

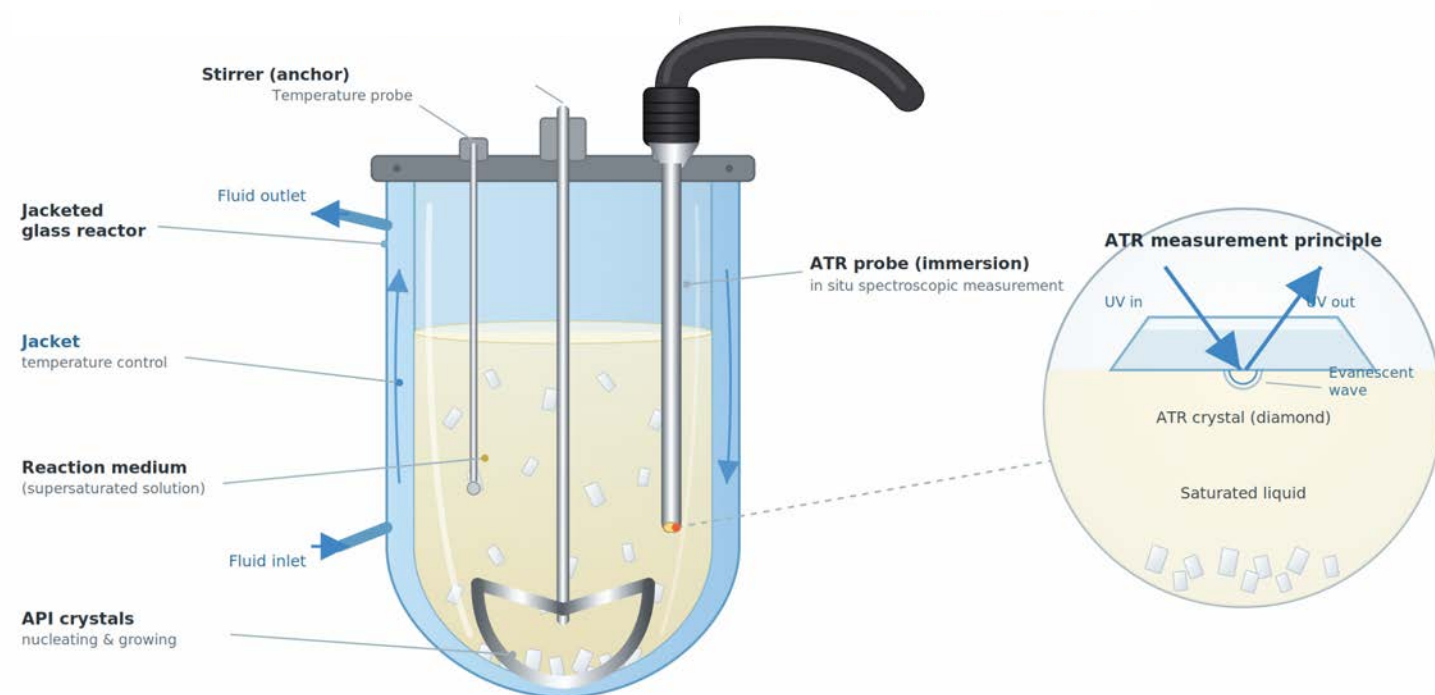


See the process in real-time to control it

Controlling the crystallization of an active ingredient governs its chemical quality and end-use properties (polymorph, particle size, filterability). The decisive lever is monitoring concentration and supersaturation, which are the driving force(s) of the process, in real-time. ATR-UV spectroscopy meets this need, giving simultaneous access to the solubility curve, the metastable zone width and concentration, and even extends to non-absorbing molecules through the refractive index. Simple, inexpensive and ATEX-compliant thanks to optical fibers up to 2 m long, it is a robust alternative to ATR-FTIR for optimizing an industrial crystallization process.

In situ monitoring of API crystallization by ATR spectroscopy

Jacketed glass reactor - direct measurement in the reaction medium



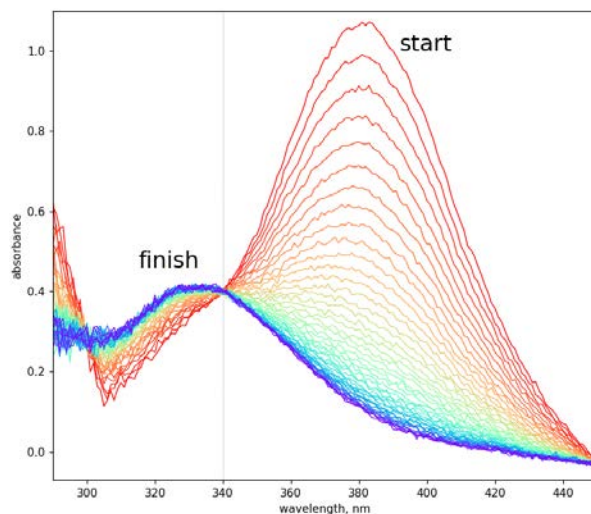
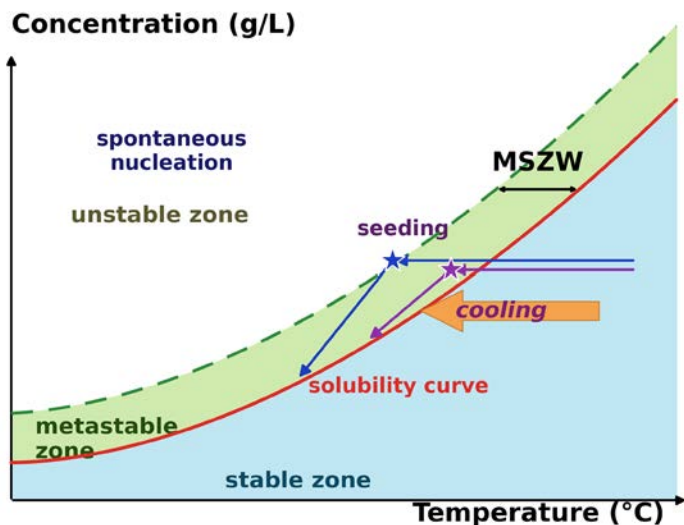
ATR probe – liquid phase

Only the dissolved API is sensed by the evanescent wave; suspended crystals do not contribute to the signal.
In-solution concentration measured continuously
→ supersaturation relative to the solubility curve.

Backscatter / Transmission in the visible

The appearance of the first crystals increases scattering (apparent absorbance).
Detection of the cloud point (onset of nucleation) and mapping of the metastable zone width (MSZW).

Example of process control to stay within the metastable zone UV-VIS measurements were performed using an ATR probe. The temporal evolution of the spectra can be readily tracked by monitoring two key wavelengths, 380 nm and 340 nm. At the start of the process, maximum absorbance is observed at 380 nm, while absorbance at 340 nm is minimal. Over time, the 380 nm peak diminishes and eventually disappears, whereas the 340 nm peak becomes increasingly prominent. Precise monitoring and control of concentration enables consistent crystal size in the production process.



In-line UV-Visible measurement for optimising crystallization control:

- Real-time monitoring of supersaturation
- Shorter cycle times and improved yield
- Improved product quality through controlled particle size and polymorphic form
- ICH Q8/Q11 compliant — directly deployable in classified areas



The ATEX option (Solvent Area)

- A customized ATEX zone II pressurized stainless-steel cabinet with Ex Op Is light source (IEC 60079-28)
- Passive certified optical probe connected with optical fiber

The multichannel option

- Monitoring of up to three channels simultaneously
- Cost advantage when several reactors must be monitored in one go: a single shared electronics unit for three probes
- Information advantage: combine an ATR probe for the concentrated liquid with a backscatter or transmission probe to characterize the particles (size and density)