$i$, $C_i$ is the API concentration in the mother liquor within and discharged from MSMPR $i$ and $g$ is the crystal growth exponent. The API solubility concentration, $C^{sat}{}_i$, is a function of $T_i$, calculated *via* a surrogate polynomial regressed from published temperature-dependent saturation data for cyclosporine.[58]

The nucleation rate in MSMPR $i$, $B_i$, is described by the power law expression in supersaturation and temperature.[18]

$$B_i = k_{b0} \exp\left(-\frac{E_{ab}}{RT_i}\right)\left(\frac{C_i}{C_i^{sat}} - 1\right)^b M_i^m \tag{15.18}$$

$k_{b0}$ is the pre-exponential factor for nucleation, $E_{ab}$ is the nucleation energy barrier, $b$ is the crystal nucleation exponent, $M_i$ is the slurry density in MSMPR $i$ and $m$ is the exponent of the slurry density. All crystallisation kinetic parameters are taken from previous work.[42,51]

The one-dimensional population balance model is described by a system of ordinary differential equations (ODEs).

$$G_1 V_1 \frac{dn_1}{dL} = F_{N+1} n_{N+1} - F_1 n_1 \tag{15.19}$$

$$G_i V_i \frac{dn_i}{dL} = F_{i-1} n_{i-1} + F_{N+i} n_{N+i} - F_i n_i \qquad i = 2 \ldots N. \tag{15.20}$$

$F_{i-1}$ and $F_i$ are the volumetric flowrates of streams entering and leaving MSMPR $i$, respectively, $F_{N+i}$ is the recycle volumetric flowrate entering MSMPR $i$, $N$ is the total number of crystallisers, $n_i$ is the crystal population density function in MSMPR $i$ and $L$ is the characteristic length of the crystal. For the process without recycle, $F_{N+i}$ terms are equal to zero. The system of ODEs formed by the population balance equations are satisfied by the boundary condition, $n_i^0 = n_i\,(L = 0) = B_i/G_i$, corresponding to the population density of nuclei.

The slurry density in MSMPR $i$, $M_i$, is calculated from the population density function as follows:

$$M_i = k_v \rho_{API} \int n_i L^3 \, dL \tag{15.21}$$

$k_v$ is the crystal volume shape factor (= π/6 for spherical crystals, assumed constant for linear crystal growth) and $\rho_{API}$ is the crystal density. A value of $\rho_{API} = 1.3$ g cm$^{-3}$ (average for solid APIs[88]) is assumed.

Steady-state mass balances assume no accumulation and account for volumetric changes due to API crystallisation. The general mass balance equations for processes are:

$$F_0 C_0 + F_{N+1}\left(1 - \frac{M_{N+1}}{\rho_{API}}\right) C_N + F_{N+1} M_{N+1} - F_1\left(1 - \frac{M_1}{\rho_{API}}\right) C_1 - F_1 M_1 = 0 \tag{15.22}$$