Spray drying

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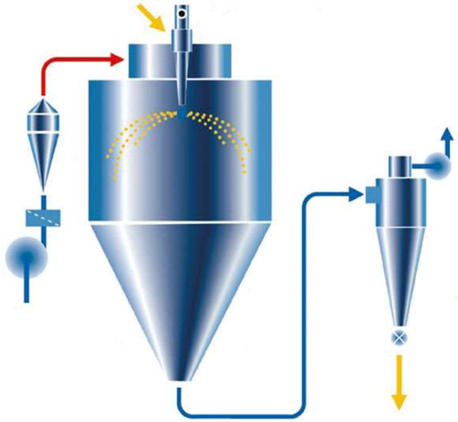


Presentation outline

- Definition, principle, applications
- Plant design
- Drying chamber, Air flow patterns, Atomization
- Theory
- Critical process parameters
- heat & mass transfer
- Drying kinetic
- Particle engineering
- Scale-up

Introduction

how does a spray dryer work?

https://youtu.be/KL4-SpP-Ghk

https://youtu.be/6Jj4RkvgH0c

Introduction: Definition

- Drying of an atomized solution or suspension in contact with a stream of hot gases, under condition which permit the recovery of dried product.

- Spray drying operation can be divided in 3 major operations
  - Atomization of the solution or suspension
  - Liquid droplets are mixed with hot gas in the drying chamber where evaporation and drying of the produced liquid droplets take place.
    - Design of drying chamber must provide adequate residence time for the droplets to be dried
  - Separation of dried particles from drying gas

Introduction: Pros&cons

- **Advantages:**
  - High rate of drying due to high surface , heat & mass transfer are very quick → drying time from 5 to 40 s.
  - Particles remain at or close to the wet buble temperature (adiabatic saturation temperature) of the drying gas → Product is protected from high T
  - Little or no decomposition of material being drying
  - Absence of pretreatement steps such as precipitation and filtration, which are often required in conventional drying
- **Disadvantages**
  - High investment
  - Could leads to a low bulk density of produced material
  - Dried material loading
  - Requires secondary drying

Introduction: *interest (1/2)*

- ***Why spray -drying can be chosen?***
  - ***Method for removing water or other liquid from the liquid stream***
  - ***To obtain dry extracts when no crystallization is possible during synthesis of small molecules***
  - ***Dry powder aerosols & heat sensitive materials***
  - ***To obtain dry extracts of active raw materials from plants***
  - ***To manage solid properties : Improved drug or excipient compressibility by managing density, flowability, and specific surface area***
    - ***Directly compressible Lactose is obtained by spray drying***
    - ***The spray dried crystals of Acetazolamide were characterized by an excellent compressibility and the absence of capping tendency while the pure polymorphic forms I and II could not be compressed into tablets***
  - ***Encapsulation***
    - *Matrix microcapsules containing drug substance and a biodegradable polymer are usually prepared by spray drying in order to obtain controlled drug release formulations*

Introduction: *interest (2/2)*

- Increased bioavailability
  - Spray drying can be used to enhance the solubility and dissolution rate of poorly soluble drugs. This usually occurs via the formation of pharmaceutical complexes or via the development of solid dispersions,
- Complex formation
  - Cyclodextrins can be used to increase the solubility and bioavailability of poorly water soluble drug substances: binary complexes containing carbamazepine and -β cyclodextrin prepared via spray drying showed faster drug release in comparison with the physical mixtures because of an improvement in drug solubility
- To fix mixing homogeneity (formulation)
- Alternative to freezing for biologic pharmaceutical drug product
- To mange supra high concentrated for biologic pharmaceutical drug product
- Economical process for high tonnage products

Introduction: *applications*

- Spray drying is a very widely applied technique used to dry aqueous or organic solutions , suspensions and emulsions in:
  - Food industry : baby and infant food, dry milk, soups, instant coffee tomato paste, eggs…
  - Chemistry : polymers (emulsions), aluminium chlorohydrate, ammonium nitrate, ammonium phosphate, magnesium hydroxide, zinc oxide, zinc sulphate, bleach powders, carbides (titanium, silicon, tantalum, niobium), catalysts for inorganic and organic chemical reactions, ceramic metals, detergents, dyestuffs, pigments
  - Agro chemistry : formulations of pesticides, herbicides ….
  - Flavor encapsulation
  - Electrical insulating material consists of spray dried aluminium oxide
  - pharmaceutical and biopharmaceutical industry: spray drying is often selected to transform the active pharmaceutical ingredients in a powder and to manufacture solid dosage forms containing peptides, proteins or poorly water soluble active pharmaceutical ingredients.

Introduction/ *Example of formulation : pesticides or herbicides*

Jet milling

↓

Dispersion in water + surfactant

↓

Spray drying

Inlet :250

Outlet: 85/100

- *The spray drying leads to easily flowable and porous particles, which are directly used by the customer (dispersion in a tank prior to spray on plantation)*
- *High surface area (jet milling) but not dusty → EH&S advantage for the customer farmer*
- *Formulated with surfactants : enhances permeation in plants*

Introduction/ *Example of formulation by spray drying :Instantaneous coffee*

Coffee extraction

↓

Preconcentration

(30-35% solid

↓

Spray drying

Inlet :220/300

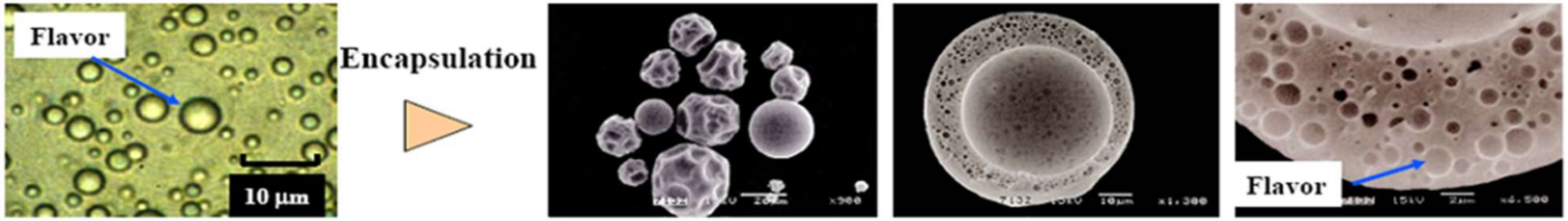
Outlet: 85/100

- *The spray drying leads to easily flowable and porous particles (100-400µ)*
- *water penetrates quickly in pores an coffee dissolution is quick*
- *Pressure nozzles and/or spray drying + agglomeration are used*

Introduction/ Flavour encapsulation

Microencapsulation of flavor is a technology of enclosing flavor compounds in a carrier matrix

- *Improving the chemical stability of flavor compounds*
- *Providing controlled release of flavor compounds from micro-encapsulated flavor products*
- *Providing a free flowing powder with improved handling properties.*



Flavor emulsion (Liquid state)

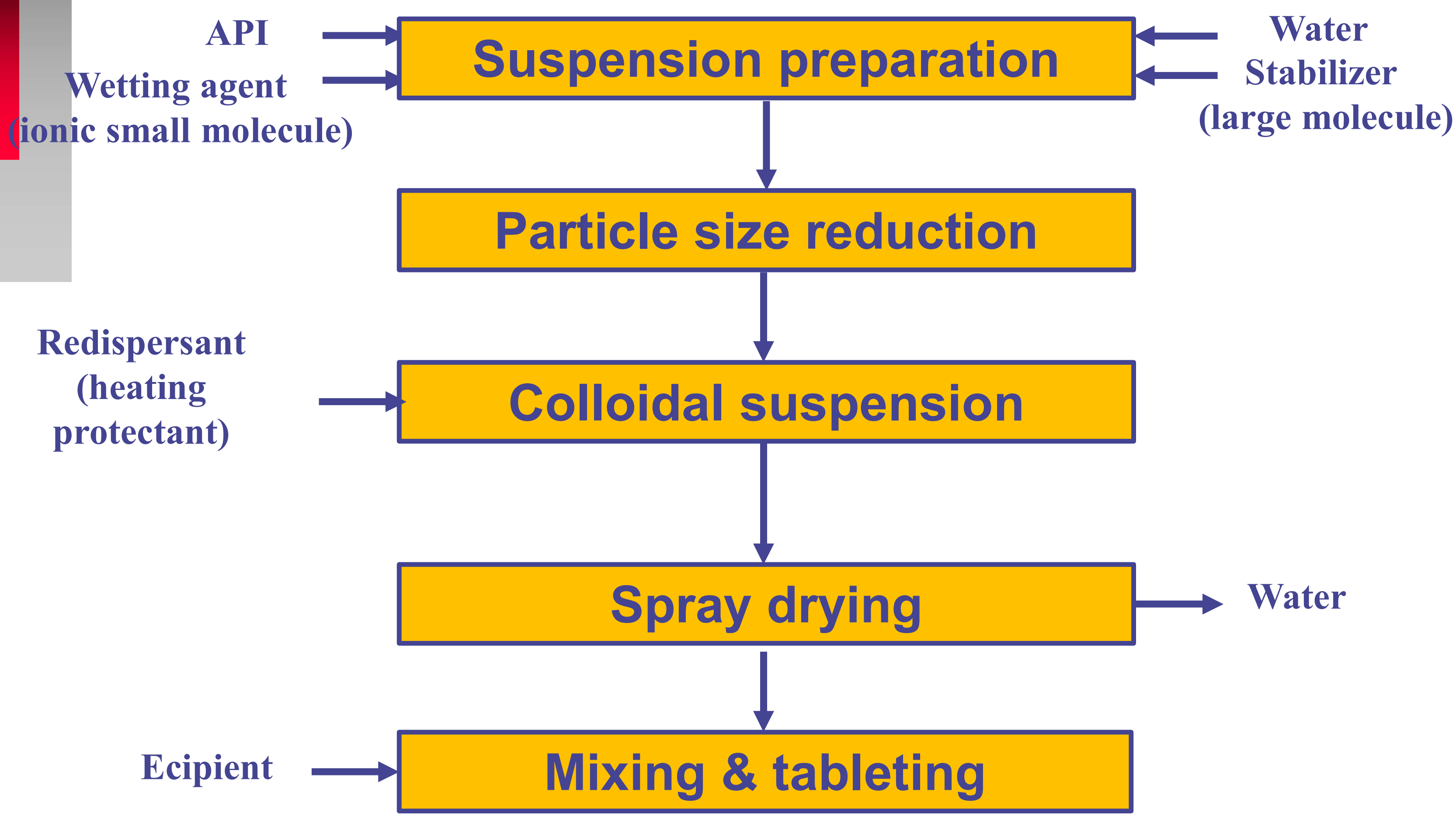
Encapsulated flavor powder (Solid state)

Various encapsulated methods have been proposed. Among them, *spray drying* is the most common technique to produce flavor powders from food flavor emulsion.

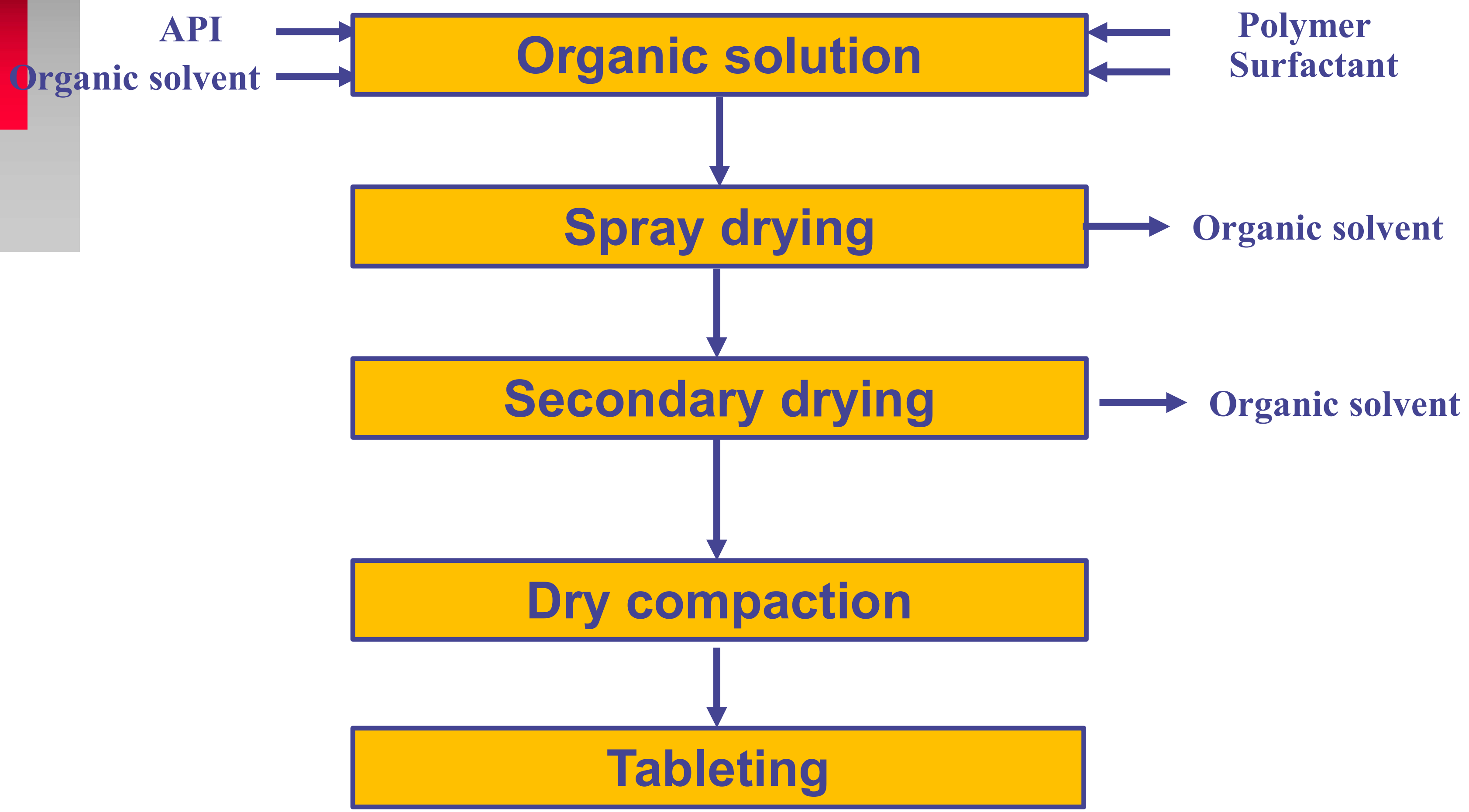
Introduction/ *Use of Spray drying in pharmaceutical industry*

- **Various uses of Spray drying in Pharmaceutical Industry**
  - ***Drying Technique for chemical APIs***
  - ***Drying technique for biotech APIs & vaccines***
  - ***Granulation by spray drying : standard or fluid bed spray drying***
  - ***Drying technique for the production of nanocrystalline suspension by top down process***
  - ***Bioavailability enhancement/modification by spray drying: solid dispersions- Depot formulations***
  - ***Inhalation compounds by spray drying***
  - ***Alternative to freezing for biologic pharmaceutical drug product***
  - ***To mange supra high concentrated for biologic pharmaceutical drug product***
  - ***Spray chilling***

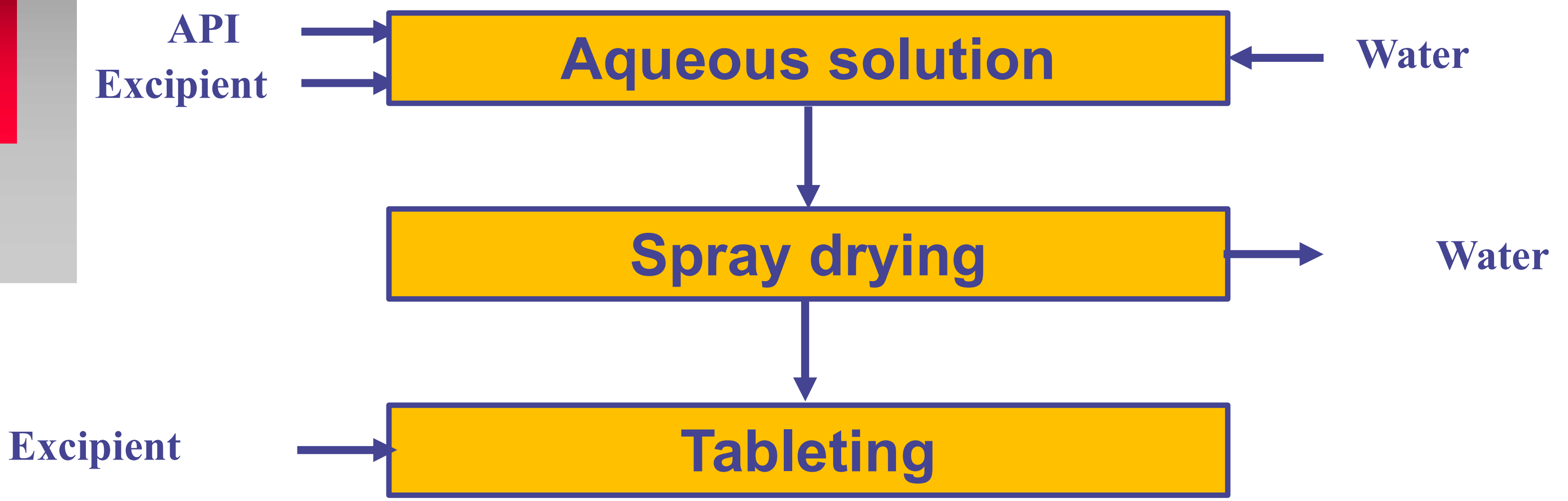
Introduction/ *process flow chart for the manufacturing of nano-crystalline drug product*



Introduction/ *process flow chart for the manufacturing of amorphous solid dispersion*



Introduction/ *process flow chart for Spray drying as a granulation technique*



- ***Spray drying of API suspension including classical water soluble like mannitol can lead to direct compression products***
- ***It could be a way to formulate nanoparticles suspensions or jet milled solids. Could even form a kind of "standard" formulation.***

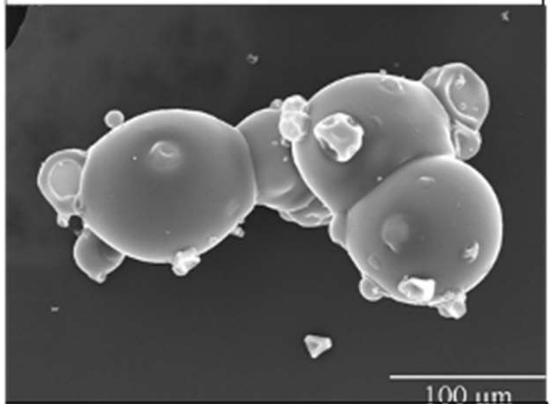
Granulation

- ***Double effect spray dryers : with fluidized beds***

Fluid Bed at the exit of FSD4 at Hovione

Example 1:

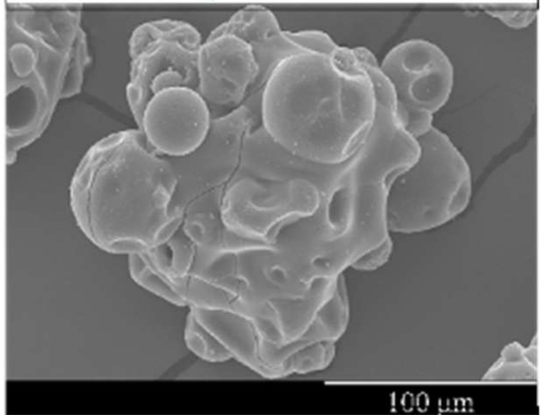
- **FSD**
- poor bulk density
- not direct compressible



Bulk density < 0.2 g/ml
D_v50 ~ 260 µm

Example 2:

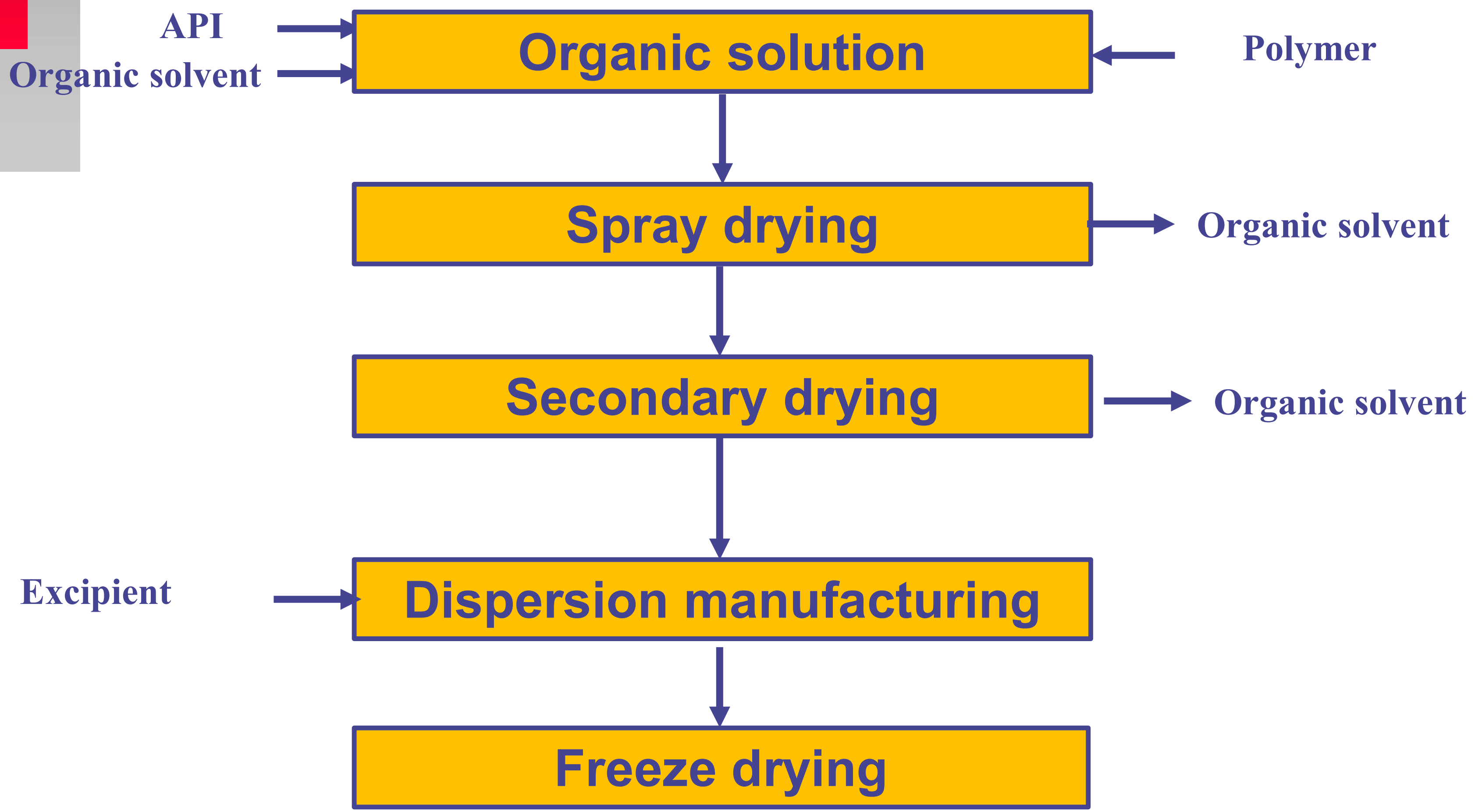
- **FSD**
- good size and density
- direct compressible



Bulk density ~ 0.6 g/ml
D_v50 ~ 180 µm

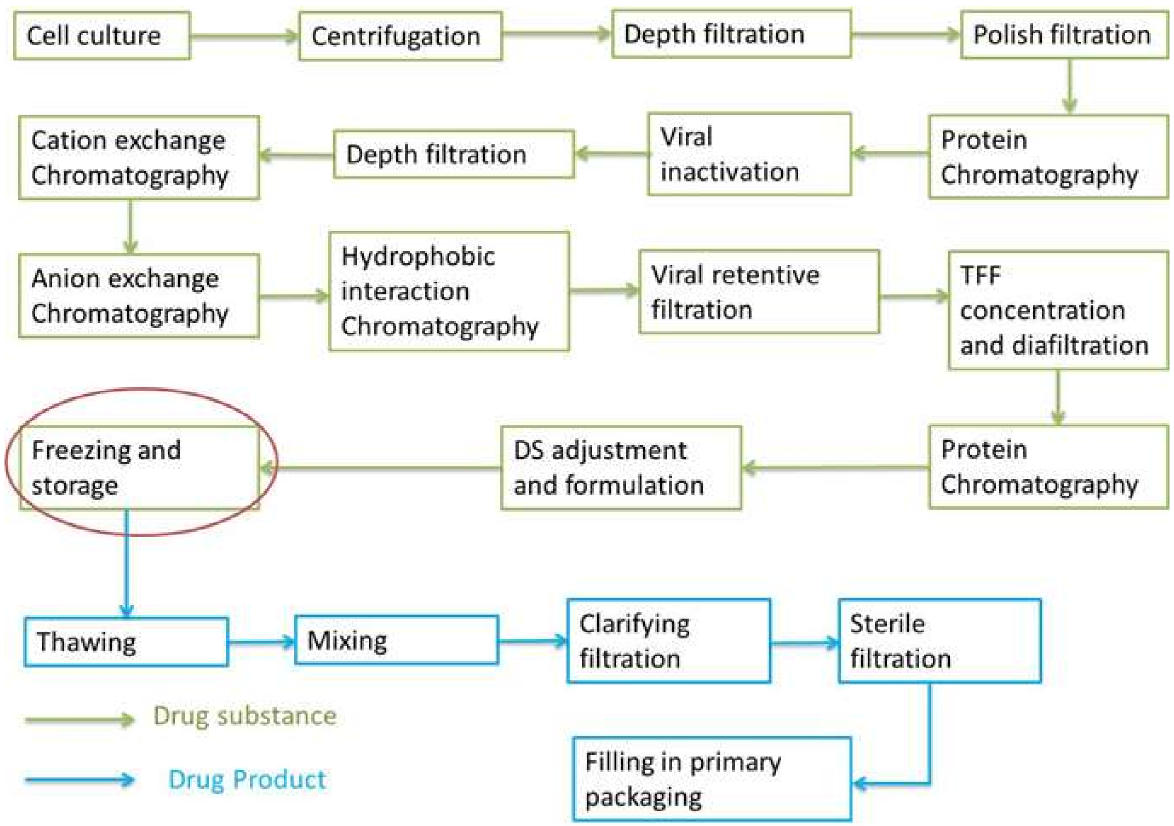
Introduction/ *Spray drying as a microencapsulation technique*

Sustained release



Introduction/ *Alternative to freezing of biologic drug product*

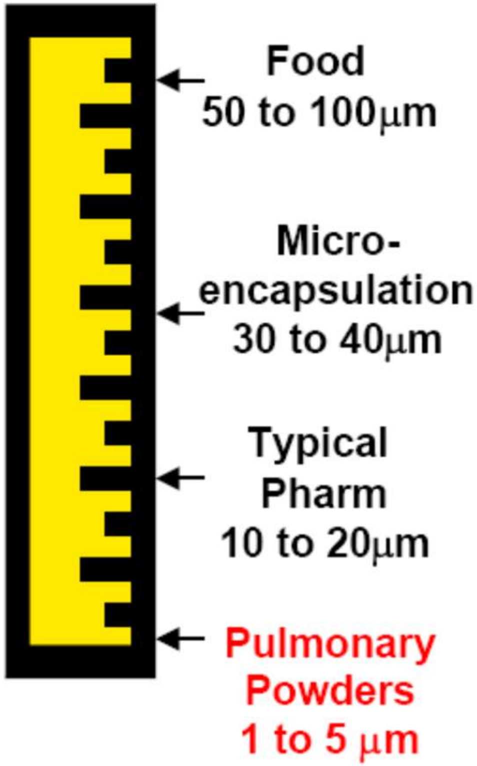
Most of products are with high-value



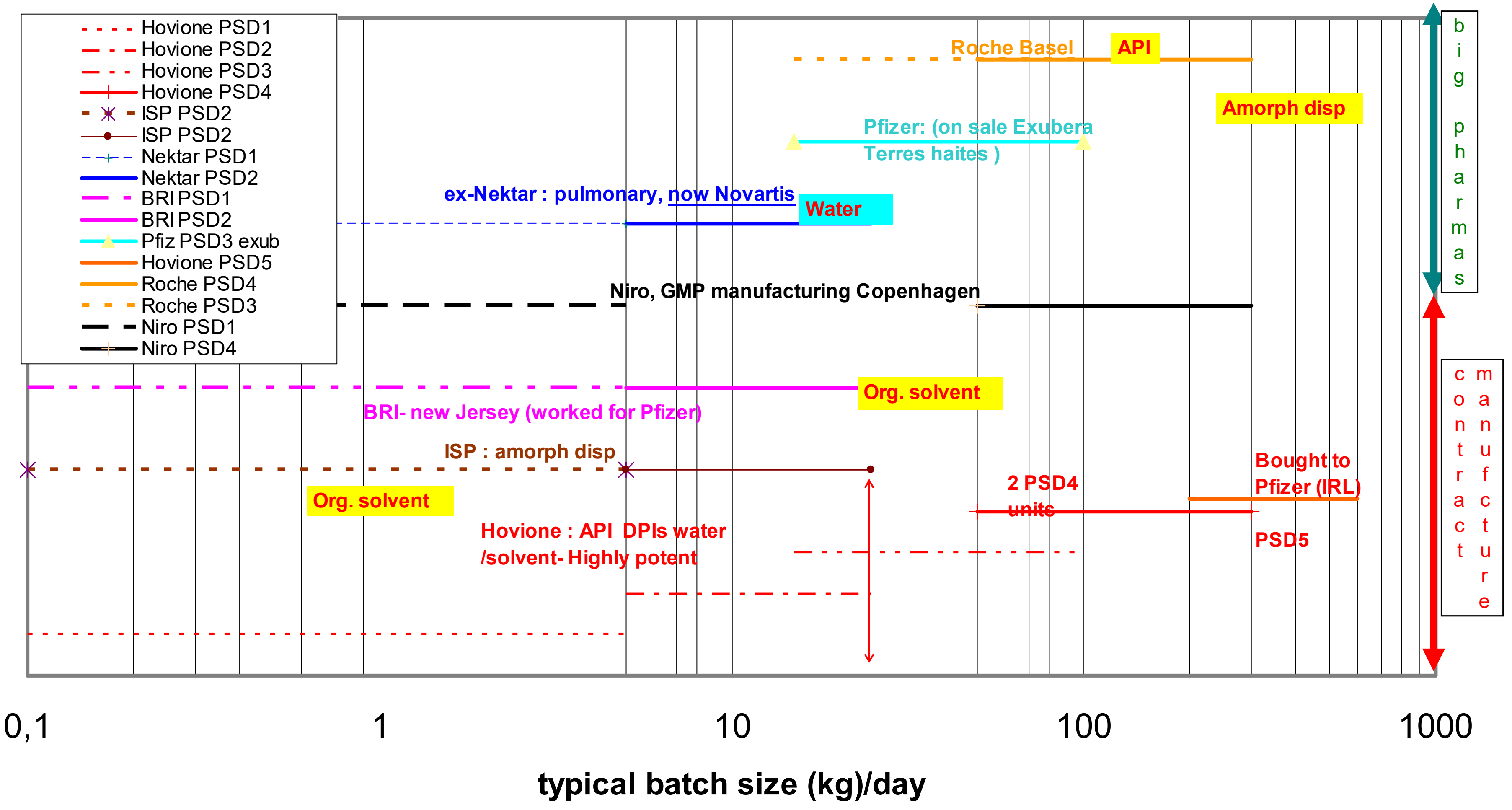
Spray-drying pulmonary products

- Feedstock
- ***Atomization***
- *Drying*
- ***Powder Collection***

- Spray Drying enables
  - Homogenous particles
  - Controlled size with:
    - Low moisture
    - Small particle size (<5 μm)
    - High drug purity



Introduction/ *Known capacities (western countries only)*



Plant design

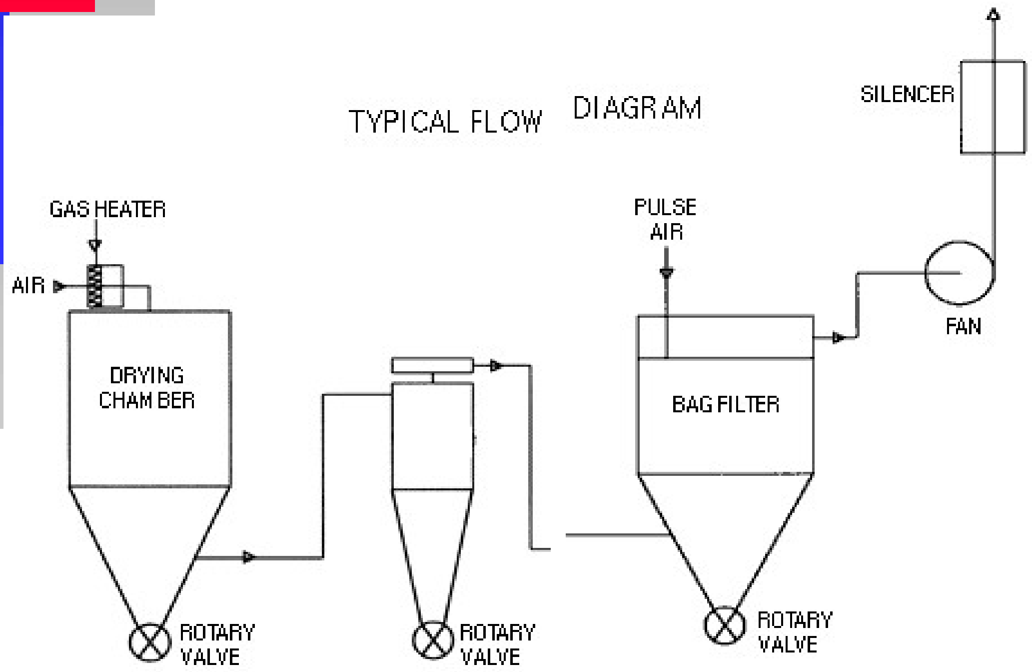
- Different types of spray dryers
- Air flow pattern
- Atomization technology

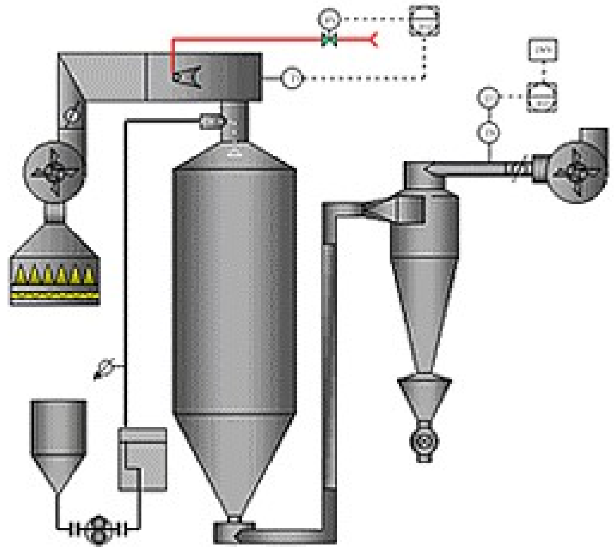
Plant design: *Typology of spray dryers*

- *Typical spray dryer*
- *Multiple effects spray dryers*
- *Loop spray dryer*
- *Spray chilling / prilling*

Plant design: *Typical spray drying installation*

- **Solution/suspension is sprayed in hot air. Particles are extracted at the bottom of the spray dryer and /or at the bottom of the cyclone separator**



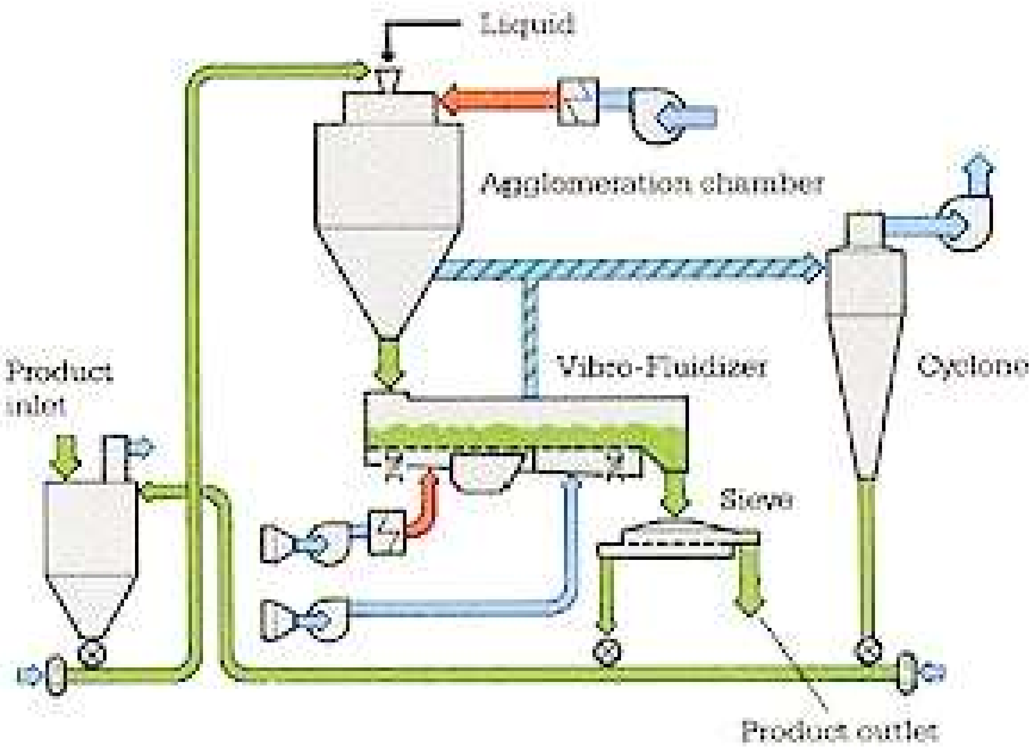


Drytec ltd, England

Plant design:

Multiple effect spray dryer

Rewet agglomeration



- ***Fines are re-circulated in the spray dryer and granulated.***
- ***Interest → big particles, but poor density***

Drytec ltd, England

Plant design:

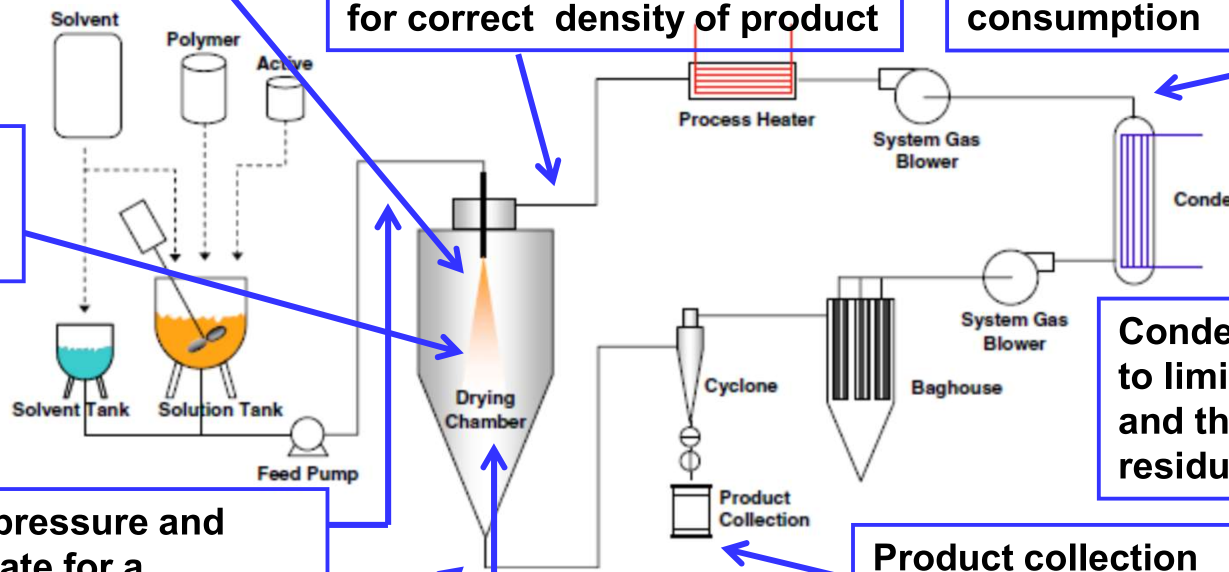
Closed pressurized loop for flammable solvents

Drying process where hardware and formulation are optimized to meet drug product specification

Limited inlet gas temperature for correct density of product

Nitrogen as drying gas for elimination of explosion risk and closed loop to minimize nitrogen consumption

Dryer designed for sufficient gas flow



Condenser temperature to limit gas composition and therefore product residual solvent

Constante feed pressure and constante feed rate for a constante particle size

Product collection design for high yield

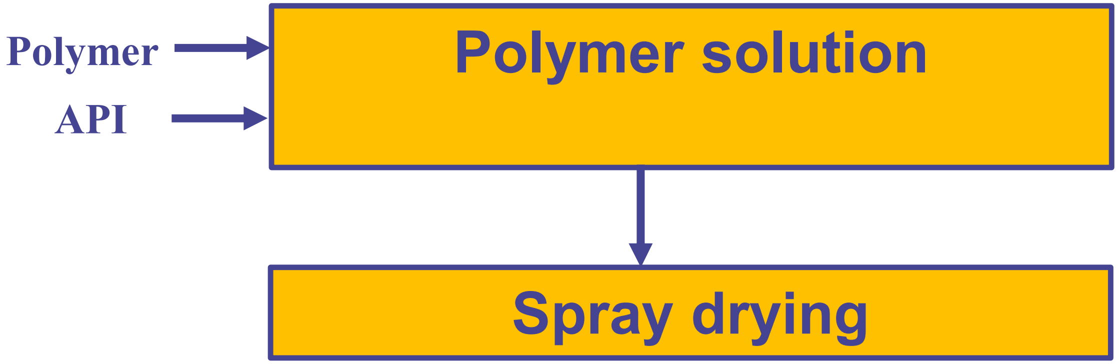
Outlet temperature = (drying and product temperature)

Drying chamber design for sufficient residence time

Plant design:

Spray chilling

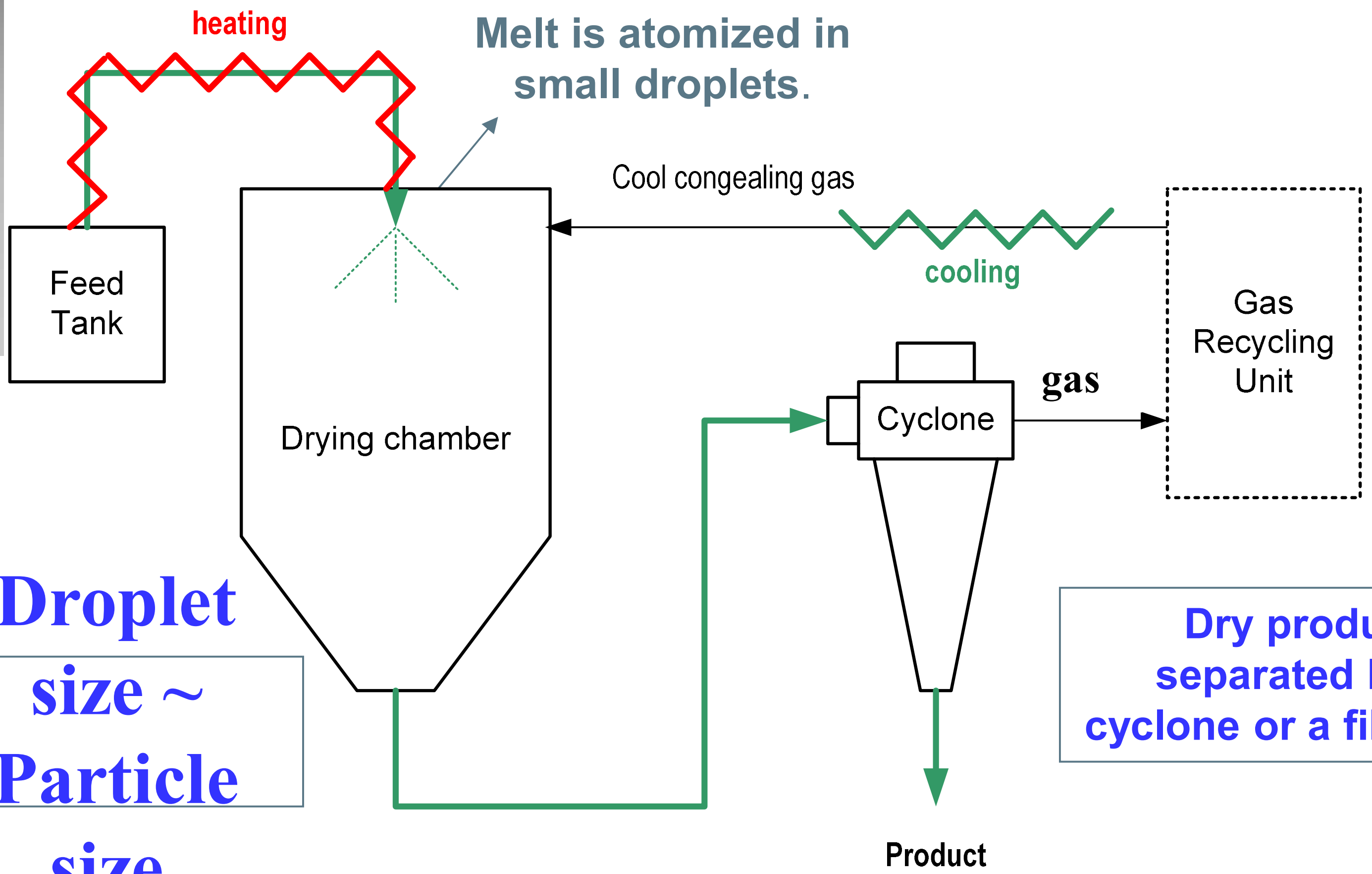
- ***Possible variant of spray drying: This process is an alternative to spray drying for the encapsulation of solid particles. The transition of a melt from a soft or fluid state to a rigid or solid state by cooling is called spray chilling.***



- **Applications : agrochemistry, explosives, taste masking, pharma**

Plant design

Conventional Spray Congealing



Droplet size ~ Particle size.

Dry product separated by a cyclone or a filter bag

Example of products : encapsulated vitamins

Prolonged releaze product

Plant design:

Prilling

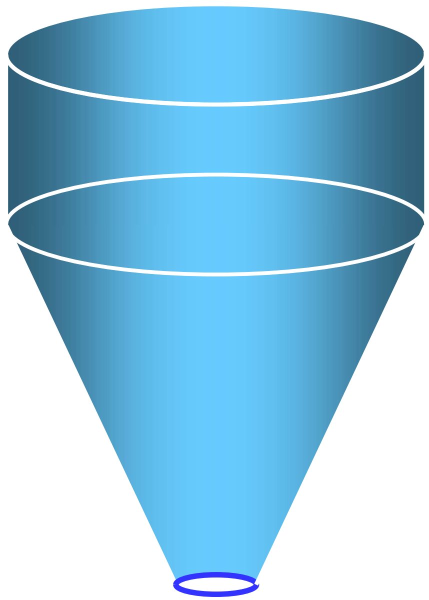
- ***Chilled air is disperser at the bottom of a high tower.***
- ***Melted, liquefied product is fed at the top of the prilling tower via a spraying or atomizing nozzle to disperse liquid droplets into the chilled air.***
- ***the nozzle is often vibrated to help a very good calibration of particles.***
- ***As the droplets fall they cool and solidify individually forming spherical balls referred to as prills.***
- ***The prills collected at the bottom of the tower and are discharged through a rotary airlock.***

  - **Applications : agrochemistry, explosives, taste masking**
  - **Modified release**

Plant design

Shape of drying chamber

- ***Spray dryer chambers are in the shape of a cylinder converging to an inverted cone at the bottom.***
- ***The shape of the chamber is selected according to the shape of the atomizing device that is to be used in a given type of dryer and on the desired product properties***
- ***Drying chambers can be divide in 2 categories : tall and small***
  - ***Tall chambers are characterized by the ratio of their height to diameter exceeding 5:1***
  - ***Small chambers usually have a ratio of height to diameter around 2:1***
    - ***more frequently used, mainly because they allow the usage of both atomizing discs and nozzles***



Plant design:

Example of pharma execution (Hovione)

Plant design:

Scales of production…

- *From few kg/y to million of tons/y*
- *From <0.1$/kg to 500 k$/kg*

Büchi

Minor mobile

PSD1

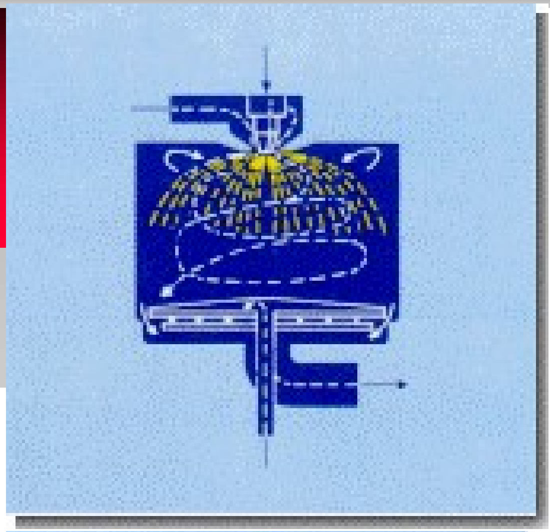
Plant design

Available scales for the pharma applications

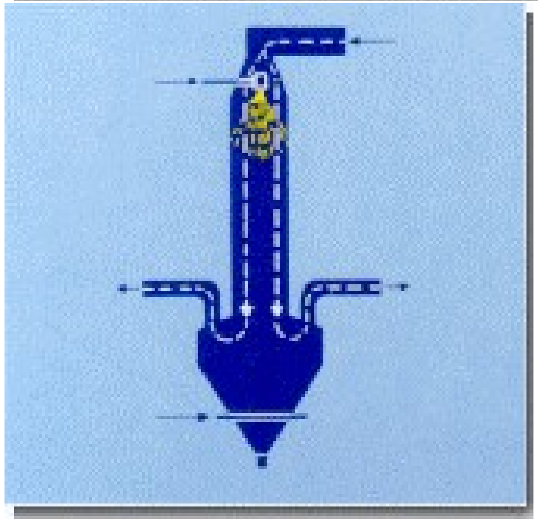
- **Niro PSD (Pharmaceutical spray dryer) :**
  - **PSD 1 (= “minor mobile”) 80 kg/h N2- ~2 kg/h water- 8 kg /h DCM**
  - **PSD 2: 360 kg/h N2**
  - **PSD3 :700 kg/h N2**
  - **PSD4 : 1250 kg/h N2**
  - **PSD 5 : 2500 kg/h N2**

Plant design

Examples of special execution (Kilburn)



- For very heat - sensitive products : flat bottom with side air ports and air sweeper to cool particulars before collection; centrifugal atomization; low headroom.



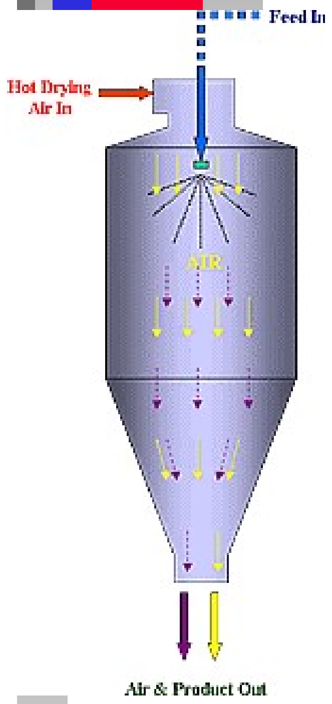
- For large fragile particles (e.g. coffee): tower with co-current, liner air flow; setting zone with air inlet separates and cool products; pressure nozzle atomizer.

Plant design:

Air flow pattern

- *Co current flow*
- *Counter current flow*
- *Mixed (fountain) flow*

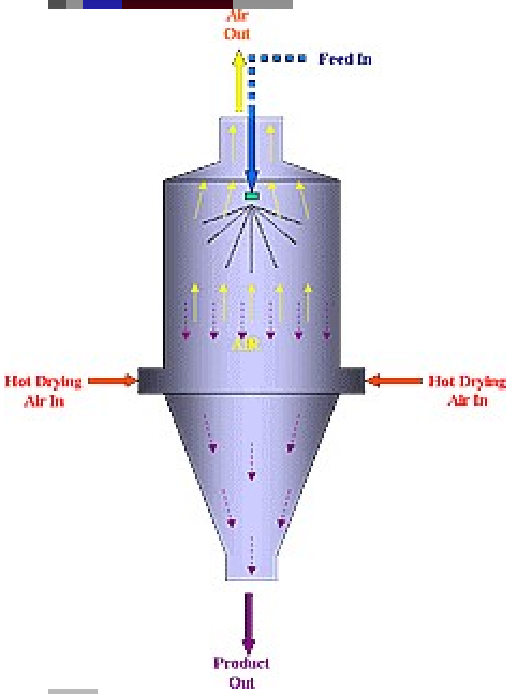
Plant design
Co current flow



- Drying air streaminlet and the atomizing device are both placed in the upper part of the drying chamber.
- Co current flow : liquid droplets are submitted to the highest gas T → the thermal energy of the drying gas is utilized to evaporate the abundant solvent → the product is heated the least.
- Is used for thermally sensitive products (eg food, flavours, pharmacy)
- Is less efficient (like any co-current heat exchanger)
- In cocurrent dryers, both atomizing discs and nozzle-based constructions are used.
- The atomizing device chosen is influenced by the drying chamber shape and the powder properties desired.

Plant design

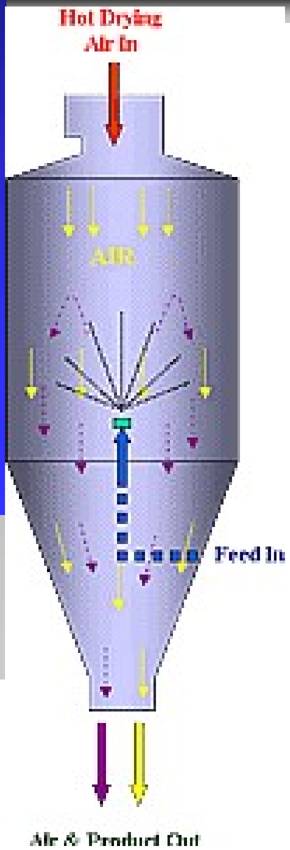
Counter current flow



SDS documentation

- *Counter current flow spray dryer: drying air inlet placed opposite to the descending dispersion droplets*
- *The atomization of feed occurs in the direction of the bottom of the chamber, and the drying air is supplied from the bottom*
- *nozzles are the most preferred type*
- *Interest : higher residence time*
- *Only for dense and non thermally sensitive & non combustible (The final temperature of the product is higher than the outlet/exiting air temperature.*
- *products, typically mineral products*
- *Products which require a high T treatment*

Plant design
Fountain spray dryer



SDS documentation

- *Fountain spray dryer (Mixed case): The term "combined flow systems" refers to dryers in which the feed is atomized in the direction of the upper part of the chamber, counter-current relative to the drying air*
- *Interest : higher residence time, handling coarse product in small chambers*
- *Non (too) sensitive products*

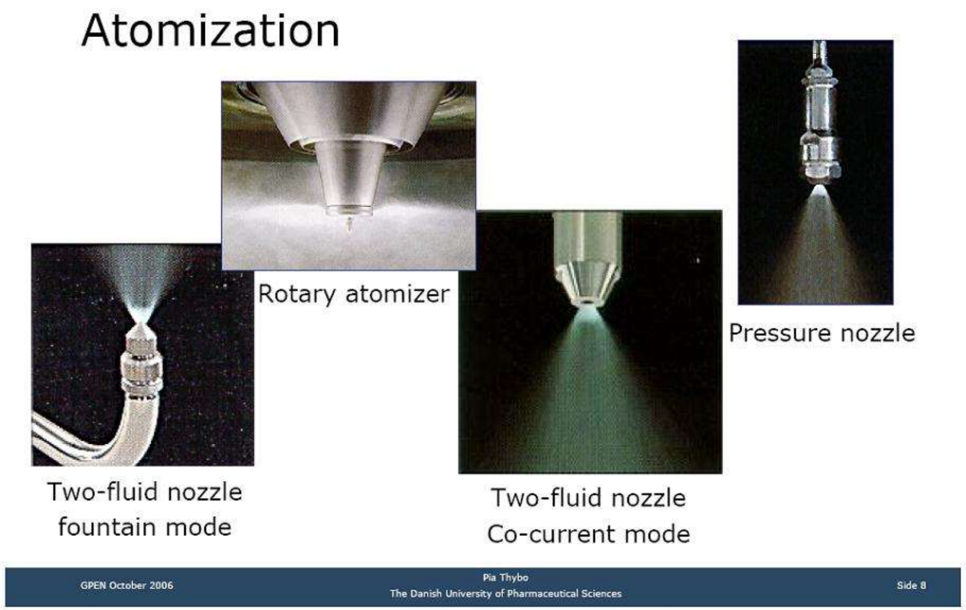
Plant design

Atomization technology

- *Atomization refers to the formation of a liquid suspension in a gas*
- *Atomization causes the formation of very large surface areas that are exposed to the drying gas*
- *This large surface area facilitates the heat transfer from the heated drying gas to the atomized fluid particles that results in evaporation of the solvent in seconds, and mass transfer back into the gas phase.*
- *As a result, the drying material never reaches the inlet temperature of drying gas.*

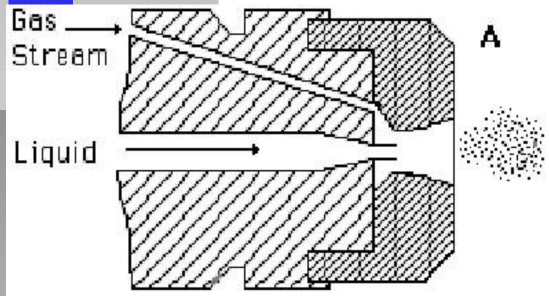
Plant design
Atomization technology

- ***The atomization effect can be achieved using several types of devices. The basic devices include***
  - ***Rotary atomizers;***
  - ***Hydraulic (pressure) nozzles;***
  - ***Pneumatic nozzles; and***
  - ***Ultrasonic nozzles.***



Plant design:

Bi-fluid (pneumetic) nozzle



- *Principle : liquid jet is disrupted by air flow due high frictional forces over liquid surfaces*
- *the relative velocity between the liquid and gas is the main driving force of the atomization process*
- *Advantage : very versatile*
  - *Broad dispersion, fine particles*

Example of correlation

$$d_{50} = \frac{A}{(V_{rel}^2 \cdot \rho_a)^{\alpha}} + B\left(\frac{M_{air}}{M_{liq}}\right)^{-\beta}$$

A, B : parameters depending from nozzle and liquid properties (viscosity, surface tension)

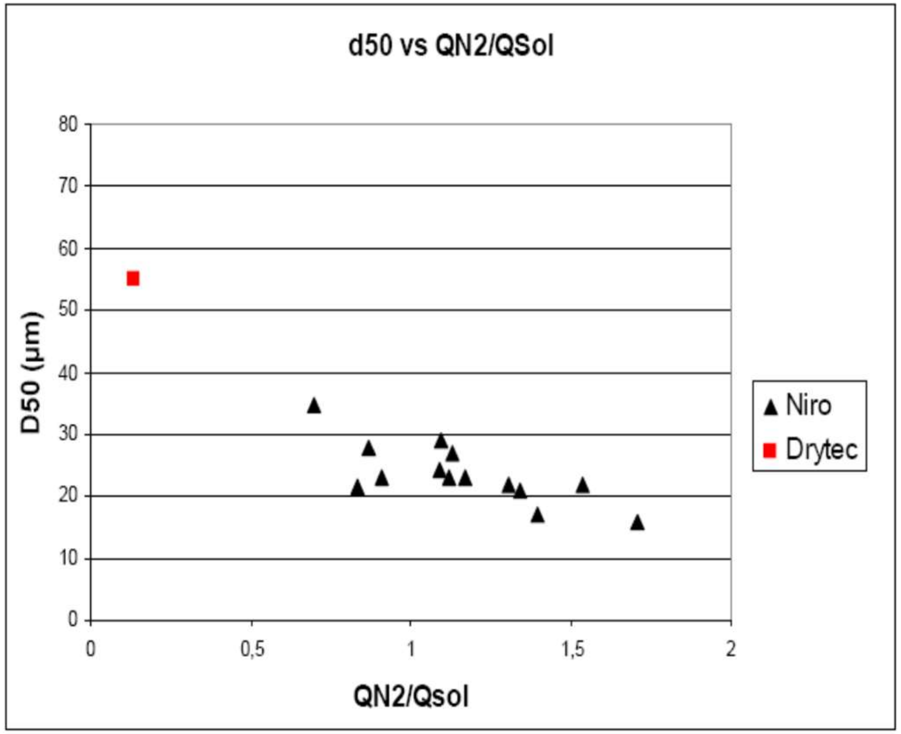
Vrel : relative air/liq velocity

Mair/Mliq : air to liquid mass ratio

Plot design

Example of a bifluid nozzle

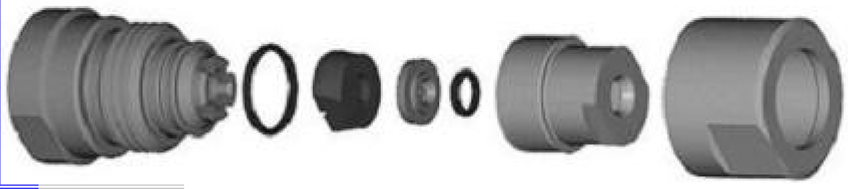
- The impact of the gas/liquid flows is critical
- Higher is the ratio gas/liquid, lower is the particle size



Tests on a Niro minor mobile and on a Drytec (equiv to PSD2) pilot

Plant design

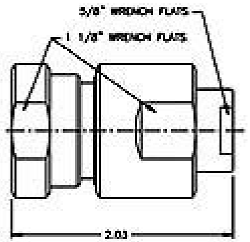
Pressure (one fluid) nozzles



Q in ml/s

P in kPa

μ in Mpa/s



Example of correlation

$$d_{3/2} = \frac{2774.Q^{0.25}}{P^{0.5}} \mu$$

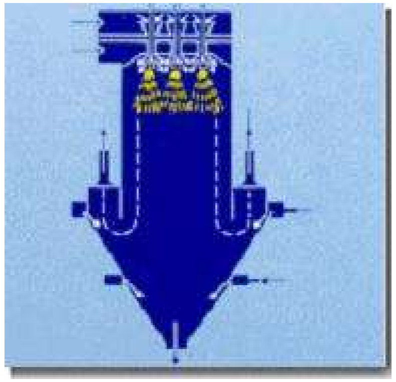
- *Principle : liquid is accelerated in turbulent, regime through a small orifice (0.4-4 mm):*
- *P ~Q² (for a given orifice)*
- *P in the range 20-200 bar*
- *Not suitable for high viscosity feed*
- *can produce particles within a narrow range of sizes (50–400 μm)*

→ Requires a special high pressure pump

Plant design

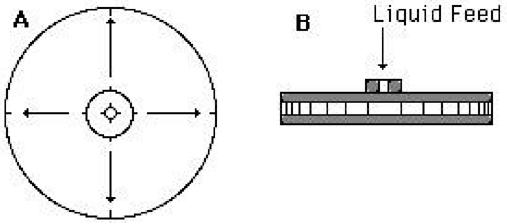
Pressure nozzles

- ***Pressure nozzles require special high pressure pumps***
- ***Flow and droplet size cannot be changed independently → need to customize the nozzle for the flow***
- ***PSD is narrow, and much bigger particles(up to 300 μ) can be obtained***
- ***Q <3 m^3/h/nozzle → multi nozzle installations***
- ***Pressure nozzles are very good devices for routine production of coarse product***



Plant design

Atomizer wheels



- *shape of horizontally fastened wheel or discs, to which the feed is supplied*
- *Principle : accelerating the liquid off the edge of a spinning wheel (10.000 -30.000 rpm)*
- *Size of particles depends of d, N (rpm), liquid flow and physicochemical data.*
- *Produces more wall deposit*

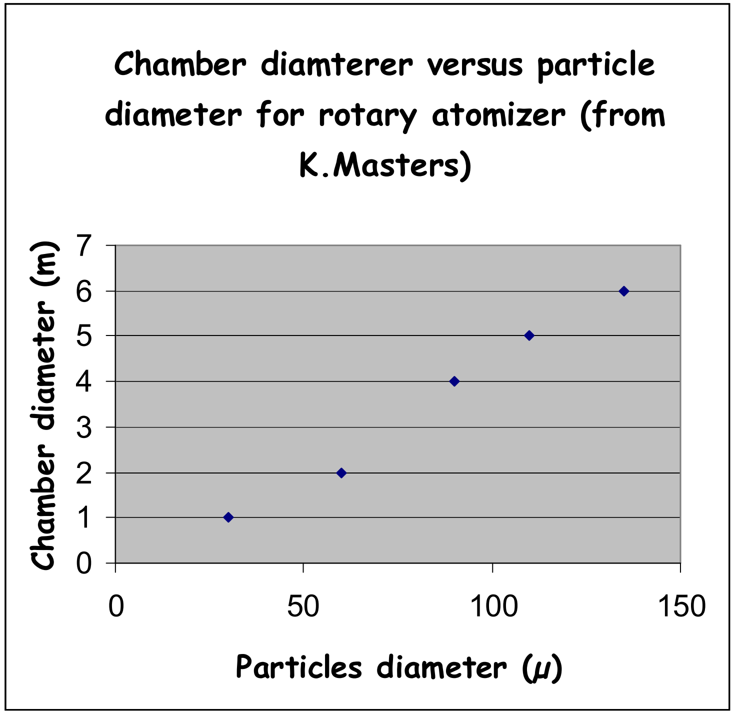
$$d50 = \frac{KQ_l^a}{N^b d^c (n_o h)^d}$$

Q_l: kg/hliq; n_0 numbers of vanes, K =1.2-.1.7x10^{-4} m, a :0.1-0.2, b : 0.8; c: 0.6 d0.1-0.2

Plant design

Atomizer wheels, continued

- *Horizontal ejection velocity is very high (50-150 m/.s)*
- *A large diameter is needed to avoid wall deposit (H/D : 0.6 to 1)*



Drying chamber needs to be selected according the desired particle size

Plant design

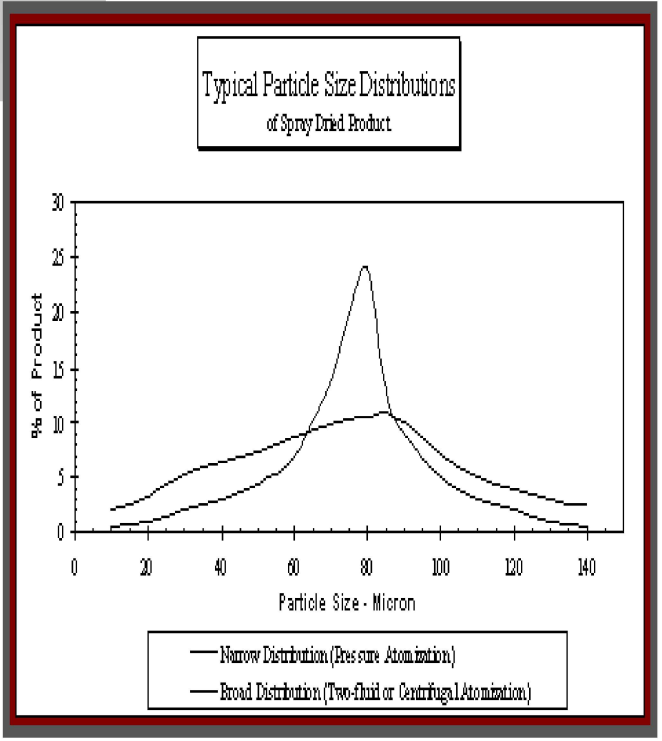
Atomizer selection (from K.Masters)

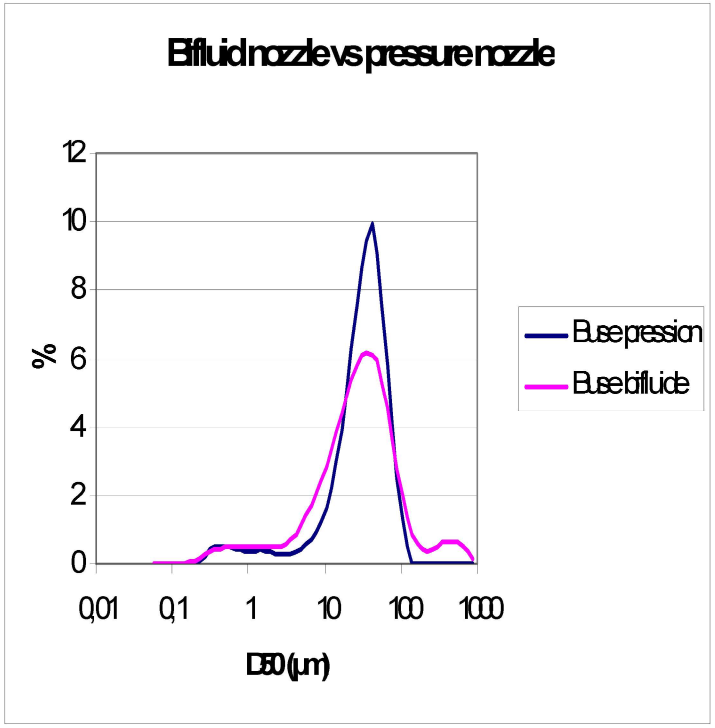
	rotary	Pressure nozzle	2 fluid nozzle
FLOW			
Co-current	X	X	X
Cuntercurrent	No	X	X
Mixed	No	X	X
FEED PROPERTIES			
Low viscosity sol/sklurry	X	X	X
High viscosity sol/slurry	X	no	X
Abrasive	X	no	X
Paste	X	X	X
FEED RATE			
<$3 m^3/h$	X	X	X
>$3\ m^3/h$	X	Multiple nozzles	Multiple nozzles
PARTICLE SIZE			
30-120 μ	X	X	X
120-250 μ	no	X	no

Plant design

Particle size selection form different nozzles

- *Bi-fluid and rotary atomizers tend to give finer particles/broader distributions*
- *Pressure nozzle give tighter distribution, generally bigger particles*





Plant design

Atomizer selection

- Use bi-fluid nozzle in pilot plants, because of very versatile performances, or for very fine particles
- Use rotary atomizers for multipurpose plant, with great diameter chamber
- Use pressure nozzle for mono- product plants, especially when tight distributions are required

Theory

Process design

- Critical process parameters

Theory

Critical process parameters

- ***Inlet temperature of air: higher the temperature of inlet air, faster is the moisture evaporation but the powder is subjected to higher temperature, which may impact he chemical/physical quality***

- ***Outlet temperature of air: it control final moisture content of powder.***

- ***Viscosity: high viscosity hinders correct drop formation. As the viscosity is lowered, less energy or pressure is required to form a particular spray pattern.***

Theory

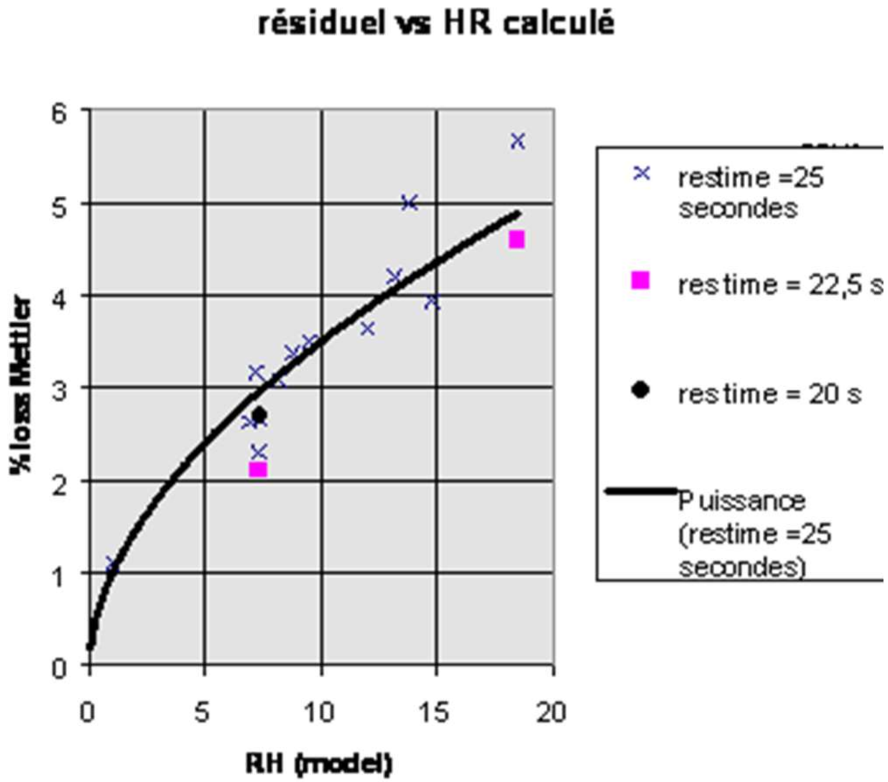
Critical process parameters

- Solid content: care must be taken with high solid loadings (above 30%) to maintain proper atomization to ensure correct droplet formation.
- Surface tension: addition of a small amount of surfactant can significantly lower the surface tension. This can result in a wider spray pattern, smaller droplet size, and higher drop velocity
- Feed temperature: as the temperature of a solution to be sprayed is increased, the solution may easily dry as it brings more energy to the system.
- Volatility of solvent: a high volatility is desirable in any drying process.
- Nozzle material: most pharmaceutical applications use stainless steel inserts. However, tungsten carbide nozzles are often available and have excellent resistance to abrasion and good corrosion resistance for most feedstock.

Theory

Critical process parameters: Close loop ,Spray drying :role of condenser T

- The condenser temperature is critical in the quantity of solvent recycled.
- This is very sensitive for easily boiling solvents (e.g DCM)
- High RH of gas results in a high solvent residual content→ Risks :
  - Stickiness (amorphous products)
  - Physical / chemical instability



Theory

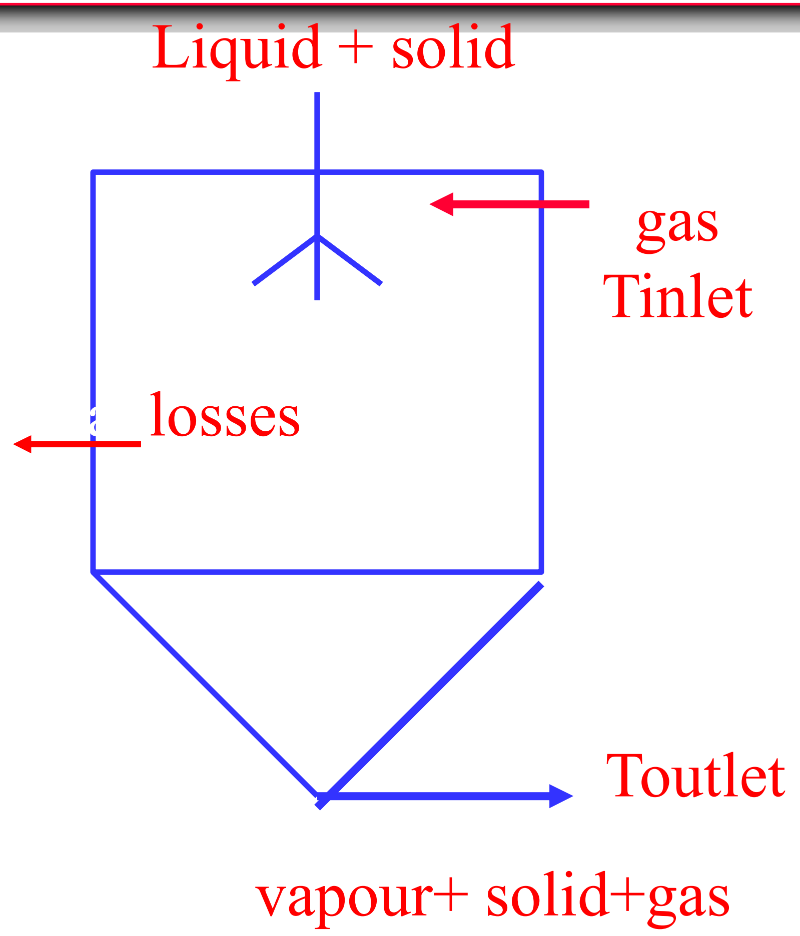
- Heat and mass balance
- Drying kinetics
- Particle engineering

Theory

Heat and mass balance

Heat given by cooling the gas (0)=

Latent heat of vaporisation (1) + (heating vapour and solid to outlet T)(2) + heat losses (3)



$$(0) = Q_g*Cp_g*(T_i-T_o)$$

$$(1) \quad = Q_l*L \text{ (latent heat at RT)}$$

$$(2) \quad = (Q_l*Cp_{vapour}*+Qs*Cp_{solid})*(T_o-RT)$$

$$(3) \quad \sim h.S*(T_o-RT)$$

Typical value of h = 2-3 kcal/h.m²°C

Theory

Heat and mass balance continued

- ***Moisture balance :***
  - ***Input = Output***

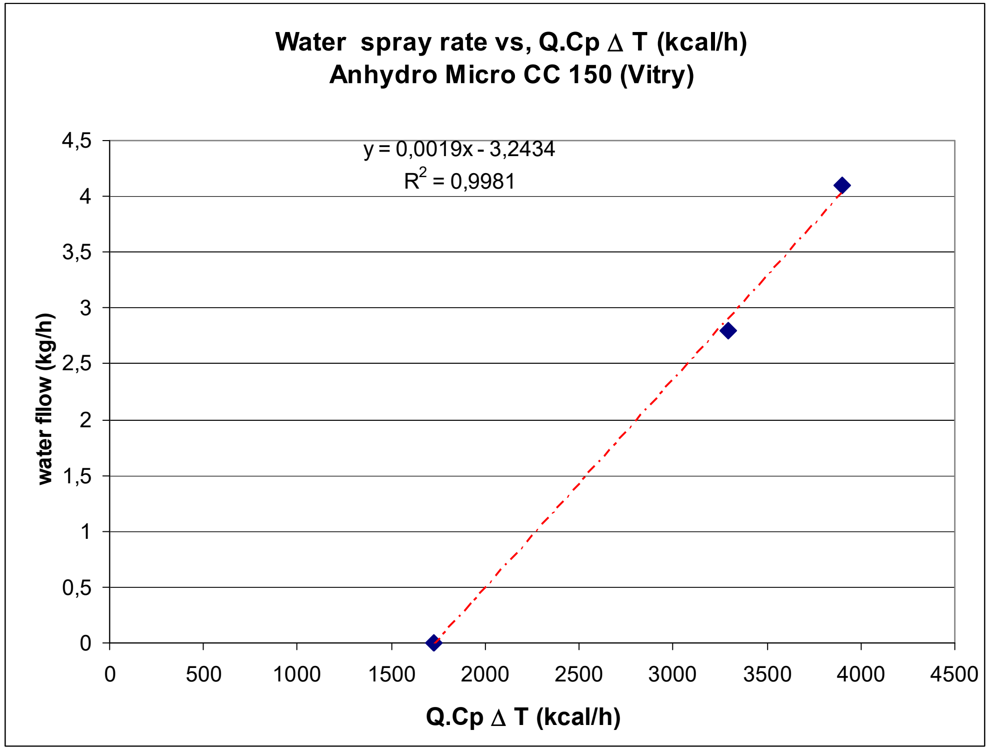
$Q_{liq} = Q_g * (M_o - M_i)$, M : kg solvent/kg gas

$\underline{M_o < M \text{ saturation at } To}$

Theory

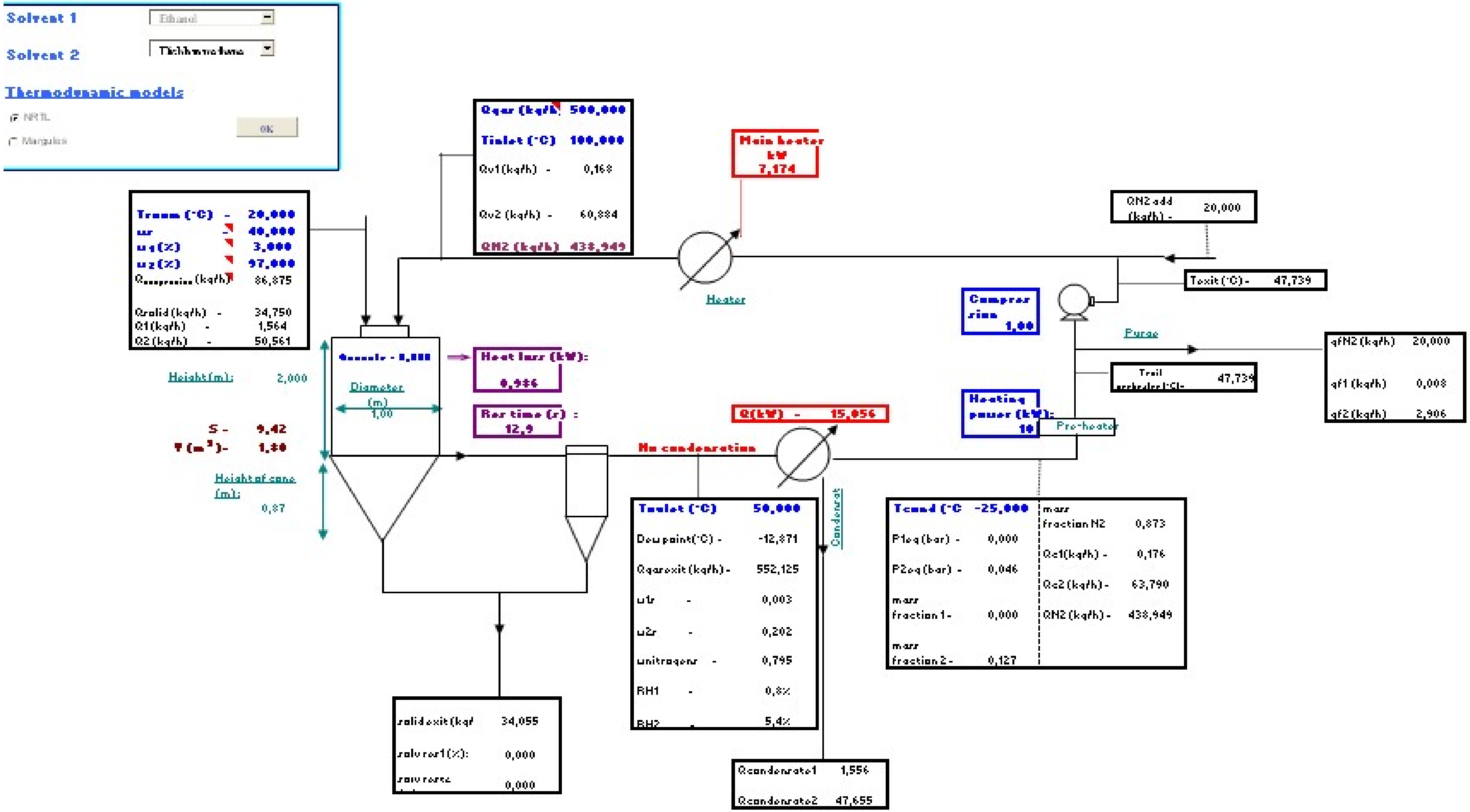
Heat balance application : OQ tests of evaporative capacity

- A nice OQ (or PQ) test is to determine the heat '(loss) transfer coefficient , by
  - 1 measuring the inlet/outlet DT without drying
  - 2 measuring the inlet/outlet DT with drying several water/solvent flow



Theory

Heat balance application : Use of the simulation tool



Theory

Use of the simulation tool

Input Data :

- Heat transfer coef
- Gaz flow
- Temperatures : in/out, condenser
- Feed composition
- SD Geometry

→

Deliverable data :

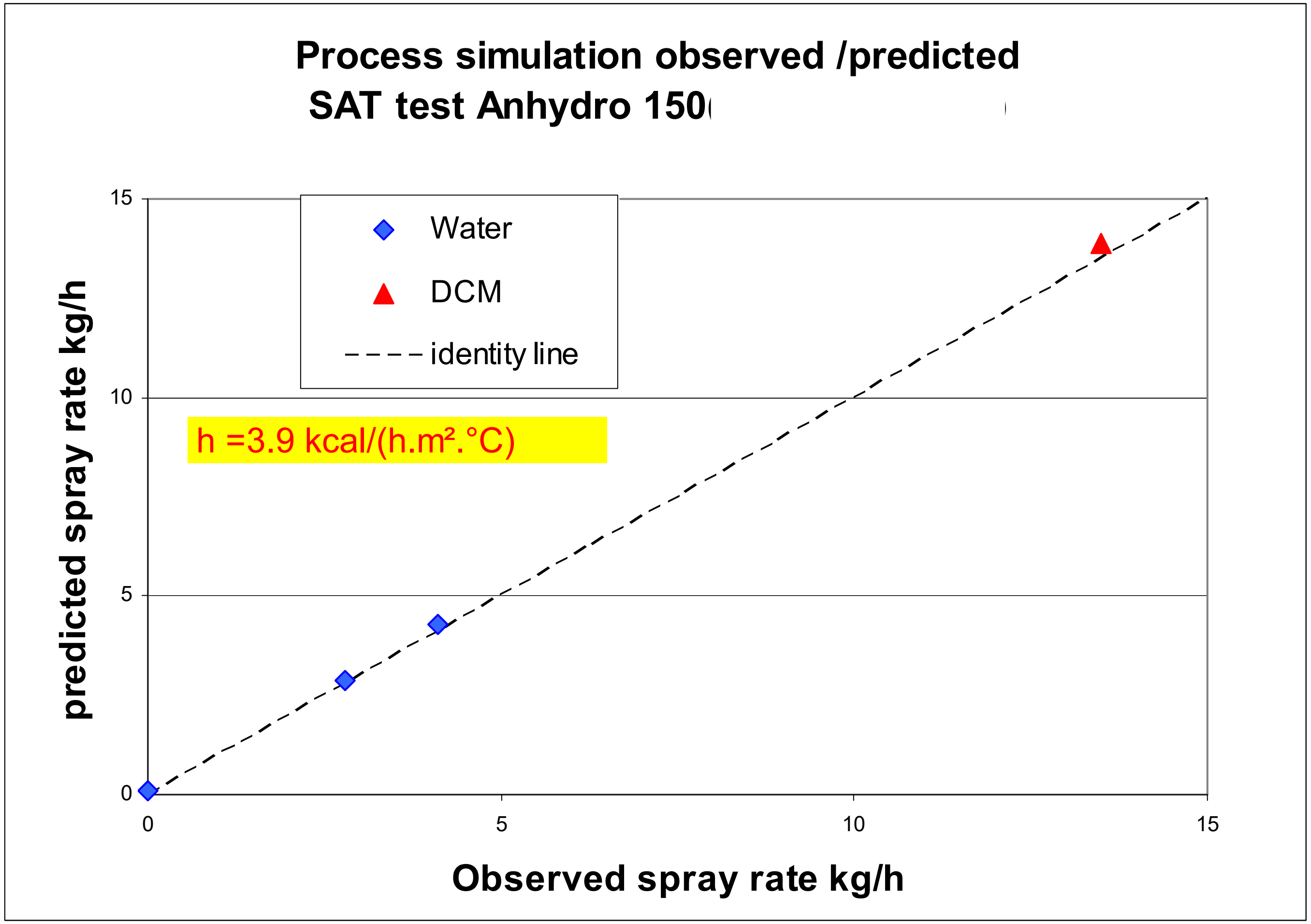
- Spray rate (kg/h)
- Gas composition and relative humidity at the exit
- Volatile organic compounds emissions
- Utilities : heating and cooling needs (kW)
- Productivity : per batch, per week, year …

Specificity Use of binary solvents

(even not available at Niro & others !!!)

Theory

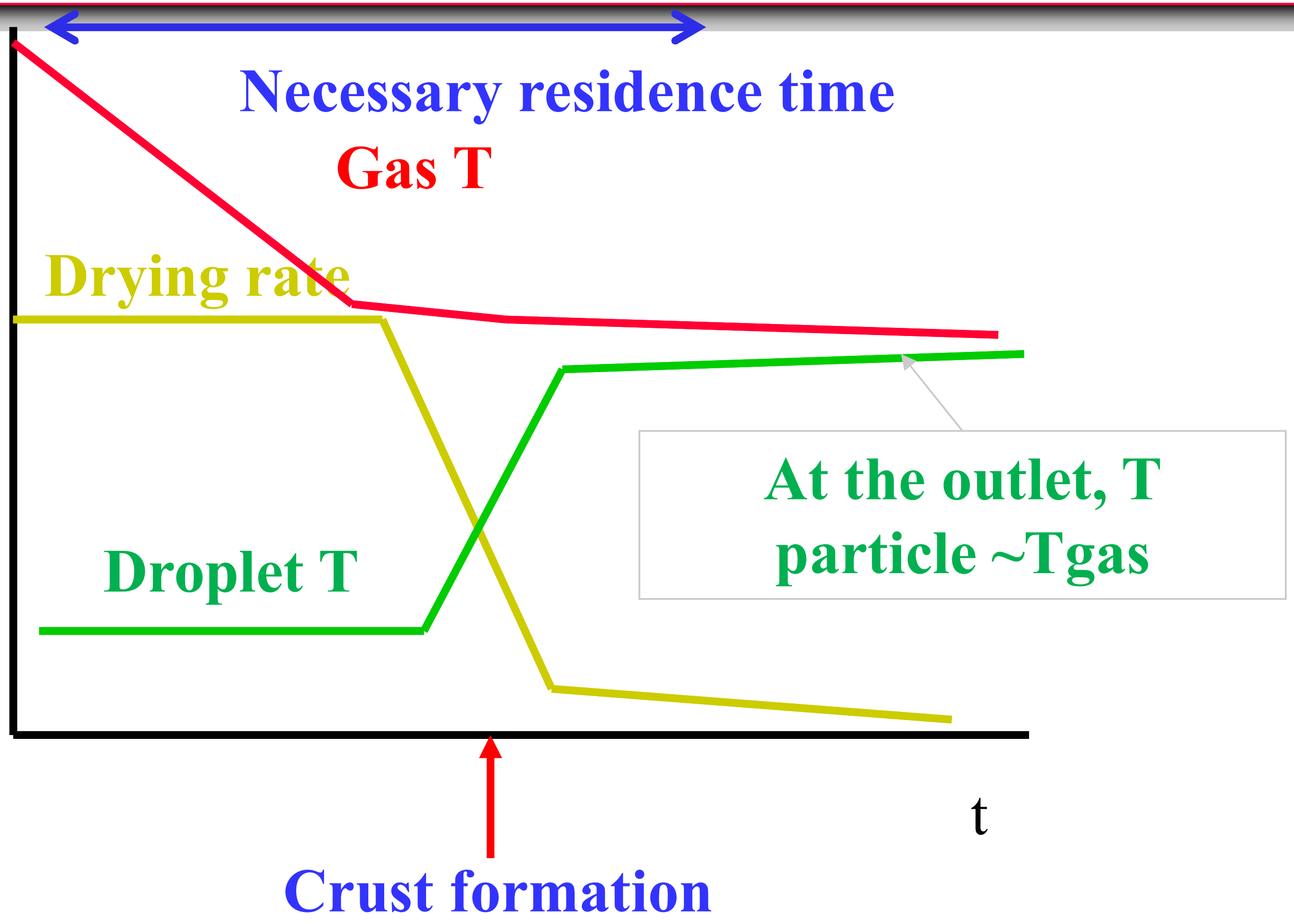
Use of the simulation tool- interest



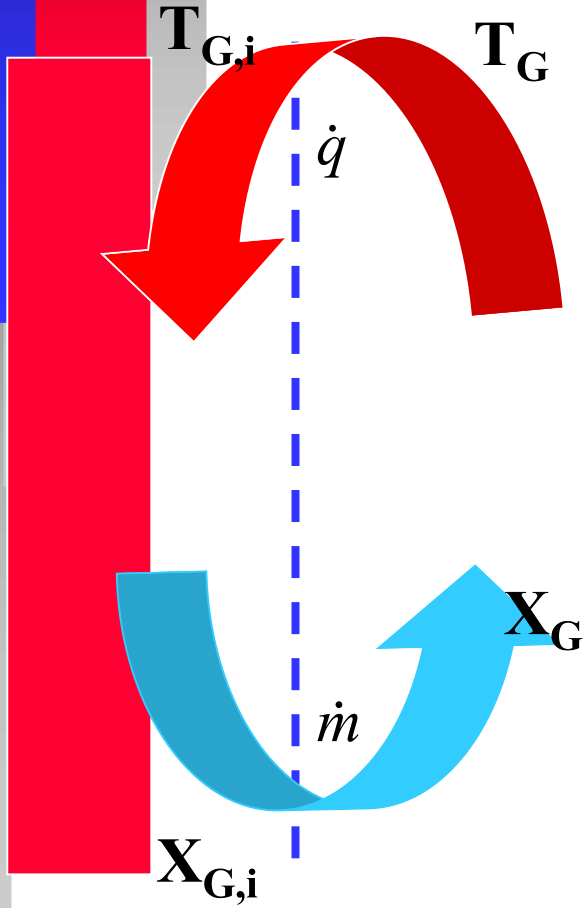
Very good quality of the predicted spray rate

Theory:

Drying kinetics



Theory
Heat and mass transfer



- ***Coupled heat & mass transfer limitation at the beginning***

As long drying is quick , the temperature of the droplet remains low. If $X_{G,i}$>> X_G,the surface T remains constant (wet bulb T)

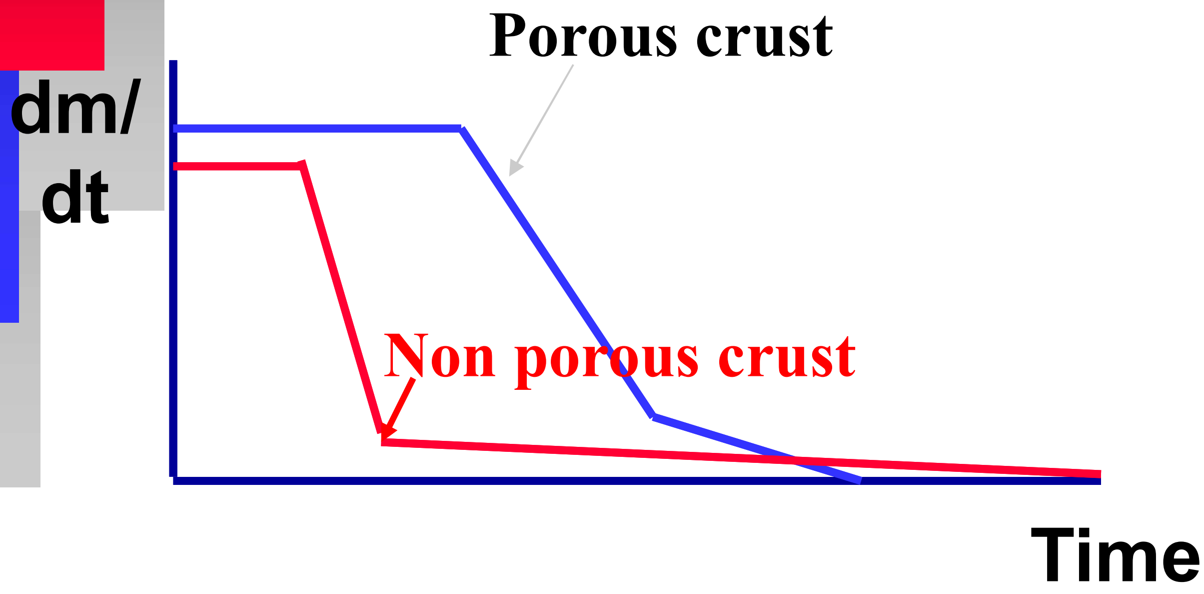
$$\dot{q} = h_T(T_G - T_{G,i})$$

$$\dot{m} = k_M(X_G - X_{G,i})$$

Theory

Second part of drying:

- *Crust can be porous (crystallization) or not (polymers) → great impact on drying kinetics*

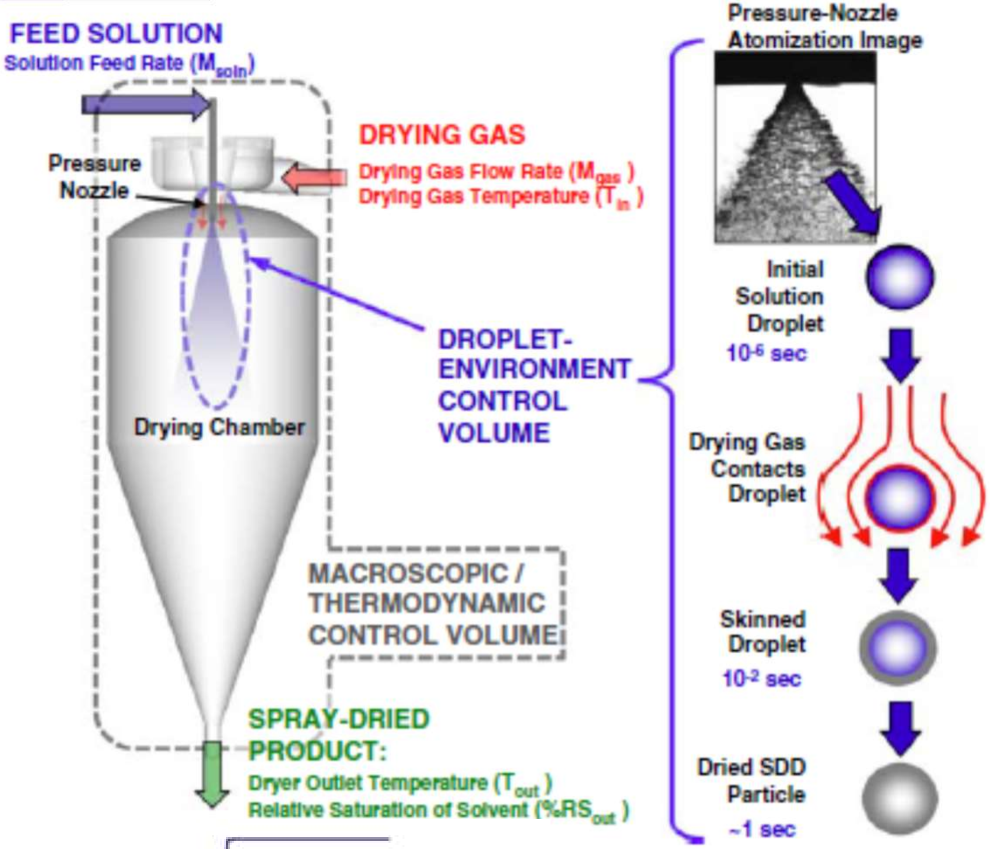


Theory

Particle engineering

- Paricle engineering

Physical situation and key control volumes of the spray-drying process



$$d_p = \sqrt[3]{x_s \times \frac{\rho_d}{\rho_p}} \times d_d$$

- *particle size can be controlled by the atomization conditions and morphology can be manipulated by the solids concentration and drying temperature.*

Jean Claude Eugène Péclet
1793-1857-Physicist

Theory:

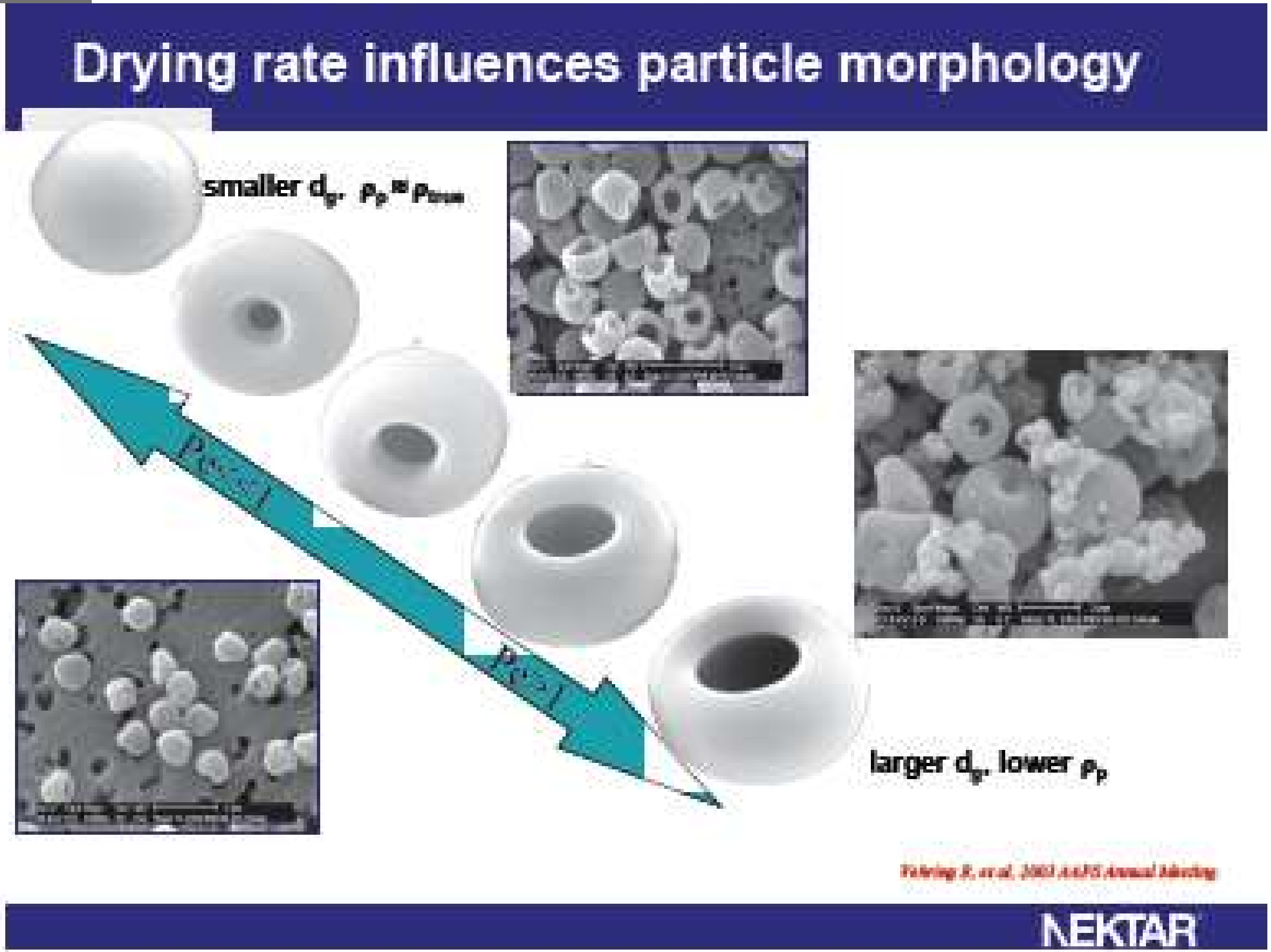
Peclet number approach

- *Ratio between droplet evaporation rate and diffusional motion of the solutes (Peclet number) is used to explain the different paths of particle formation.*
- *Low Pe number → the diffusion motion of the solutes is fast compared to the velocity*
  - *The droplet shrinks while the solutes migrate to the droplet center*
  - *Later on the drying, saturation (or supersaturation) is reached and dense and solid particles are produced.*
- *high Peclet numbers, the evaporation predominates and the surface becomes rapidly enriched in solutes that precipitate.*
  - *A dried layer is formed instantaneously at the droplet surface. Hollow, light and porous particles are formed*

Theory

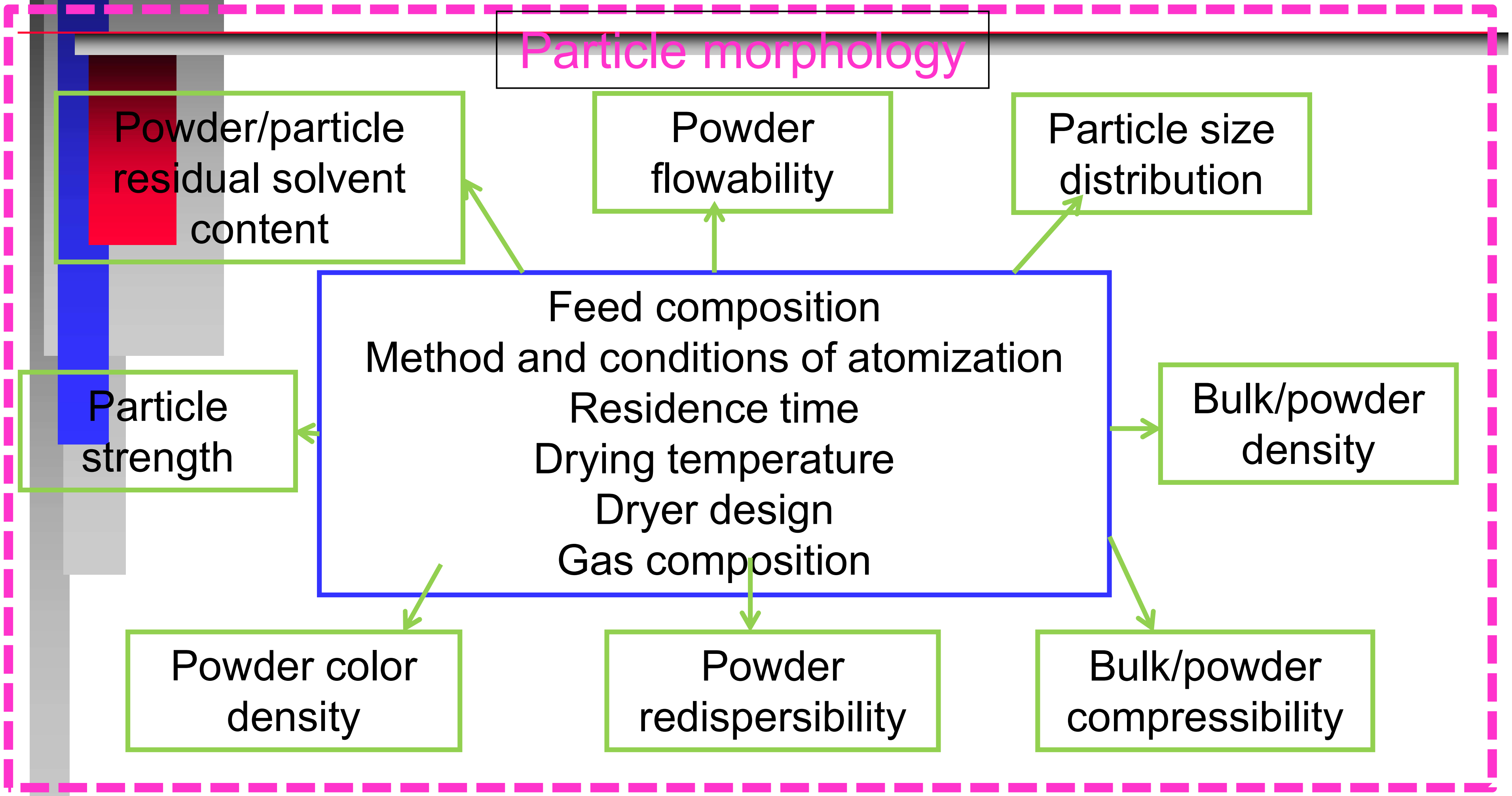
Peclet number approach

Jean Claude Eugène Péclet
1793-1857-Physicist



Theory:

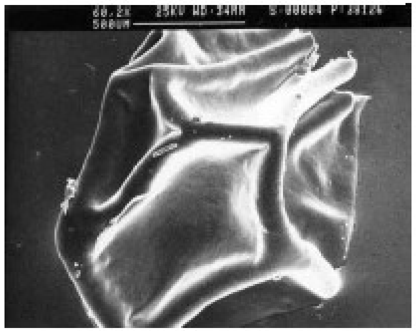
Impact of process conditions on morphologgy and proprties of particles



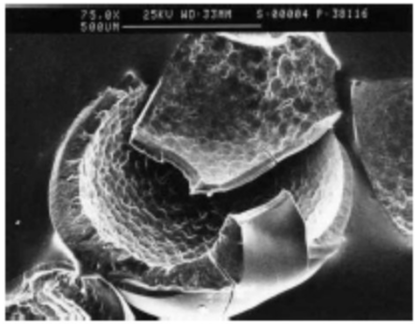
Theory

Impact of process conditions on morphologgy of particles

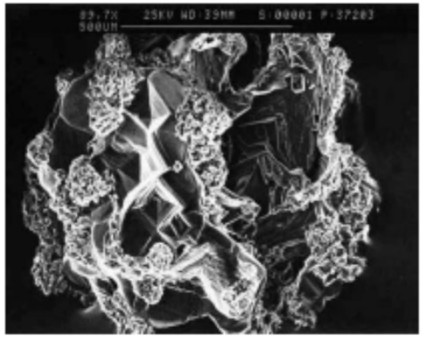
T (70°C) < boiling température



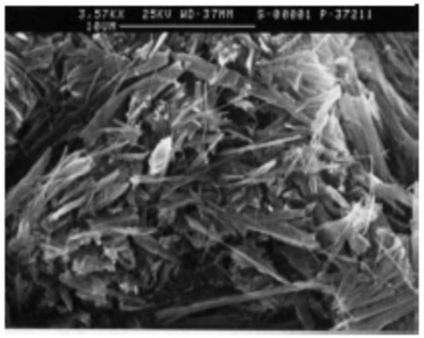
Co-dried egg and skimmed milk. conc. 15% w/w, Drying temp. 70°C.



Semi-instant skimmed milk. conc. 15% w/w, Drying temp. 70°C.



Sodium chloride. conc. 15% w/w, Drying temp. 70°C.



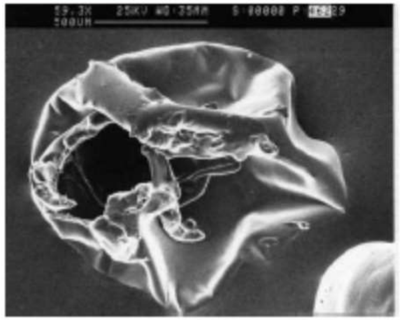
Sodium benzoate. conc. 15% w/w, Drying Temp. 70°C.

- ***Solid precipitation occurred by the formation of a skin. This covered the whole droplet surface within seconds, trapping the bulk of the droplet liquid internally.***
- ***During evaporation, the particle gradually decreased in size and became darker and . finally opaque as the skin thickened, solid or hollow particle are formed depending on the material being dried.***

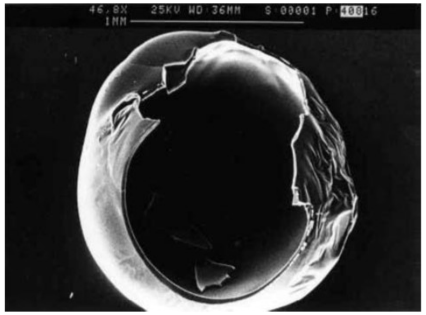
Theory

Impact of process conditions on morphologgy of particles

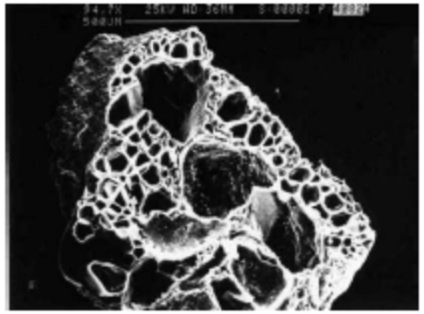
T (200°C) > boiling temperature



Semi-instant skimmed milk. In. conc. 15% w/w, Drying temp. 200°C.



Gelatine. conc. 15% w/w, Drying temp. 200°C.



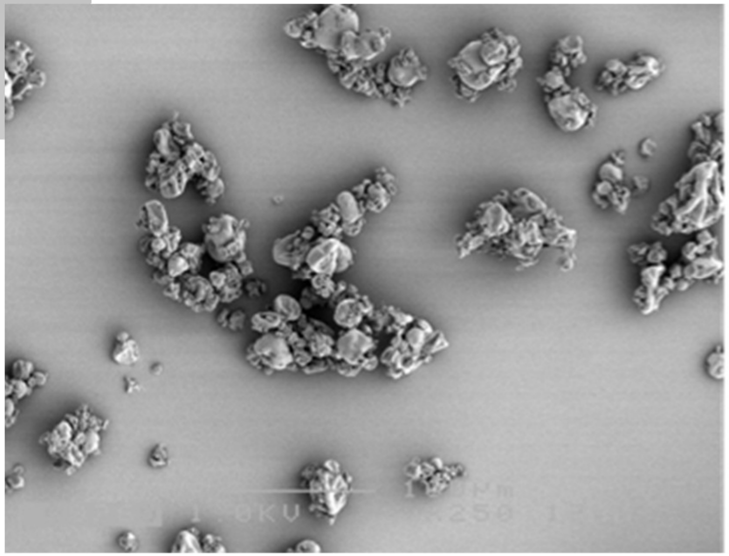
Sodium dodecyl sulphate. conc. 15% w/w, Drying temp. 200°C.

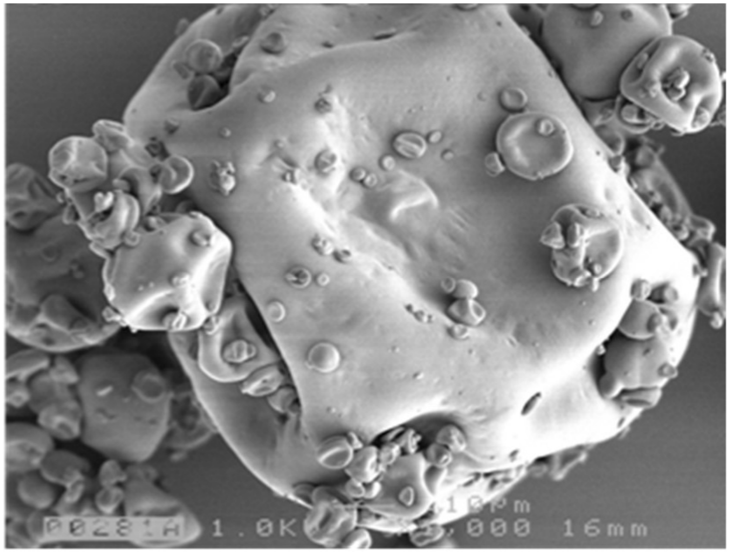
- ***skin covered the whole droplet surface instantaneously; this was rapidly followed by internal bubble nucleation. The bubbles***
- ***expanded to violently distort, and eventually rupture, the skin surface causing the particle to collapse***
- ***Formation of a hollow particle with, in the majority of cases***

Theory

Example of matrix system (API X)

Collapsed and hollow particle are formed





Theory

Drying effect on particle structure

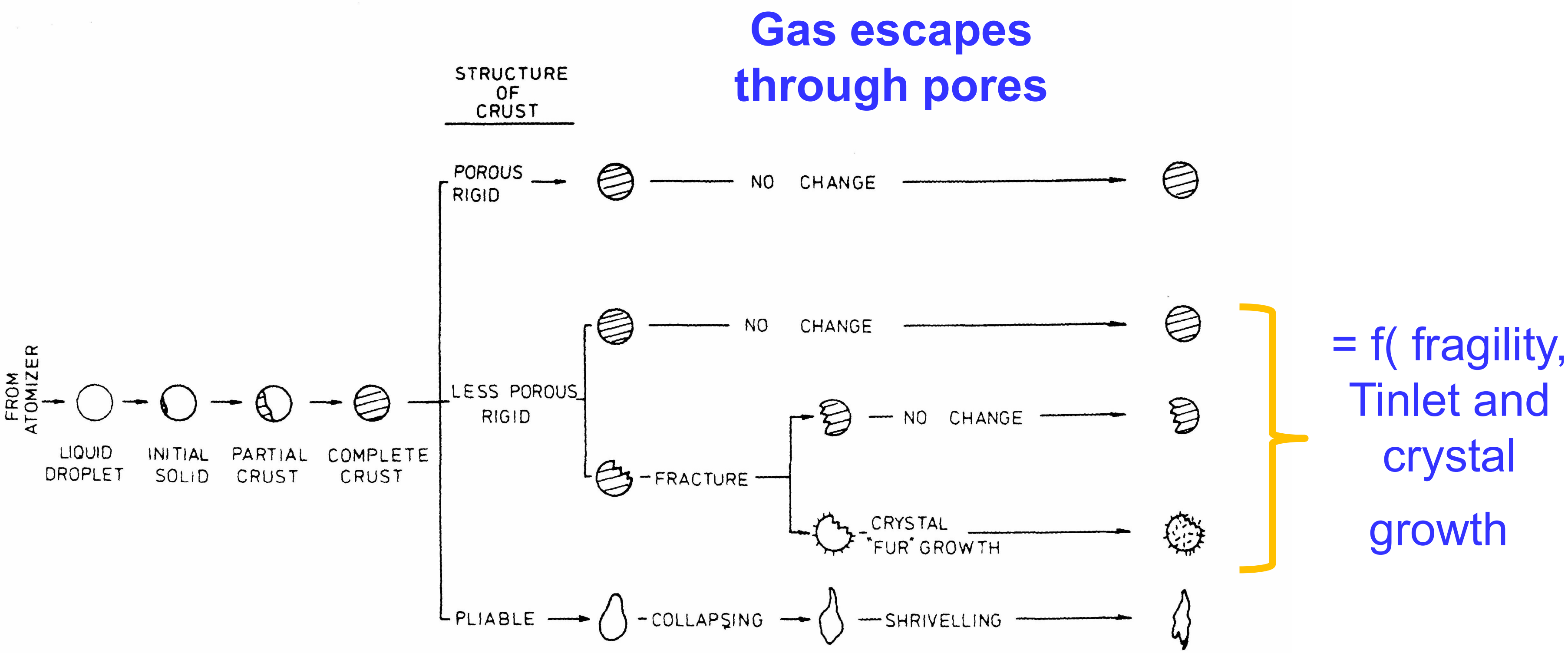
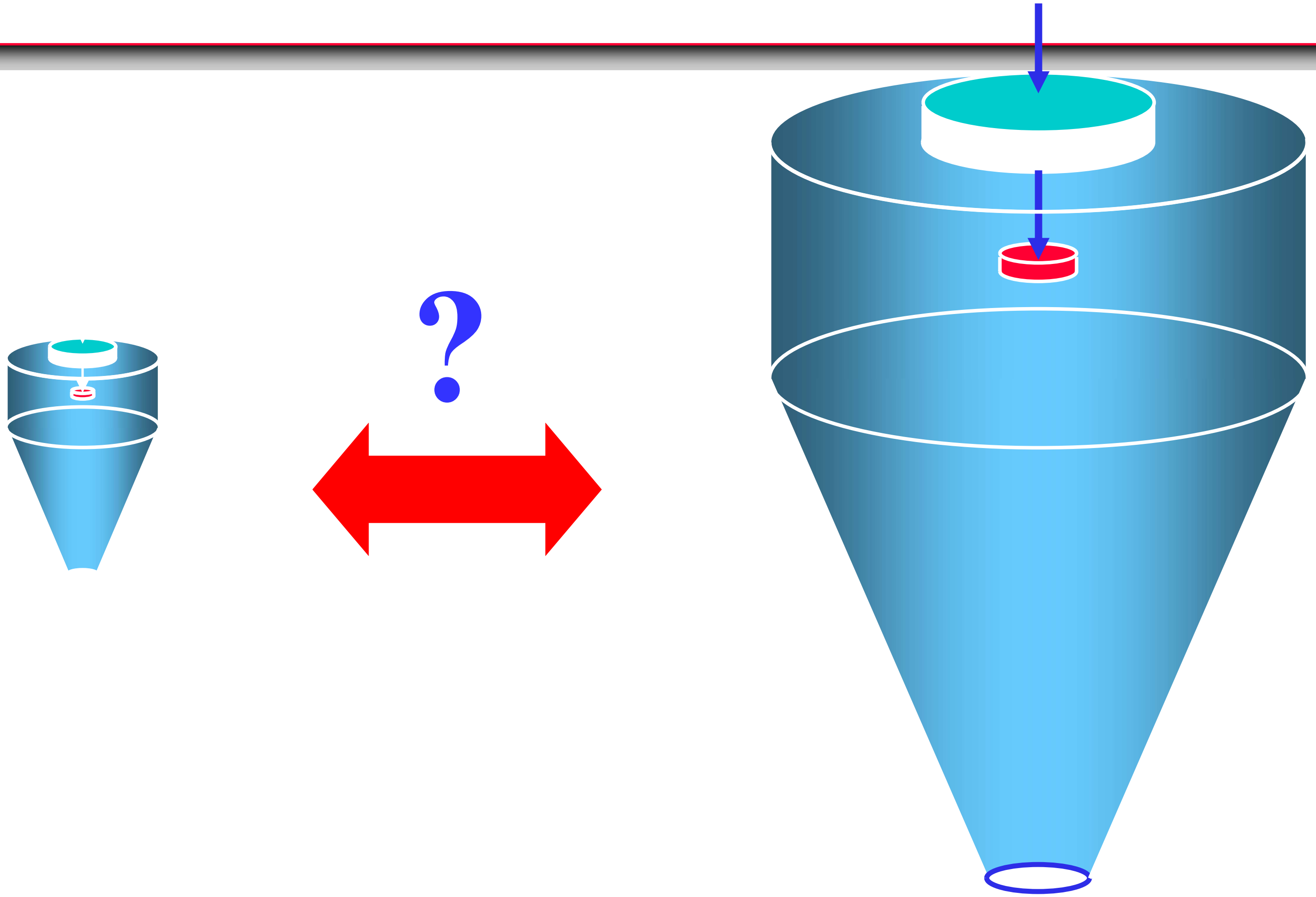


Figure 8.7 Characteristics of droplet undergoing drying (outlet drying air below boiling point) (based on Charlesworth and Marshall[45])

Scaling Up (or Down)



Scale-up/ scale-down what will change ?

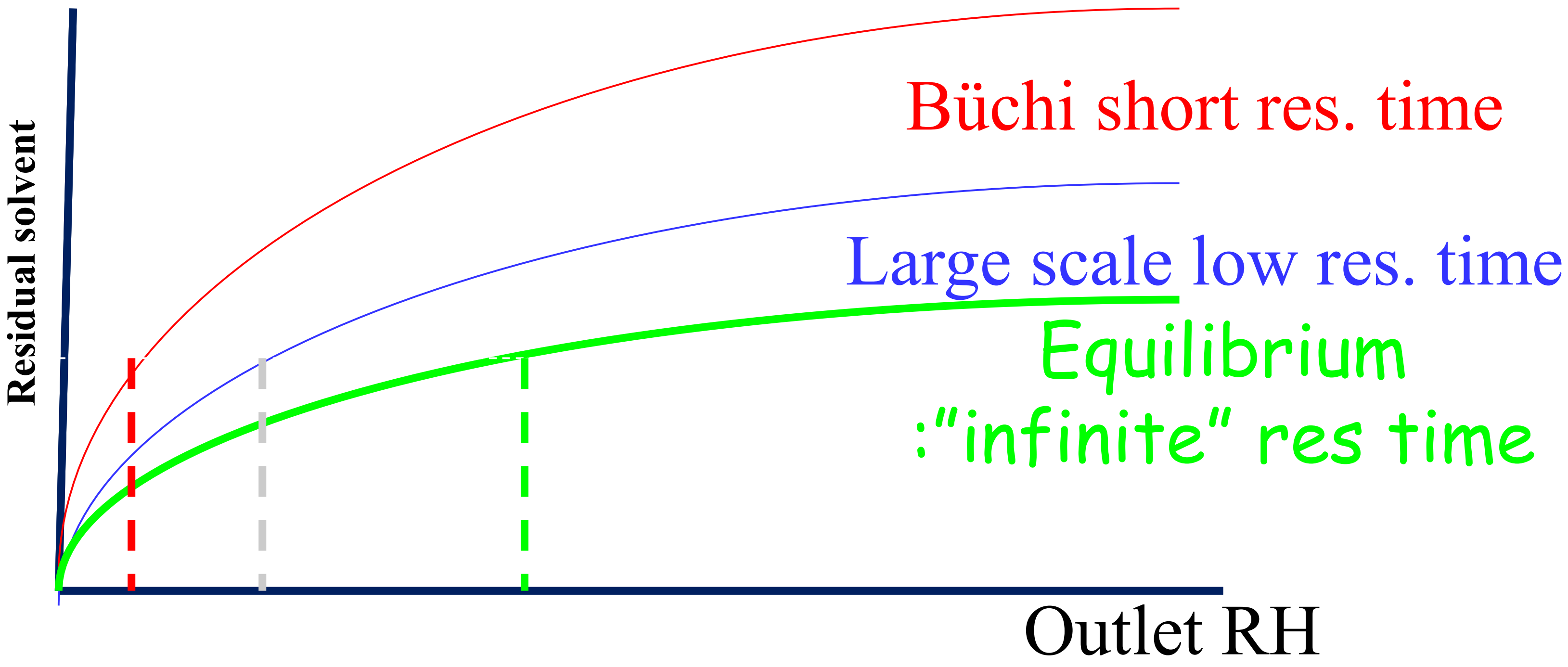
- Atomization :
  - Small scale system can only support 2 fluid nozzles
  - Only small particle size can be reached
- The yield is always bad : (typically 50-70% in a Büchi)
- Residence time is very short (2-3 seconds in a Büchi vs 20-40 s in a large unit)
- Heat losses are up to 50% in a Büchi and less than 10% in a large unit ➔thermal story is significantly different (Peclet and particle shape also)
- The product is poorly representative- but “big trends” like amorphisation or not , aggregation of nanos etc… can certainly be seen

Scale-up/scale-down

- *When moving to PSD 1(minor mobile) or Anhydro MC150, the products is much more representative- still not fully*
- *Much larger particles can be obtained , but very large (> 100 µ) can certainly not be obtained*
- *Most probably using a pressure nozzle will stay a challenge – bifluid nozzle is the most adapted to this chamber size*
- *Can be used for phase I or non pivotal phase II*

Scale-up Scale down

- ***Residence time effect :***
  - **Due to short residence time at a given outlet RH, the “Buchi” product will be more wet.**



Scale-up

Solvent consumption

Please consider the environment before …spray drying

- ***Never forget the economic and environmental aspects !!***
  - **A 6 % solution with 20% active means :**

    ~80-100 kg solvent/kg API

    80-100 t/ solvent /t API

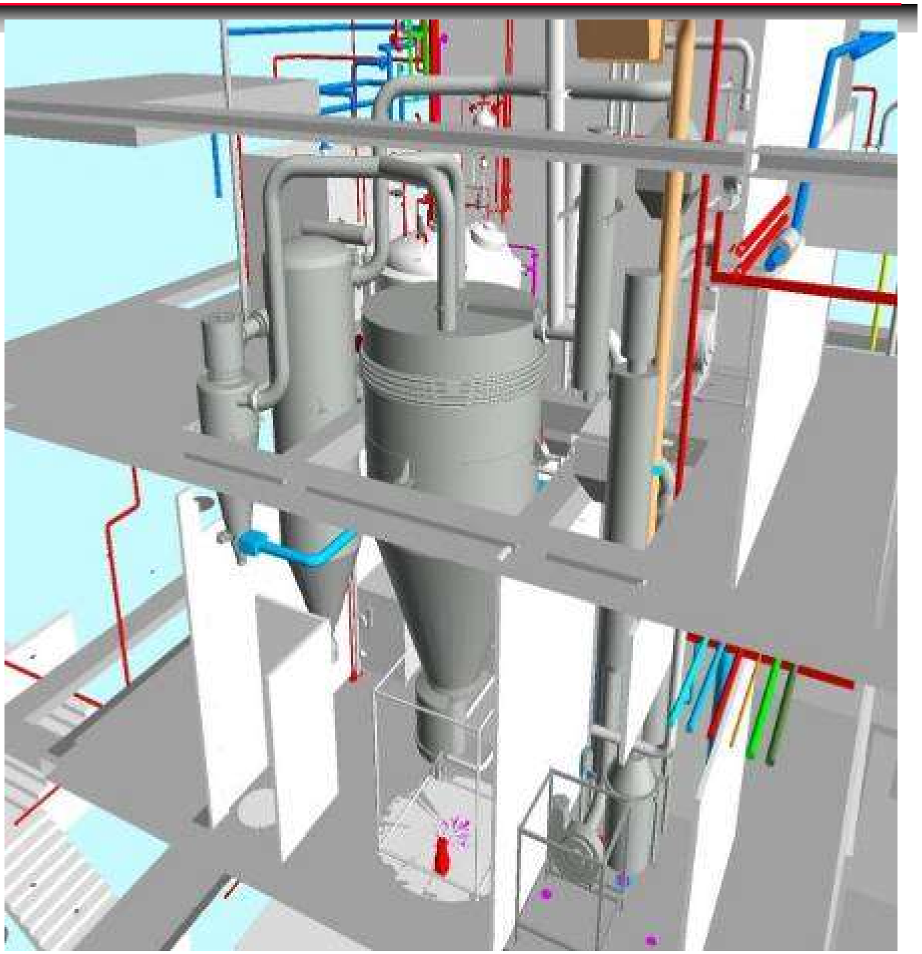
= 2400-3000 t solvent for a 30 t/y API !!! =

240-300 tank trucks /year !!

Sacle-up

Implementation : high buildings are required

- ***Spray drying is a room consuming technology***
- ***It is a solvent consuming technology***



Scale-up

Large investments(*) : examples of "PSD 5" installations

- Probably the 2 largest units of this category worldwide

Pfizer now HOVIONE

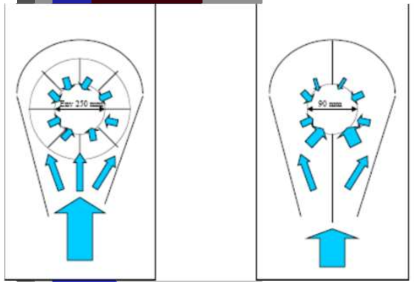
Loverceptib 80 MUS $

Cork Ireland-

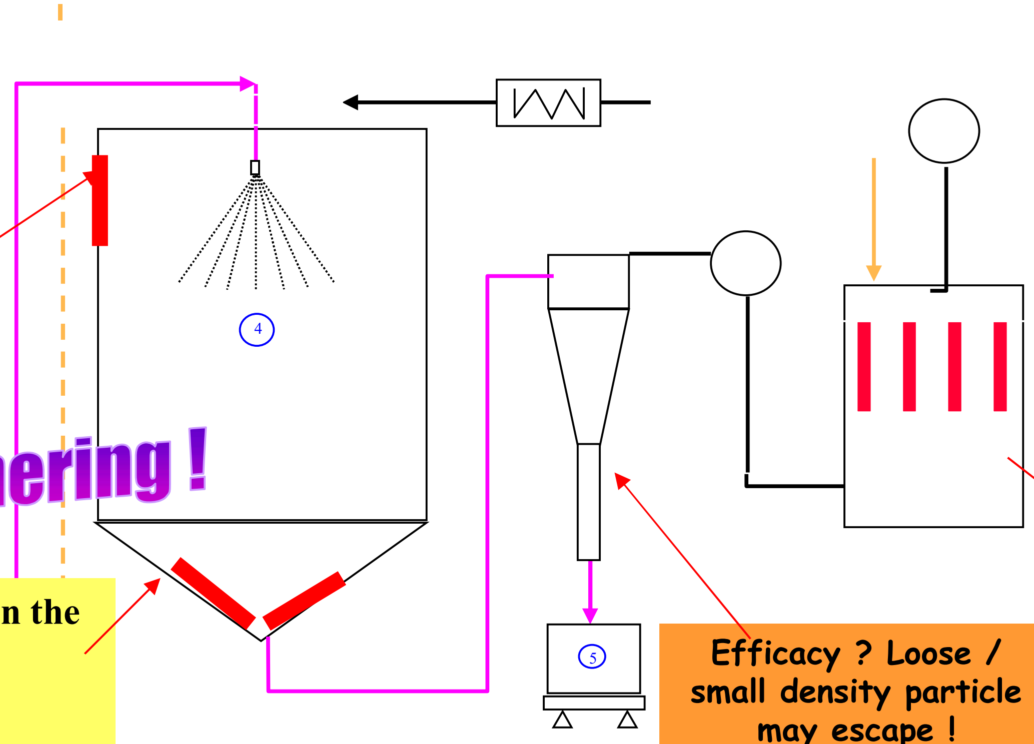
(*) especially for solvent handling units

Scale-up Practice:

Theory is OK .. But what about practice ???



Bad air disperse back flow may bring particle on the roof



Chamber : deposit on the cone

- Nozzle angle ?
- To wet powder? Tg ?
- Poor flowability ?

Efficacy ? Loose / small density particle may escape !

Blocking ?

Attrition (high efficay cyclone = high centrifuge → milling effect

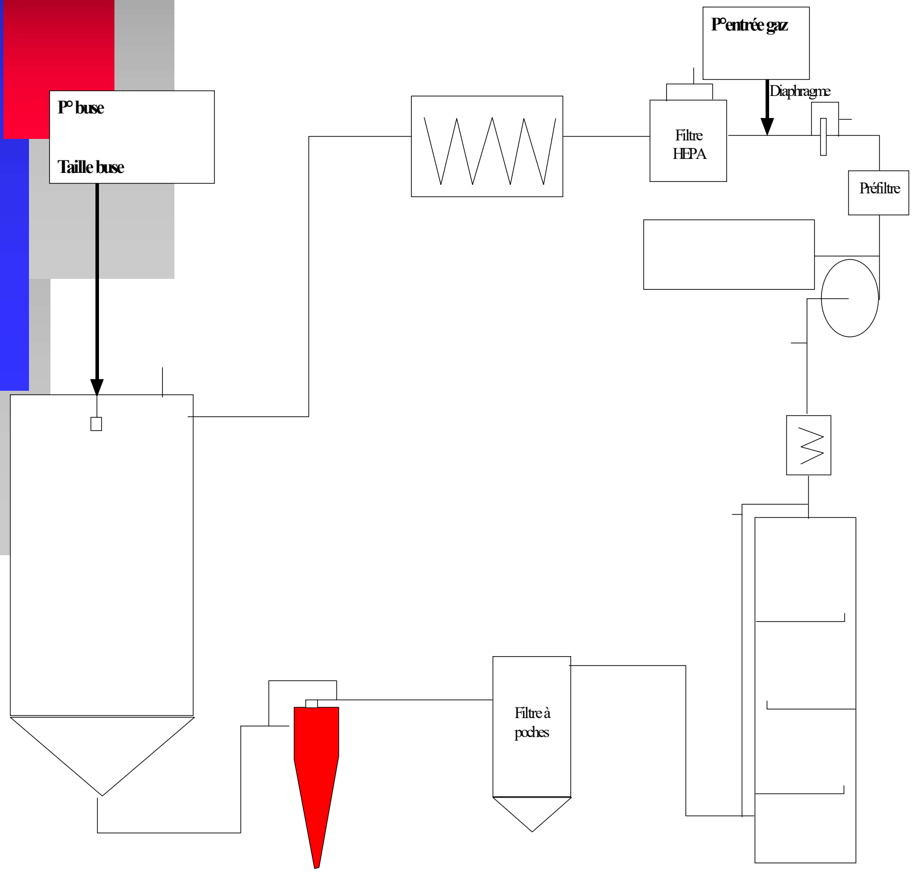
Blocking ?

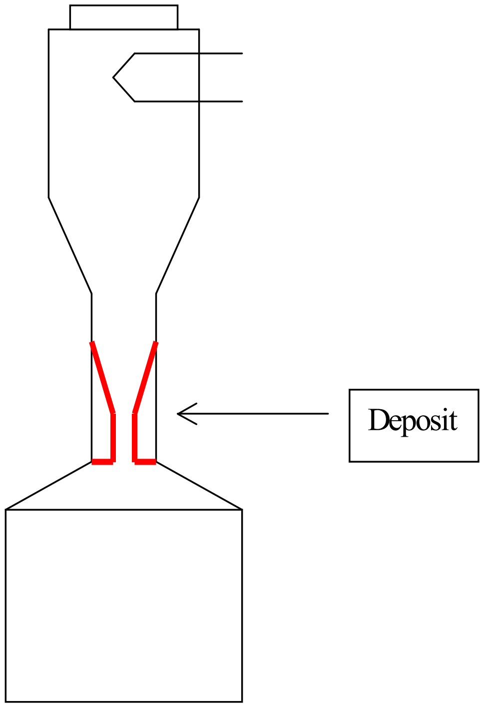
Difficult discharge ?

Dissolution of the powder layer by solvent vapor

Sacle-up practice

Cyclone issue

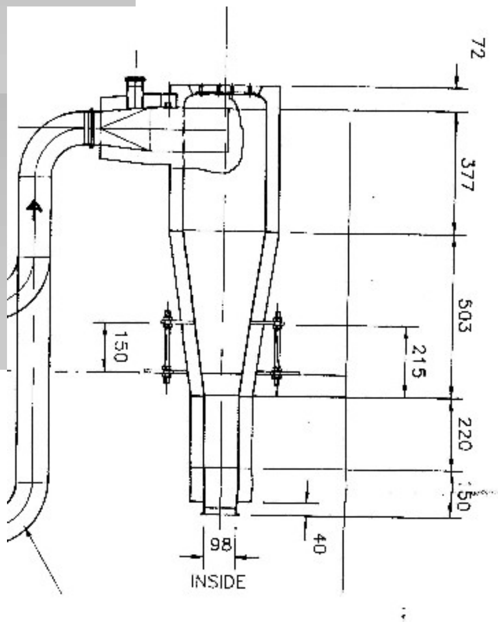




Sacle-up practice

Cyclone issue

- Severe blocking at the outlet of the cyclone observed. Discharging the product was not possible with this configuration.

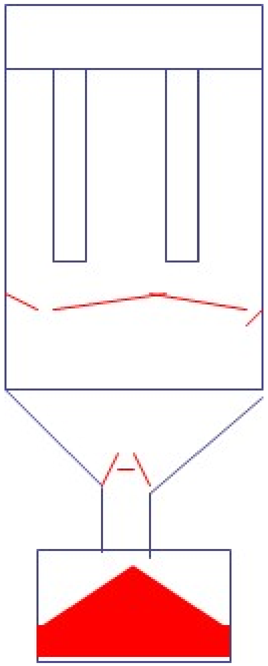


Scale-up practice:

Alternative to cyclone : filter bag option

- ***Peter's law : everything which may go wrong … will go wrong !***

No hard build-up but :

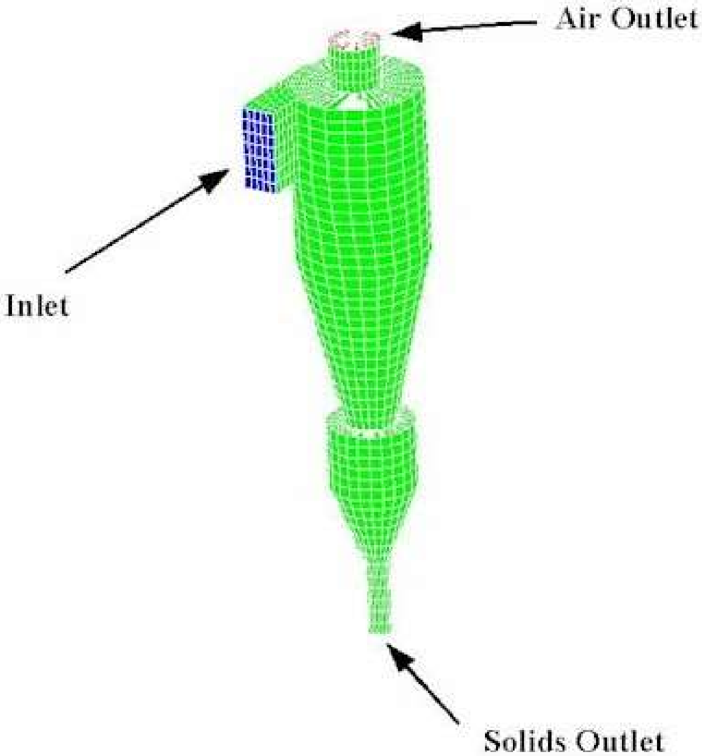


Bags uneasy to clean

Powder is arching

Scale-up practice

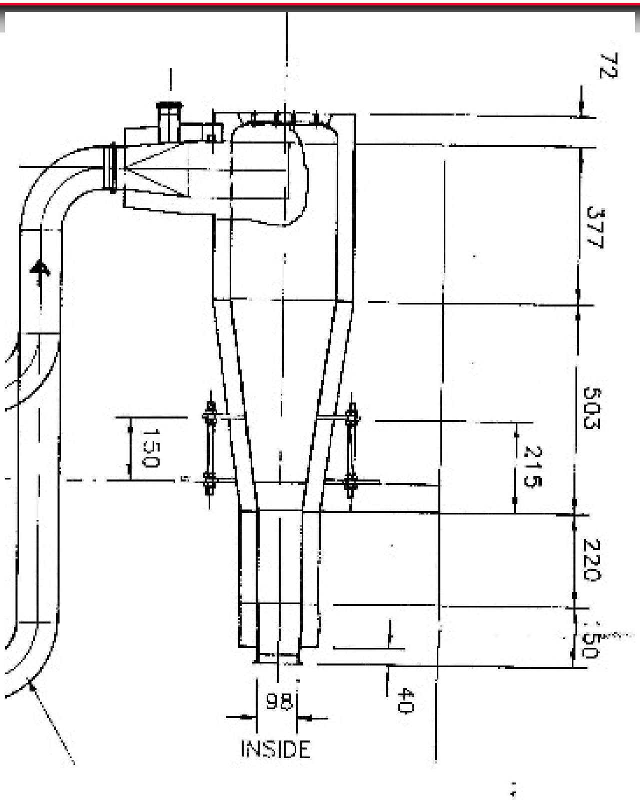
Supplier proposal to … solve the issue !

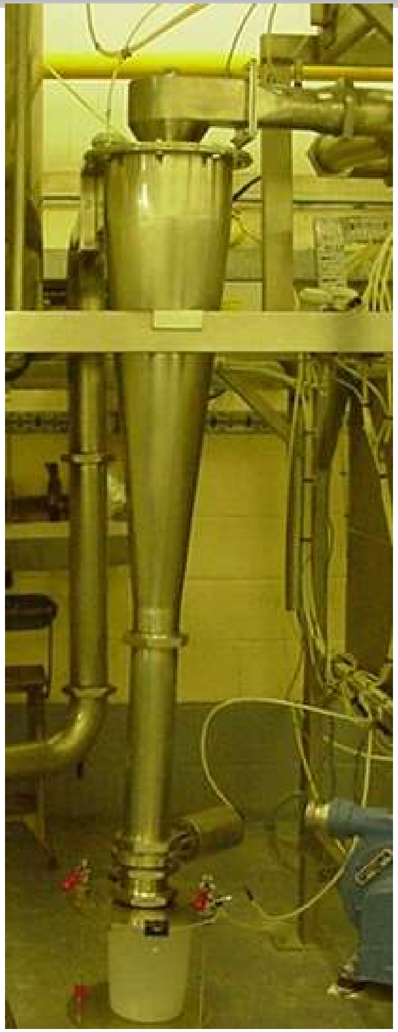


A single 50 kg Tablet in a cyclone !!

Scale-up practice

Cyclone configuration





Scale-up practice

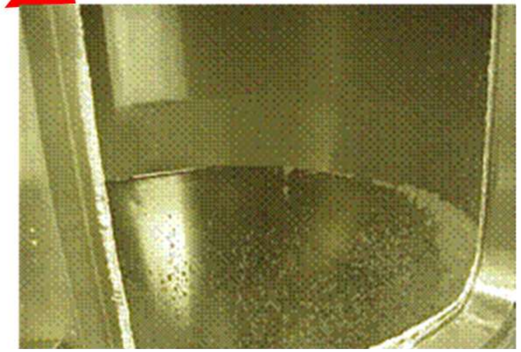
Cyclone configuration

View of the chamber

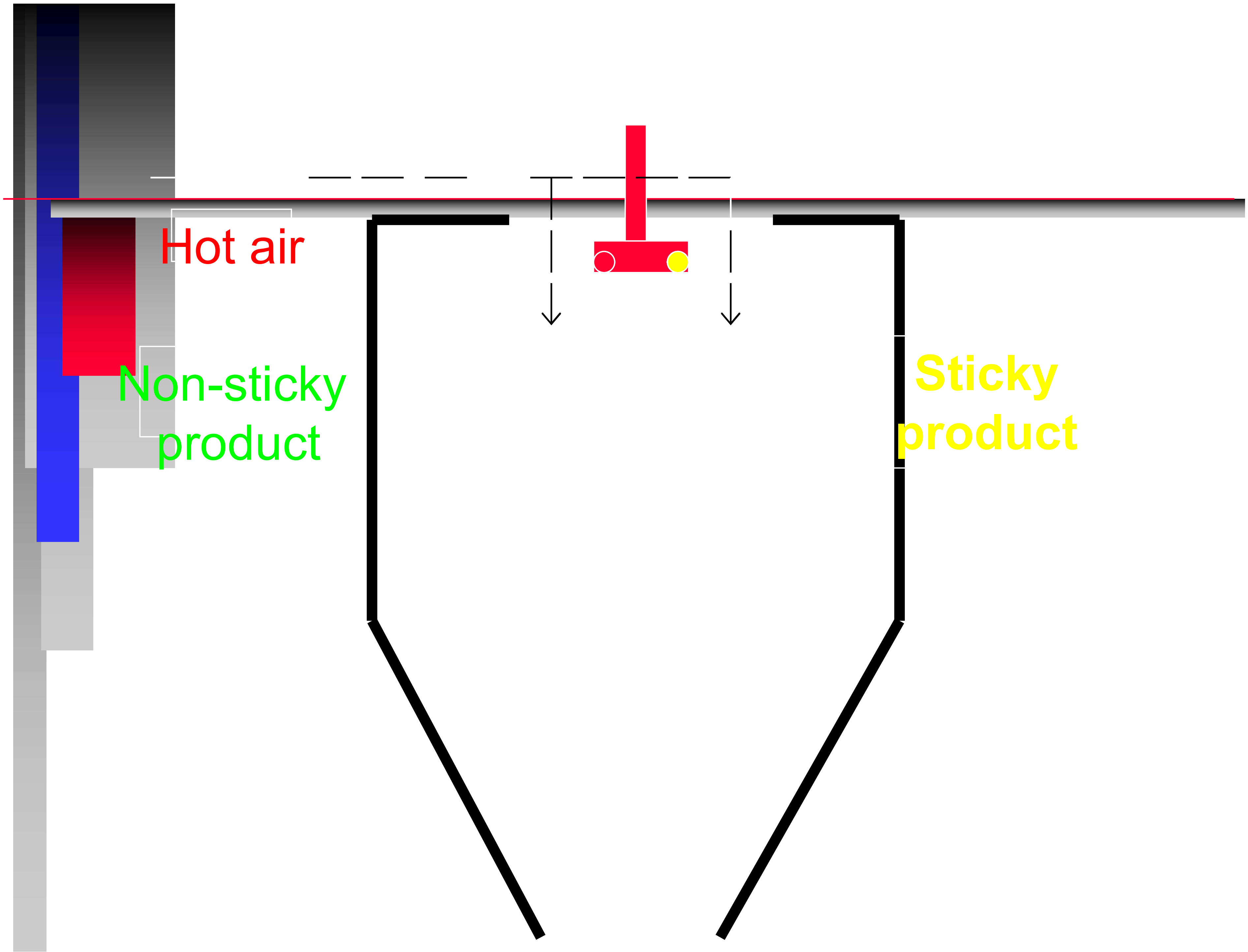
« old » cyclone

Bag filter with N2 counterflow

« optimised» cyclone



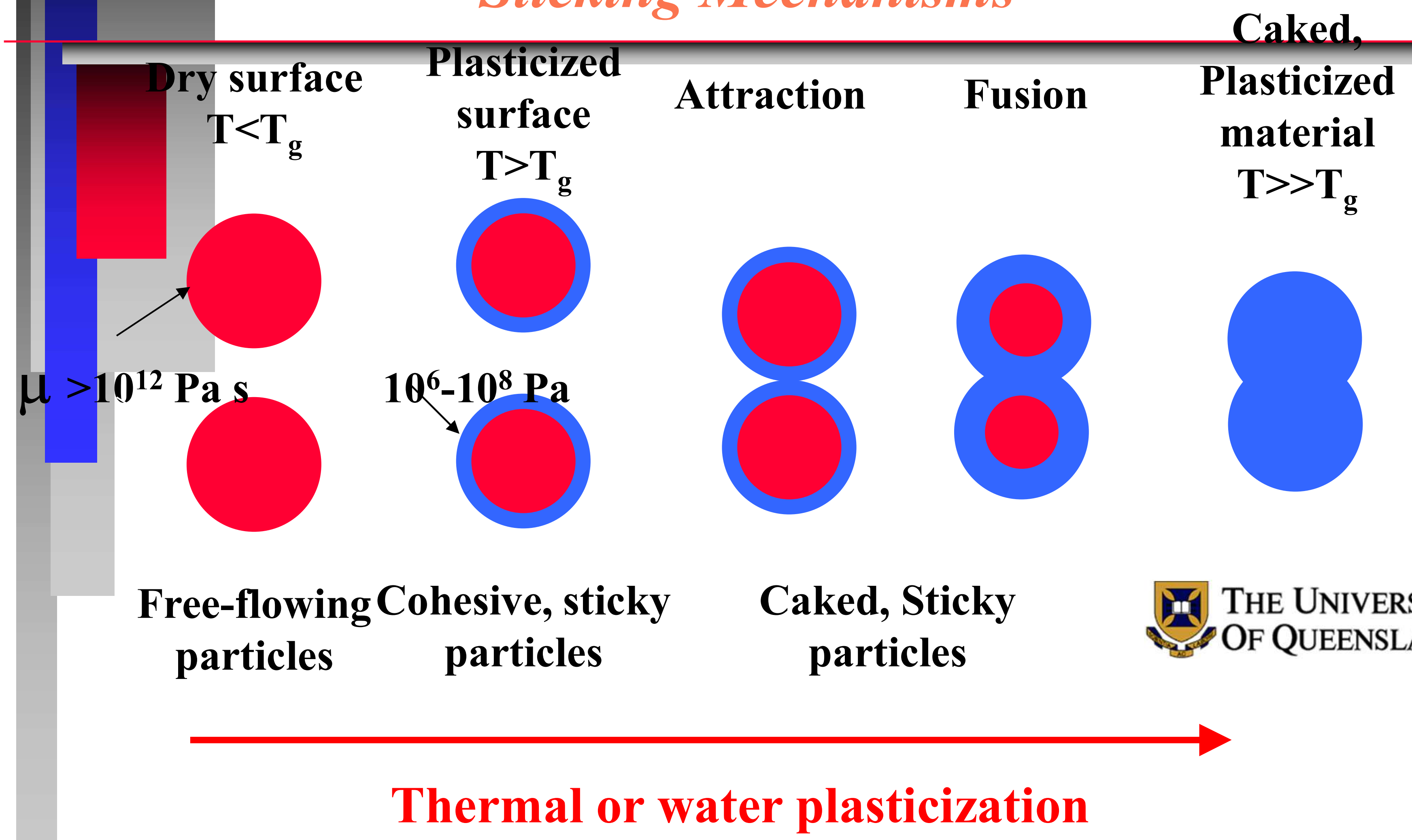
Material stickiness issues



Hot air
Non-sticky
product
Sticky
product

Theory

Sticking Mechanisms



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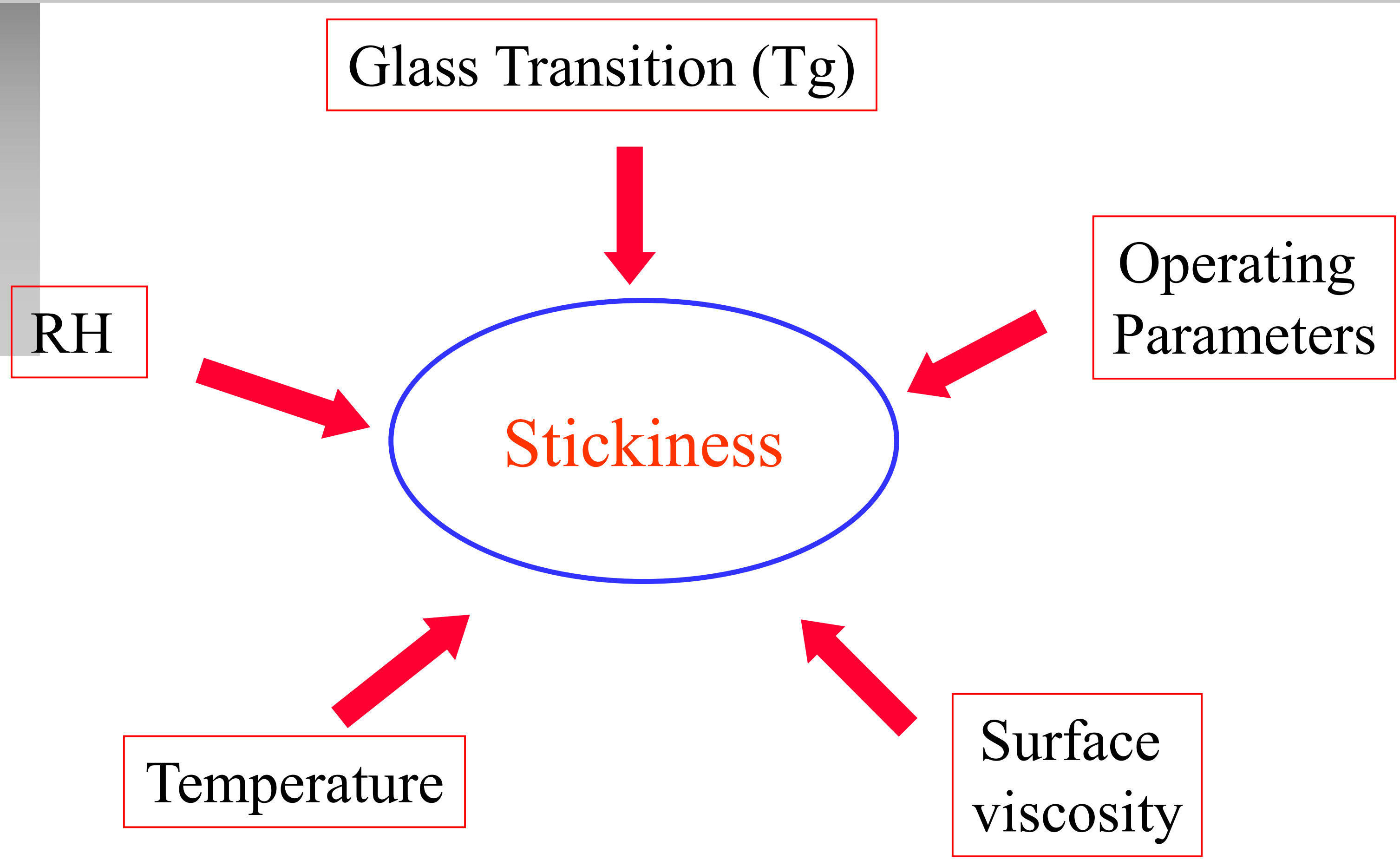
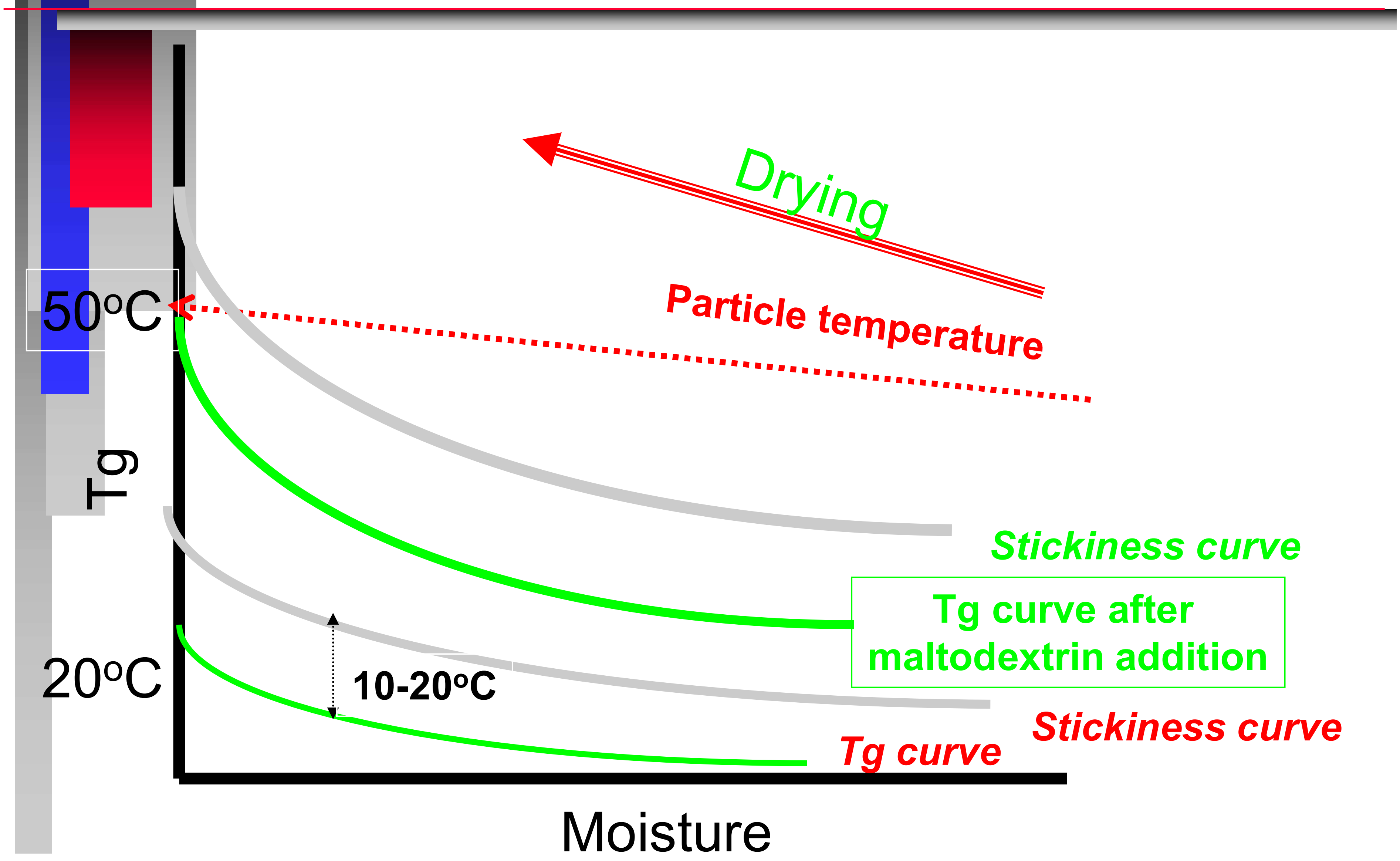
Theory

Stickiness Factors:



Spray drying of honey



Theory

The formulation acts on the Tg and changes the stickiness risk

Glass transition temperature for some common glass forming agents

Excipient	Dry Tg (°C)
Glycerol	-93
Sorbitol	-3
Fructose	13
Glucose	38
Maltose	101
Sucrose	73
Trehalose	117
Raffinose	104
Lactose	112
Mannitol	11
Sodium Citrate	170 (pH > 7)
Maltohexose	173
Leucine	140
Trileucine	70-100 (pH dependent)
Ficoll	110

$$\frac{1}{T_g} = \frac{w_1}{T_{g(1)}} + \frac{w_2}{T_{g(2)}}$$