liquid phases are of racemic composition. The PC process described can be performed also in a cyclic mode, *i.e.* successively, preferentially crystallizing the L- and D-enantiomers in an alternating manner with addition of racemic feed and the respective seed crystals in-between (see later Figure 12.8). Such a cyclic approach can also be applied to racemic compound-forming systems, in which one of the enantiomers and the racemic compound are alternately crystallized.[35,36]

More details and examples regarding various batchwise operated PC process variants are available in a review article.[21] Several process variants capable of performing PC in batch and continuous modes are introduced in Section 12.4. In Section 12.5 we will present case studies of continuous PC for the conglomerate systems of the two amino acids threonine and asparagine monohydrate.

12.3 Preferential Crystallization: Kinetics, Driving Forces and Metastable Zones

Crystallization kinetics are of essential importance for the resolution of chiral systems exploiting PC. They identify and mark possible regions for performing the kinetically controlled resolution process within a three-phase region of the phase diagram. The PC process illustrated in Figure 12.2 is redrawn in Figure 12.3 (left). After a certain process time, t, the seeded enantiomer has grown and in parallel the solution is enriched in its antipode. A current liquid phase composition, $x_{i,0}(t)$, is marked by a gray dot.

The course of the initially straight trajectory becomes curved after nucleation of the counter-enantiomer and subsequent growth of the nuclei (grey dotted line in Figure 12.3). In equilibrium a racemic composition is reached again for both the liquid ($x^{\mathrm{DL}}_{\mathrm{sat,L}} = x^{\mathrm{DL}}_{\mathrm{sat,D}}$, Figure 12.3) and the solid phases. Thus, after nucleation of the antipode, the crystallization kinetics of the unseeded component becomes faster to deplete the established enrichment. The differences in the kinetics are based on the two different and constantly changing driving forces, connected to the specific, actual chemical potentials of the particular enantiomer in the current state of the system (*e.g.* at $x_{i,0}(t)$) and the two corresponding saturated states (at $x_{\mathrm{sat,D}}$ and $x_{\mathrm{sat,L}}$, Figure 12.3). These saturated states are related to the intersection of the lines starting at the pure phase corners and going through the actual state ($\overline{\mathrm{L}x_{i,0}}$ and $\overline{\mathrm{D}x_{i,0}}$) and the extensions of the solubility isotherms for the applied temperature (dashed lines in Figure 12.3). It should be noted that the ratio between the mass fractions of the respective opposite enantiomer and the solvent is constant along these lines (isopleths, dotted grey and dotted black lines in Figure 12.3), which requires consideration in the calculation of the driving force. The dynamically changing specific supersaturations $S_i(t)$ can be expressed for polythermal conditions in a general way by eqn (12.1), where the mass (or molar) compositions of the states are used instead of the chemical potentials, which is typically sufficiently accurate for engineering purposes.