- *Chemical reaction*. Chemical reaction can be used, in which the reagents are well soluble, but the product is lowly soluble in the applied solvent system. Often fast, ionic reactions are employed, which leads to extremely high supersaturations compared to the achievable supersaturation domains by other methods. This process is also called precipitation.

The crystallization process can be conveniently described in the phase diagram. Here we use the $c - T$ phase diagram for demonstration purposes, which can easily be adapted to antisolvent crystallization. Phase diagrams are not generally used for precipitation, due to high supersaturation and extremely fast kinetics, and evaporative crystallization, where the temperature is not an adjustable parameter as the boiling point is thermodynamically linked to the solvent boiling point, concentration and pressure. In the $c - T$ phase diagram (see Figure 2.2.) there are two curves: the solubility curve and the nucleation curve. The solubility curve is determined by thermodynamics and is a function of temperature. At the solubility curve the solution is in saturation equilibrium. The nucleation curve, which is also called the metastable limit, is thought of as a region where the nucleation rate increases rapidly rather than a sharp boundary (in contrast with the solubility line). These two curves divide the phase diagram in three important zones, namely the stable zone, under the solubility line; labile zone, over the metastable limit where both spontaneous nucleation and growth occurs, and the metastable zone. The metastable zone lies between the two curves, where the existing crystals are growing and there is no nucleation.

2.2.2 Nucleation

Nucleation is the formation of a solid crystalline phase. Nucleation mechanisms are commonly lumped into one of two categories: primary and secondary nucleation.[6]

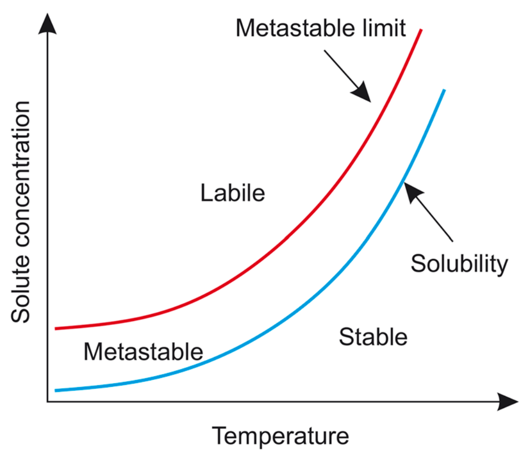

Figure 2.2 $c - T$ phase diagram with the solubility and metastable limit.