where t is the time, v is the volume, and $n(v,t)$ is the time-dependent volume-based population balance density function, with $n(v,t)\mathrm{d}v$ representing the number of particles in the volume range of v to $v + \mathrm{d}v$ per unit volume of the reactor. The volume growth rate (G) of any particle is defined as

$$G = \frac{\mathrm{d}v}{\mathrm{d}t} = k_{g1}\mathrm{e}^{\frac{-k_{g2}}{RT}}\sigma^{g}k_{\mathrm{a}}\left(\frac{v}{k_{\mathrm{v}}}\right)^{\frac{2}{3}} \tag{1.11}$$

where the relative supersaturation is defined by

$$\sigma = \frac{C - C_{\mathrm{eq}}}{C_{\mathrm{eq}}} \tag{1.12}$$

T is the absolute temperature, R is the universal gas constant, k_{g1} and k_{g2} are the growth rate constants, g is the growth rate order, and k_{a} is the shape factor of the particle used to calculate the surface area of particles.

The nucleation rate expression is

$$\dot{N}_{\mathrm{heterogen}} = k_{b1}\mathrm{e}^{\frac{-k_{b2}}{RT}}\sigma^{b}Ar \tag{1.13}$$

where b is the order of the nucleation rate and Ar is the surface area of the excipient per unit volume of the crystallizing solution.

The mass balance of API particles can be written as

$$\frac{\mathrm{d}C}{\mathrm{d}t} = \frac{(C_{\mathrm{i}} - C)}{\tau} - \frac{\dot{N}n_{\mathrm{c}}}{Ar_{\mathrm{v}}} - \frac{k_{\mathrm{a}}\left(\frac{1}{k_{\mathrm{v}}}\right)^{\frac{2}{3}}k_{g}S^{g}}{V_{\mathrm{m}}}\int_{0}^{\infty} n(v,t)v^{2/3}\,\mathrm{d}v \tag{1.14}$$

where $k_{g} = k_{g1}\mathrm{e}^{\frac{-k_{g2}}{RT}}$, C and C_{i} are the concentrations of solute in the reactor and in the inlet slurry, respectively, and V_{m} is the specific volume of the solute.

To simplify the analysis, the moments of the population density function are solved here. The jth moment M_j of the population density function is defined by

$$M_{j} = \int_{0}^{\infty} n(v,t)v^{j}\,\mathrm{d}v \tag{1.15}$$

The 0th moment M_0 represents the total number of solute crystals present in the system, and M_1 is the total volume of solute crystallized. As $k_{\mathrm{a}}\left(\frac{1}{k_{\mathrm{v}}}\right)^{\frac{2}{3}}M_{\frac{2}{3}}$ is the total surface area of crystals, the rate equation for the concentration of solute can be written as

$$\frac{\mathrm{d}C}{\mathrm{d}t} = \frac{(C_{\mathrm{i}} - C)}{\tau} - \frac{\dot{N}n_{\mathrm{c}}}{Ar_{\mathrm{v}}} - \frac{k_{\mathrm{a}}\left(\frac{1}{k_{\mathrm{v}}}\right)^{\frac{2}{3}}k_{g}\sigma^{g}M_{\frac{2}{3}}}{V_{\mathrm{m}}} \tag{1.16}$$