

Dividing both side by $A\Delta x$ and in the limit $\Delta t, \Delta x \rightarrow 0$

$$\Rightarrow \frac{\partial}{\partial t}(c) = -\frac{\partial}{\partial x}(uc) - k_v \rho_c \frac{d\mu_3}{dt} - k_v \rho_c B_0 L_0^3 \quad (\text{A4})$$

where μ_3 is the third moment of CSD. Often the depletion due to nucleation is neglected due to its much smaller contribution as compared to the other terms.

A3 Derivation of the Energy Balance Equation for Plug Flow Crystallizer

We write the energy balance equation in the volume element $A\Delta x$ as shown in Figure 2.18. The contributing terms are the heat transfer due to fluid flow (*i.e.*, convection) and conduction in the x direction, overall heat transfer from the crystallizer to the cooling water and the generation/depletion term due to the heat of crystallization.

$$\begin{aligned} \rho_{\text{slurry}} c_p A \Delta x T \Big|_t^{t+\Delta t} &= -u A \Delta t \rho_{\text{slurry}} c_p T \Big|_x^{x+\Delta x} \\ &+ k A \frac{\partial T}{\partial x} \Big|_x^{x+\Delta x} + 2\pi R \Delta x \Delta t h (T_{\text{cool}} - T) \\ &+ \left(-\Delta H_c A \Delta x \rho_c k_v \int_0^{L_{\text{max}}} n L^3 dL \right) \Big|_t^{t+\Delta t} \end{aligned}$$

where h is the overall heat transfer coefficient, k is the conductivity of the slurry, c_p is the heat capacity of the slurry and ΔH_c is the heat of crystallization. Now dividing both sides with $\rho_L c_p A \Delta x \Delta t$ and in the limit $\Delta t, \Delta x \rightarrow 0$, finally we have

$$\frac{\partial T}{\partial t} = -\frac{\partial}{\partial x}(uT) + \frac{k}{\rho_{\text{slurry}} c_p} \frac{\partial^2 T}{\partial x^2} + \frac{2\pi R h}{\rho_{\text{slurry}} c_p A} (T_{\text{cool}} - T) + \frac{\rho_c k_v \Delta H_c}{\rho_{\text{slurry}} c_p} \frac{\partial \mu_3}{\partial t}$$

Abbreviations

API	active pharmaceutical ingredient
CCG	constant crystal growth
CFL	courant–Friedrichs–Levy
CPC	coupled preferential crystallization
CNT	classical nucleation theory
CSD	crystal size distribution
FVM	finite volume method
GRD	growth rate dispersion
HR	high resolution
MOCH	method of characteristics