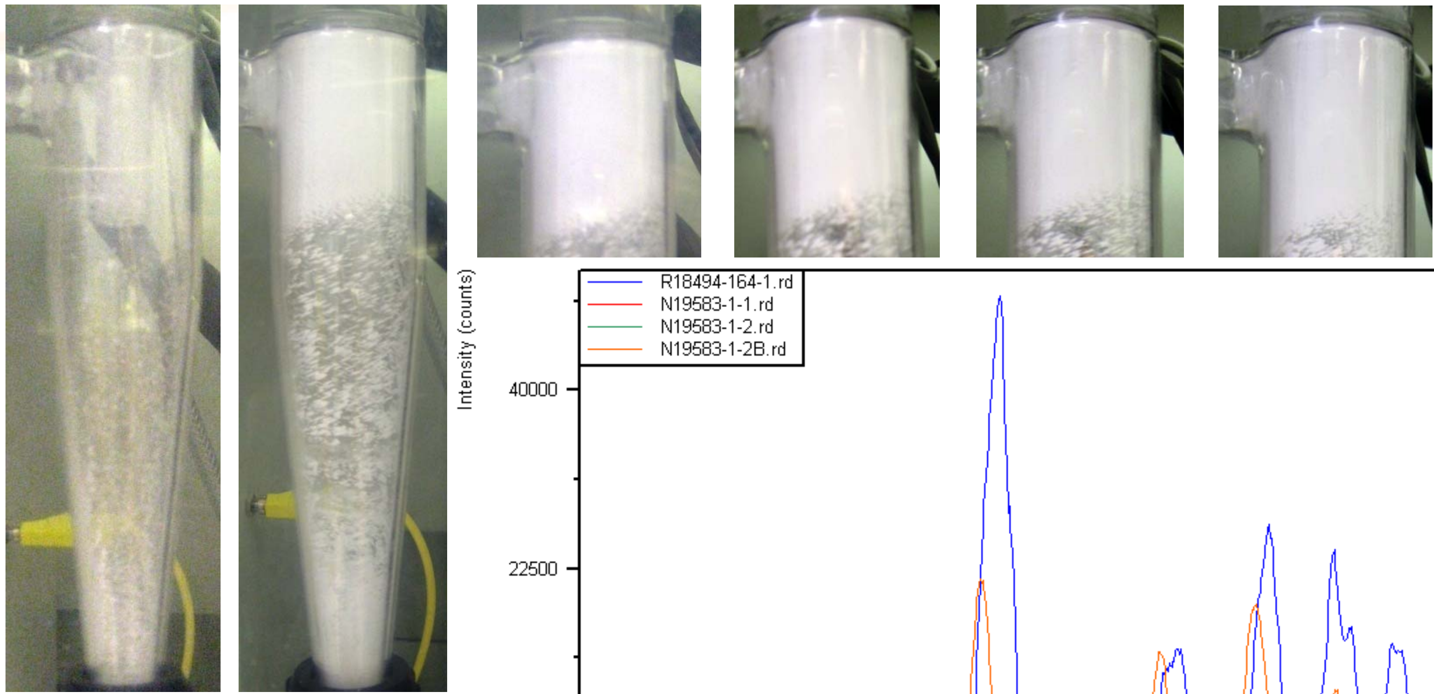
→ Efficiency >95%

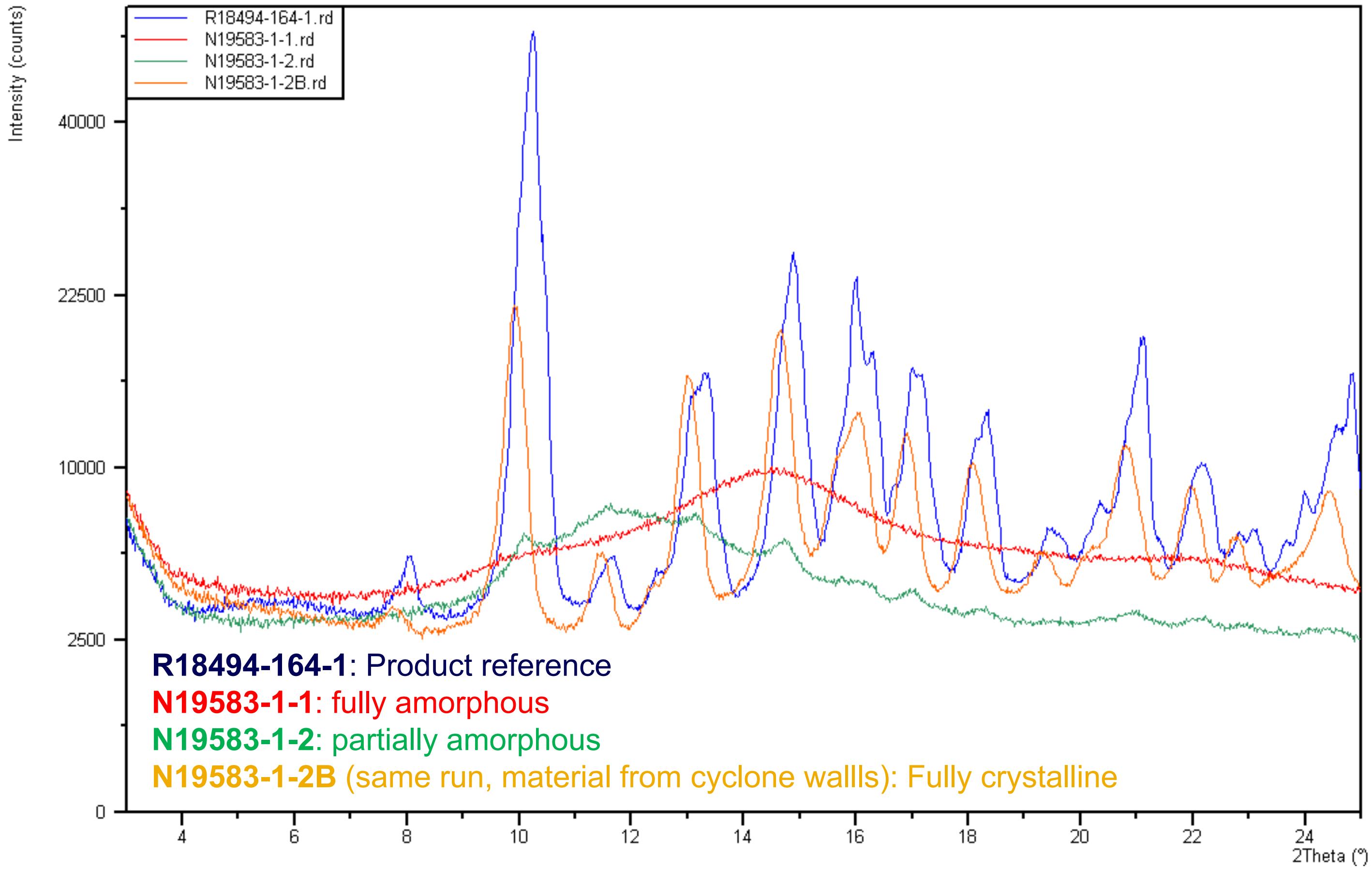


Chen & Shi (2007): A universal model to calculate cyclone pressure drop
Powder Technology Vol 171, no 3, pp 184-191.

Modelling Approach
3. Cyclone – Real Effects

30 sec | 1 min | 1:30 min | 2 min | 3 min | 5 min





Modelling Approach

IPO

Atomization Model

input attributes	**process**	**model output**
Physical Properties for Feed (solution/suspension) & gas	Atomisation parameters (flow rates) Nozzle orifice diameter	Inlet droplet size (distribution)

Spray Chamber Model

input attributes	**Process**	**model output**
Physical Properties for solvent, solid & gas Solid loading Inlet droplet size distribution	Spray chamber geometry Inlet flow rates Inlet temperatures	PSD ex spray chamber **temperature history** **moisture content**

Cyclone Model

input attributes	**process**	**model output**
PSD ex spray chamber Solid loading Physical Properties for solid & gas	Cyclone geometry Gas flow rate	**PSD in offload** (collection pot / fines filter) **Yield**

Modelling Approach

IPO

Experimental Database
Process conditions,
Equipment (scale/type),
compounds, solvents

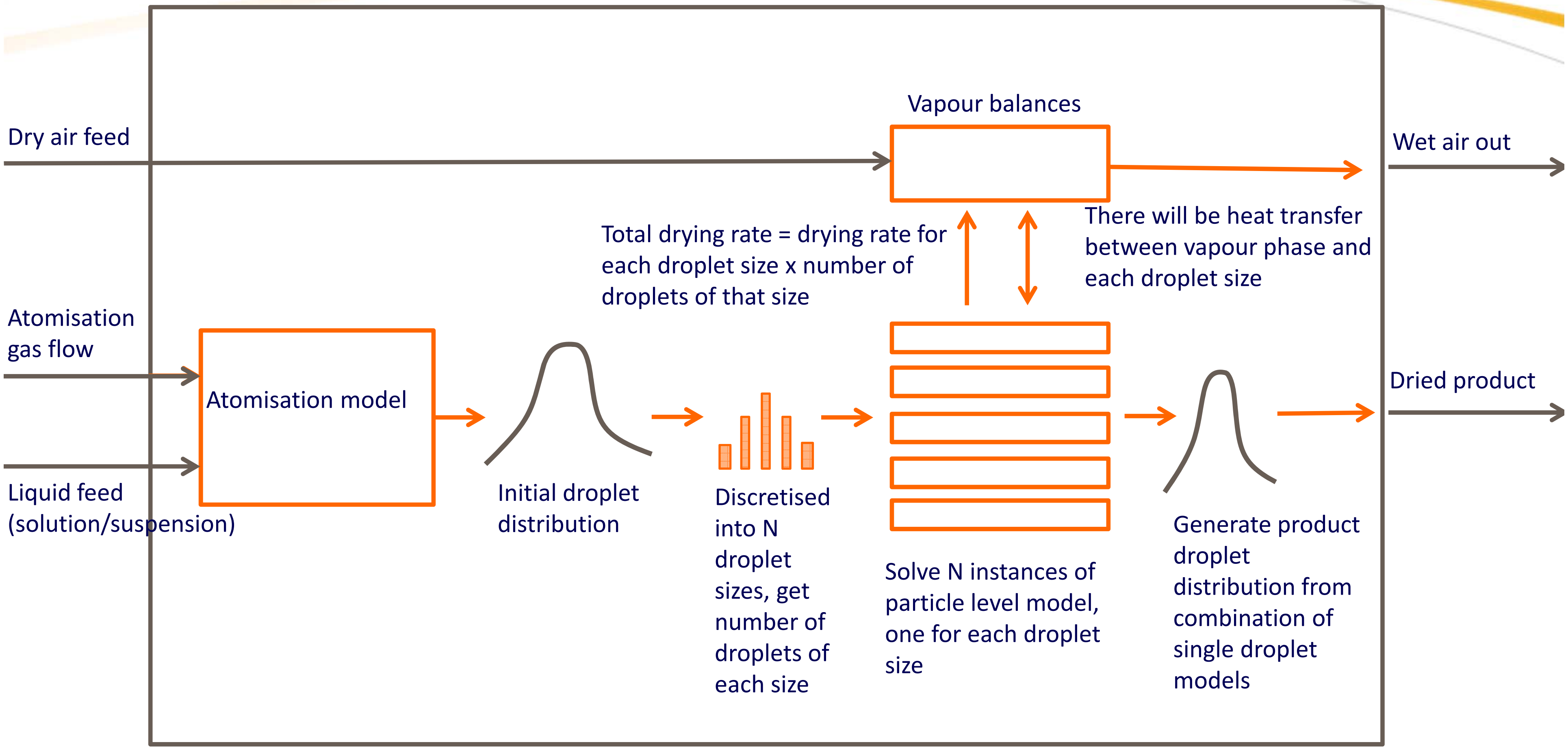
gSOLIDS model includes:
Spray chamber
Cyclone
Atomisation

Input Attributes	Process Parameters	Model Output
Physical Properties for solvent, solid & gas	Inlet flow rates (Liq,Gas, atomisation)	Temperature history
Solid loading	Inlet temperatures	Moisture content
Inlet droplet size	Spray chamber geometry	PSD in offload (spray chamber/cyclone)
	Cyclone geometry	Yield

Required additionally:
Heat loss as function of inlet temperature
Inlet droplet size distribution as function of atomisation flow rate
Droplet residence time from fluid flow / CFD modelling

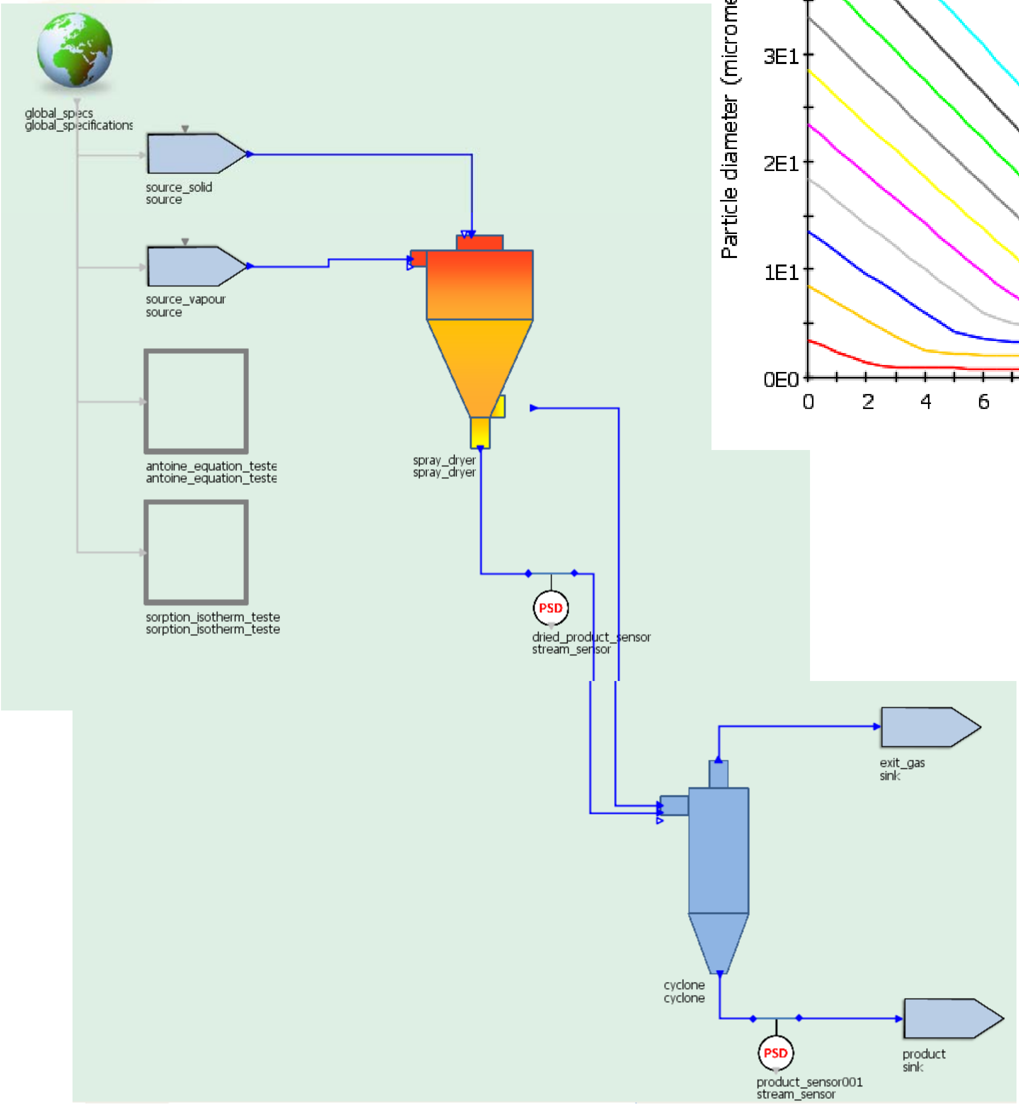
Modelling Approach

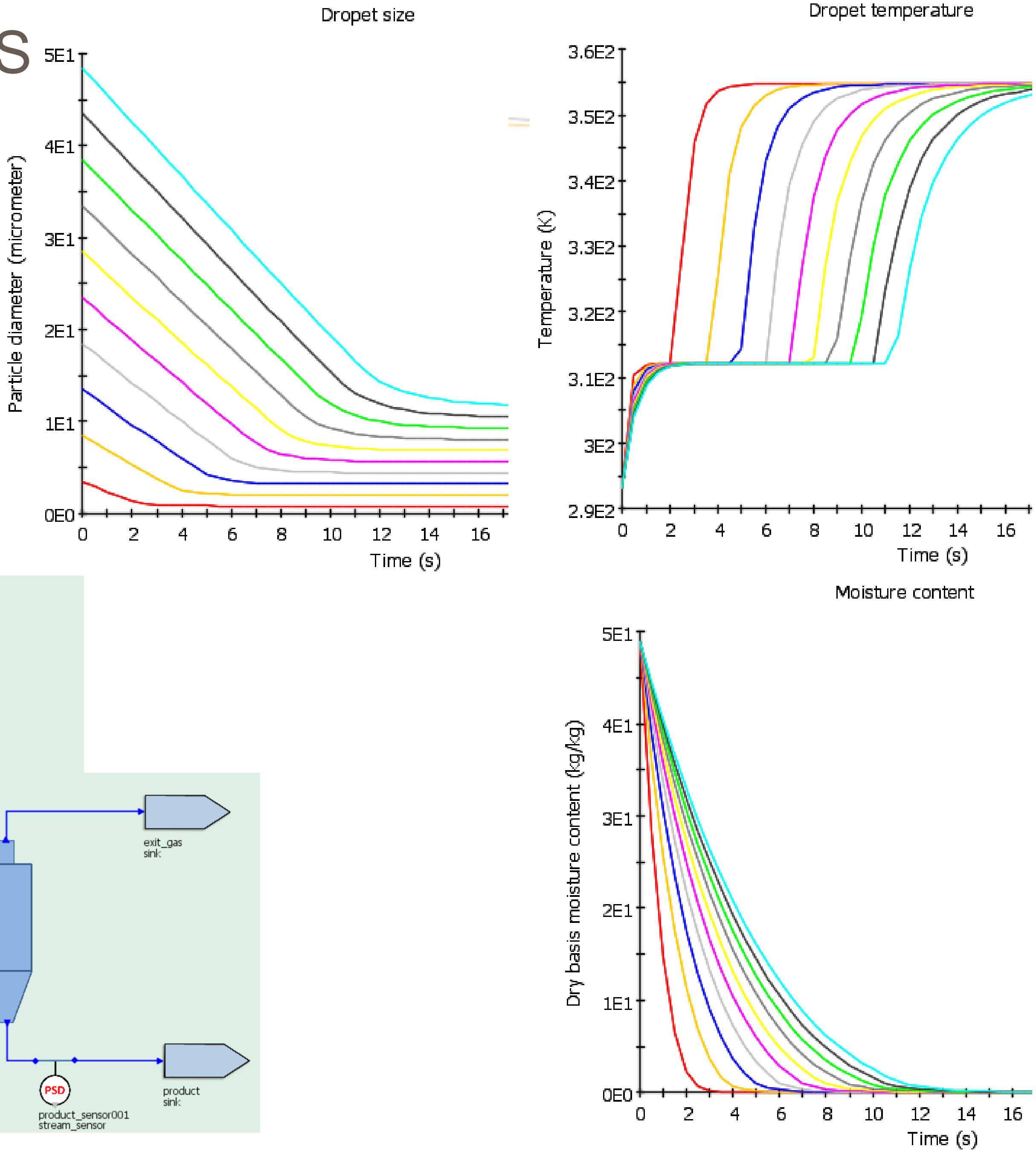
Overview



Modelling Approach

Realisation in gSOLIDS



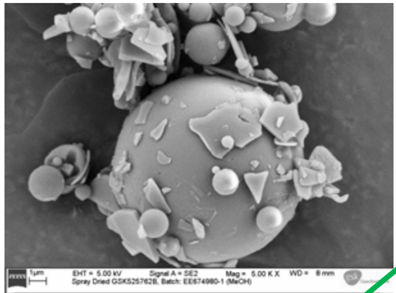


Case Study

Identify Process Conditions Cross-Scale: Modelling vs DoE

Gas inlet temperature

small, broken shells, dry



BP

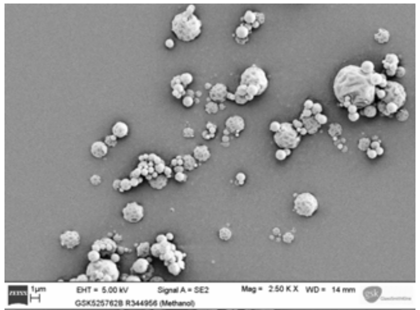
large spherical dry

Identify Optimal process conditions to make particles
- **10-20 μm in size**
- **spherical, regular shape**
- **solvent content <0.3%w/w**

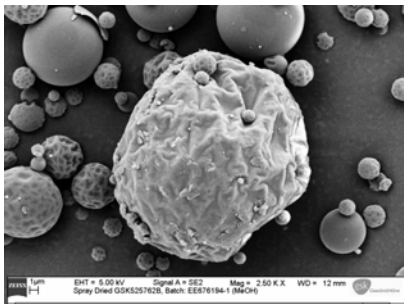
(1.) <u>Experimental</u>: 2 factors DoE, ~1+1 week using 20+200g of material at small+large scale

(2.) <u>Modelling</u>: ~1 day to identify optimal conditions + large scale validation experiment using 40g of material

too small, spherical, dry



large, spherical, too wet



Atomisation flowrate

Case Study

Strategy

- Determine unknown parameters using gSOLIDS regression:

  - Heat loss using outlet temperature

  - Inlet droplet size distribution using offload PSD

  - Droplet residence time using moisture content

- Establish correlations (empirical model-build):

  - Heat loss as function of inlet temperature

  - Inlet droplet size distribution as function of atomisation flow rate

  - Droplet residence time from fluid flow / CFD modelling

- Use model predictively:

  optimise inlet temperature and flow rates to optimise

  max temperature, outlet moisture content and PSD ex cyclone

Case Study

Results

- Determine unknown parameters using gSOLIDS regression:

  - Heat loss using outlet temperature

  - Inlet … using of… PSD

  - Droplet residence time using moisture content

	inlet temp	heat loss
	dC	W
	exp	calc
2g scale	100	749
2g scale	100	728
2g scale	180	1477
20g scale	110	165

	ALR	initial droplet size
	w/w	micron
	calc	calc
2g scale	4.09	2.6
2g scale	2.76	8.1
2g scale	1.99	*4.6*
20g scale	3.83	2.9

	residence time	
	s	s
	min (plug flow)	calc
2g scale	0.63	*0.01*
2g scale	0.63	*0.02*
2g scale	0.63	*0.01*
20g scale	1.20	*0.42*

- Values for observed heat losses in ranges seen before
- Heat losses higher for smaller scale equipment compared to 20g scale (vacuum spray chamber)
- No correlation could be established between ALR and inlet droplet size
  - Experiment no. 3 is outlier because of “broken shells”
- Inlet droplet size are <u>below</u> droplet sizes as reported in literature for 2 fluid nozzles
- Estimated residence times are below plug flow residence time

Case Study
Results

- Determine unknown parameters using gSOLIDS regression:

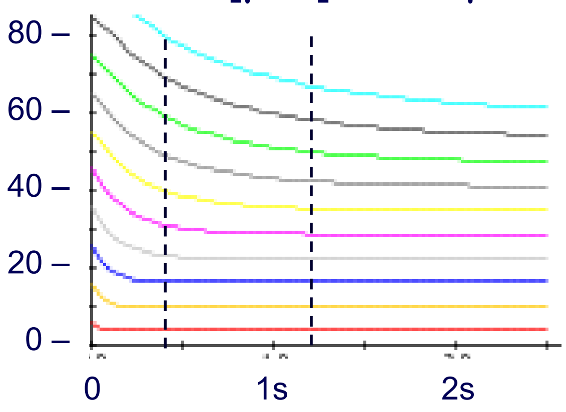
  - Heat loss using outlet temperature

  - Inlet droplet size distribution using offload PSD

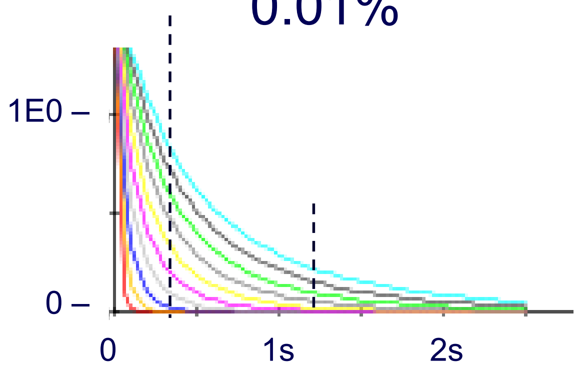
  - Droplet residence time using moisture content

	inlet temp	atomiser flow	gas flow	feed flow	ALR	initial droplet size	heat loss	residence time		outlet PSD x50		outlet temp		outlet humidity	
	dC	kg/h	kg/h	kg/h	w/w	micron	W	s	s	micron	micron	K	K	%	%
	exp	exp	exp	exp	calc	calc	calc	min (plug flow)	calc	exp	calc	exp	calc	exp	calc
2g scale	100	1.1	57.5	0.26	4.09	2.6	749	0.63	0.01	1.72	2.50	323	323	0.14%	0.14%
2g scale	100	0.7	57.5	0.26	2.76	8.1	728	0.63	0.02	5.42	5.42	324	324	0.52%	0.52%
2g scale	180	0.7	57.5	0.36	1.99	4.6	1477	0.63	0.01	3.59	3.59	356	356	0.06%	0.06%
20g scale	110	4.0	30.0	1.04	3.83	2.9	165	1.20	0.42	2.93	2.93	347	347	0.01%	0.01%

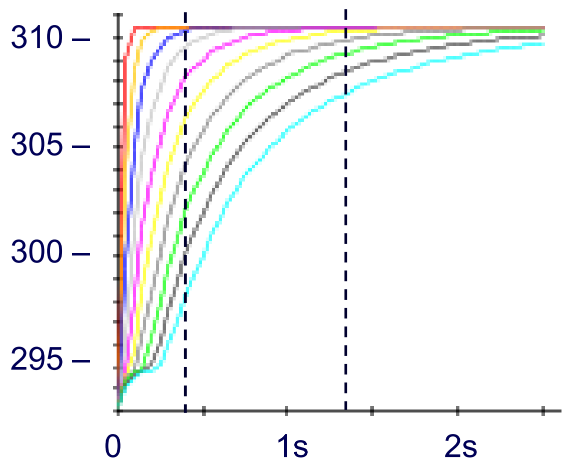
PSD [μm]: 2.93μm



moisture content [g/g]: 0.01%



droplet temperature [ºC]



Case Study
Results

- Fix residence time to minimum residence time (= plug flow)
- Vary inlet droplet size to match outlet humidity

	initial droplet size	outlet PSD x50	
	micron	micron	micron
	calc	exp	calc
2g scale	*48*	1.72	*20.1*
2g scale	*50*	5.42	*29.7*
20g scale	*78*	7.47	*52.0*
20g scale	*90*	2.93	*60.2*

- Inlet droplet sizes are above droplet sizes reported in literature
- Predicted outlet droplet sizes are much larger than observed
- Results suggest that drying in reality is hindered in comparison to model results
- Possible rationale: solvent “clinging” on the compound due to

  - Diffusion limitation (critical moisture content)

  - Physically / chemically bound (equilibrium moisture content / absorption isotherm)

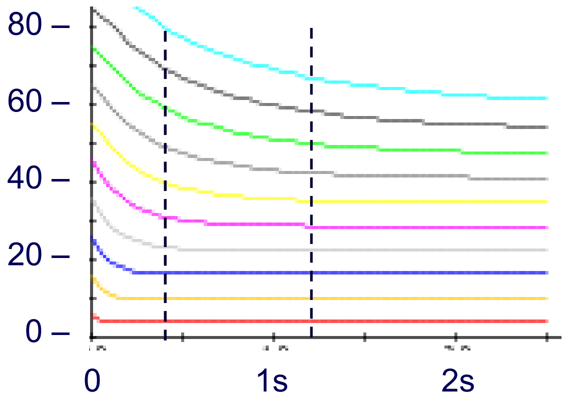
Case Study

Results

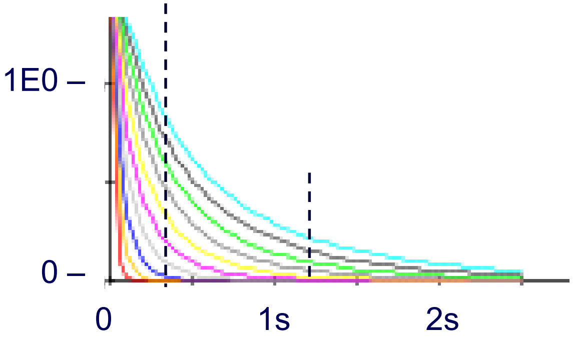
- Fix residence time to minimum residence time (= plug flow)
- Vary inlet droplet size to match outlet humidity

	inlet temp	atomiser flow	gas flow	feed flow	ALR	initial droplet size	residence time		outlet PSD x50		outlet temp		outlet humidity	
	dC	kg/h	kg/h	kg/h	w/w	micron	s	s	micron	micron	K	K	%	%
	exp	exp	exp	exp	calc	calc	min (plug flow)	calc	exp	calc	exp	calc	exp	calc
2g scale	100	1.1	57.5	0.26	4.09	48	0.6	0.6	1.72	20.1	323	323	0.14%	0.13%
2g scale	100	0.7	57.5	0.26	2.76	50	0.6	0.6	5.42	29.7	324	324	0.52%	0.53%
20g scale	110	2.0	15.0	0.93	2.15	78	2.4	2.4	7.47	52.0	340	340	1.10%	1.21%
20g scale	110	4.0	30.0	1.04	3.83	90	1.2	1.2	2.93	60.2	347	347	0.01%	0.01%

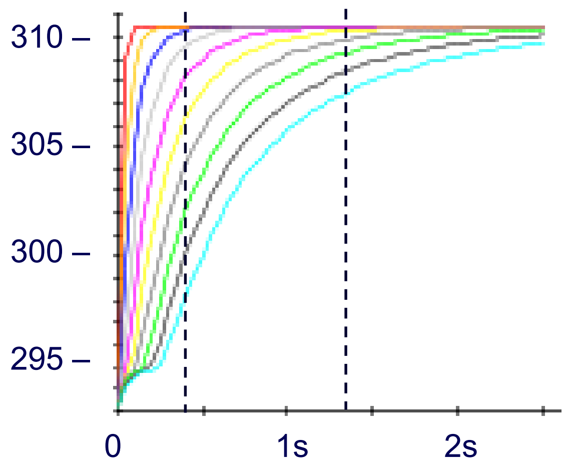
PSD [µm]: 2.93µm



moisture content [g/g]: 0.01%



droplet temperature [ºC]



Case Study
Results

- Change critical moisture content to account for hindered drying – increase from 1 to 5%
- Vary inlet droplet size to match outlet humidity

	initial droplet size	outlet PSD x50	
	micron	micron	micron
	calc	exp	calc
2g scale	20.0	1.72	*8.9*
2g scale	20.5	5.42	*13.7*
20g scale	34.0	7.47	*25.4*
20g scale	29.0	2.93	*17.2*

- Inlet droplet sizes now in expected range
- Predicted outlet droplet sizes are still larger than observed

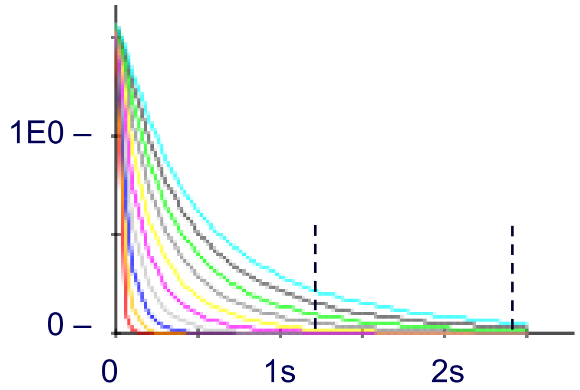
Case Study

Results

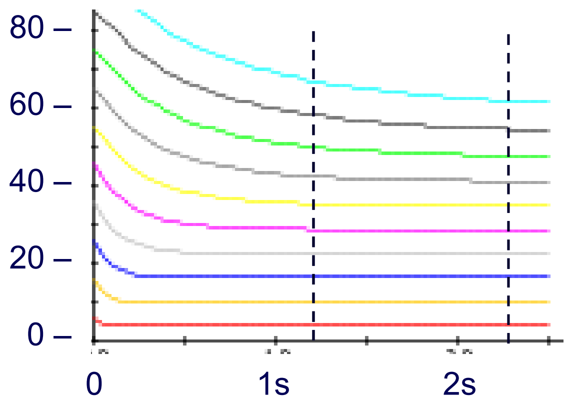
- Change critical moisture content to account for hindered drying – increase from 1 to 5%
- Vary inlet droplet size to match outlet humidity

X_E = 1%

moisture content [g/g]

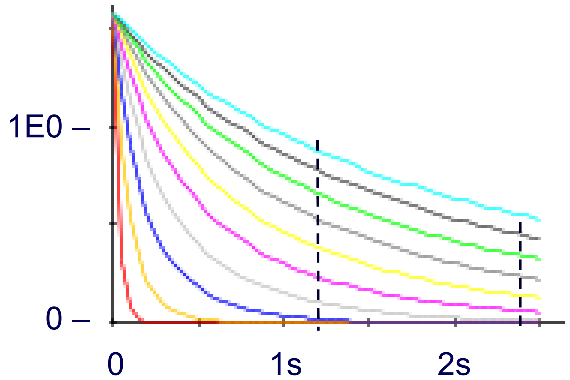


Droplet size [μm]

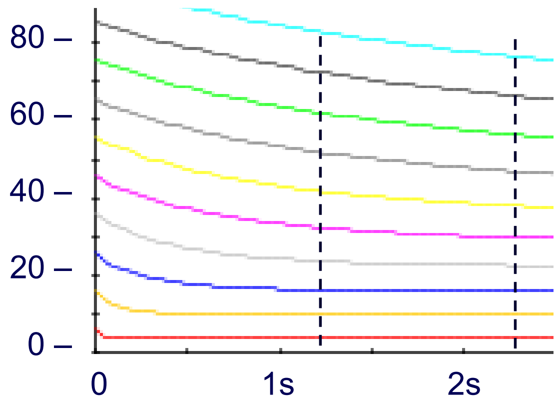


X_F = 5%

moisture content [g/g]



Droplet size [μm]



Case Study
Summary

- Model predicts qualitatively correct the 4 drying stages and principal relationships

  - PSD goes down with atomisation flow going up (wrt liquid flowrate),

  - Outlet temperature goes up with inlet temperature going up,

  - Outlet humidity increases with temperature going down and liquid flow going up (wrt total gas flow),

  - Heat loss increases with inlet temperature,

  - Inlet droplet size decreases with increasing ALR.
- **Discrepancies seen in outlet droplet sizes and/or residence times**
- **Reason: Critical moisture content higher (= diffusion limitation)/ absorption of solvent occurring for this particular compound/ solvent combination**
- **No knowledge so far about fracture, only qualitative comparison to BP of solvent**
- **More data required to make model quantitative and statistically relevant**

Using gSOLIDS to Optimise Spray Drying Operations

Conclusions

- Model performance
  - Qualitatively correct representation of phenomena occurring during suspension spray drying
  - Model can be used predictively as well as by retro-fitting input parameters
  - Retro-fitting 3 parameters from a dataset of 5 experiments took ~2h each, some runs were failing due to numerical errors
  - Platform is easy-to use, intuitive
  - Efficient link between end user & developer ensures continuous progress towards objectives
- Limitations
  - Only for suspension spray drying at the moment
  - No account for particle fracture
  - Input dataset required includes geometrical data from SD & cyclones as well as solvent&solid PhysProps data
  - No data about absorption isotherms for solid/solvent combinations available
- Learning so far
  - gSOLIDS can be used qualitatively and has the potential to be used quantitatively cross scale by 2012 eoy
  - Efforts will be put in (a) increasing the accuracy of the model and (b) adding experimental data in 2012

Using gSOLIDS to Optimise Spray Drying Operations

Next Steps

- Link to DIPPR database for solvent physical properties
- Include plug flow model for gas flow
- Build experimental datasets / generate suitable datasets from existing databank tailored for modelling
- Directly measure inlet PSD with PIV
- Build equipment models:
  - Critical moisture content for solid/solvent combinations
  - Inlet droplet size from output particle size (nozzle characterisation)
  - Droplet residence time from outlet solvent contents (spray chamber)
- Link to CFD → “multizonal” modelling
  - Improvement of residence time, drying rate
- Continue building track record of how model compares to experimental result for range of scales, compound/solvent combinations

Acknowledgements:

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