



Figure 12.3 Ternary phase diagram of two enantiomers D and L in a solvent. (a): Illustration of PC after seeding with L. A specific actual composition on the indicated time trajectory $x_i(t)$ is marked as $x_{i,0}(t)$ (dot). The current driving force for phase transfer into the solid phase (solid arrows) is depicted for each enantiomer as the intersection of the lines $\overline{Lx_{i,0}}$ and $\overline{Dx_{i,0}}$ with the corresponding dashed prolongations of the solubility isotherms valid for the actual crystallization temperature. (b): Illustration of another possible shape of the phase diagram, where the solubility of one enantiomer is significantly increased in presence of the other, which causes steeper isotherms and reduces the region exploitable for PC. In addition, non-linearity of isotherm lines is assumed caused by potential non-idealities in the system.

$$S_i(T(t), t) = \frac{x_{i,0}(t)}{x_{\text{sat},i}(x_{\text{sat},i}^0(T(t)), x_{\text{sat},i}^{\text{DL}}(T(t)))} \quad i = \text{D,L} \quad (12.1)$$

In eqn (12.1) S_i describes the relative supersaturation of enantiomer i , $T(t)$ the transient process temperature and $x_{i,0}(t)$ the current mass fractions in the system. As mentioned above, the saturation concentrations of the enantiomers i , $x_{\text{sat},i}$ at the specific temperature $T(t)$ and the composition $x_{i,0}(t)$ can be calculated by linear functions connecting the points of saturation of the pure enantiomer, $x_{\text{sat},i}^0$ and the racemic composition, $x_{\text{sat},i}^{\text{DL}}$ in the ternary phase diagram.

The maximal enrichment of a system and hence, the achievable yield of the depicted PC, is obviously strongly limited by the slopes of the solubility isotherms. This can be quantified by the so-called Meyerhoffer ratio defined as the ratio of solubilities of the racemate and an enantiomer for the same conditions.¹⁶ The supersaturation calculation for curved saturation lines needs to apply a more general approach instead of the linear functions mentioned above.

A suitable way to improve the process output is to increase the driving force for growth of the preferred enantiomer by changing the initial or the final temperature. Nevertheless, the allowable sub-cooling remains bound by the specific borders of primary nucleation at which both components crystallize