function (often referred to as CSD) is used $n(L,t)$ (# m^{-1} m^{-3}), which gives the number of crystals within the L, $L + dL$ size range at t time moment in unit volume of suspension. The CSD is governed by the population balance equation (PBE), which, assuming nucleation with constant nucleon size, growth, breakage and agglomeration mechanisms, takes the form:

$$\begin{aligned}&\frac{\partial\left[Vn(L,t)\right]}{\partial t}+V\frac{\partial\left[Gn(L,t)\right]}{\partial L}\\&=V\left[B\delta\left(L-L_n\right)+B_{\text{agg}}-D_{\text{agg}}+B_{\text{bre}}-D_{\text{bre}}\right]+F_{\text{f}}n_{\text{f}}\left(L,t\right)-Fn(L,t)\end{aligned}\tag{2.28}$$

with the $n(L,t = 0) = n_0(L)$ initial, and $\lim_{L\to\infty}n(L,t) = 0$ boundary conditions. The initial condition gives the initial distribution in the crystallizer (seeds), whereas the boundary condition states that the crystals have finite size. $n_{\text{f}}(L,t)$ denotes the CSD in the feeding stream: it is 0 if the crystallizer is fed with liquid only, but $n_{\text{f}}(L,t)$ can represent a continuous seeding CSD of an upstream crystallizer. B_{agg} and B_{bre} are birth (source) functions, which describe the rate of production of new crystals of size L by agglomeration and breakage. D_{agg} and D_{bre} stands for death (sink) functions for the rate of consumption of crystals of size L by agglomeration and breakage. The commonly used nucleation, growth agglomeration and breakage functions are described in the first section of this chapter. The set of ordinary and partial differential eqn (2.23)–(2.26) represents the closed model of the continuous cooling MSMPR crystallizer.

There are numerous practical simplifications that can be made to simplify further the model equations.

Assumption 1. *Constant volume, density and specific heat.*

For instance, assuming constant suspension density, specific heat and crystallizer working volume, which is a reasonable approximation of many pharmaceutical crystallization systems, the characteristic differential equations for the crystallizer are greatly simplified:

$$\frac{\mathrm{d}c}{\mathrm{d}t}=-\rho_{\text{c}}k_{\text{V}}\left[BL_n{}^3+3G\int_0^{L_{\max}}L^2n(L,t)\mathrm{d}L\right]+\frac{c_{\text{f}}-c}{\tau}\tag{2.29}$$

$$\frac{\mathrm{d}T}{\mathrm{d}t}=-\frac{\Delta H_{\text{c}}\rho_{\text{c}}k_V}{\rho c_{\text{p}}}\left[BL_n{}^3+3G\int_0^{L_{\max}}L^2n(L,t)\mathrm{d}L\right]+\frac{T_{\text{f}}-T}{\tau}-\frac{UA}{V\rho c_{\text{p}}}\left(T-T_{\text{cool}}\right)\tag{2.30}$$

$$\begin{aligned}&\frac{\partial n(L,t)}{\partial t}+\frac{\partial\left[Gn(L,t)\right]}{\partial L}=B\delta\left(L-L_n\right)\\&+B_{\text{agg}}-D_{\text{agg}}+B_{\text{bre}}-D_{\text{bre}}+\frac{n_{\text{f}}\left(L,t\right)-n(L,t)}{\tau}\end{aligned}\tag{2.31}$$

where $\tau = V/F$ denotes the mean residence time. For a process simulation, the model-equations are solved simultaneously, with one of the suitable numerical solution methods presented in the fifth subsection of this chapter.