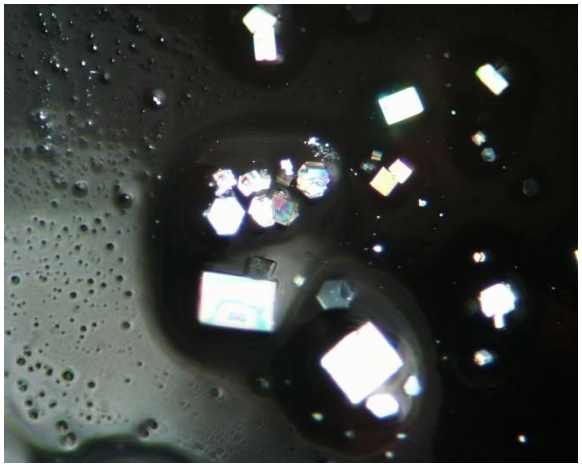
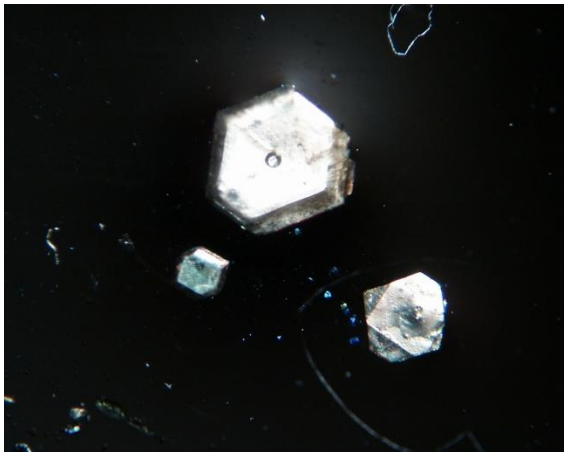
Recrystallization

- Purification
- Grow crystals suitable for XRD
  - Well formed
  - Single
  - Large enough (0.2 - 0.5mm in 2 of 3 dimensions)





Experimental considerations

- Solvent choice
- Nucleation sites
- Mechanics
- Time

Solvent choice

- Do
  - aim for moderate solubility
  - remember “like dissolves like”
- Don’t
  - use “floppy” solvents, e.g. long alkyl chains
  - use highly volatile solvents
- Typical solvents include
  - acetonitrile, MeOH, EtOH, iPrOH, ether, MeCl2, ethyl acetate, toluene, and THF to name a few.

Nucleation sites

- Crystallization begins at defect sites
  - scratches in glassware
  - dust or lint
- A few sites are necessary
- Too many will result in small crystals

Mechanics

- Crystal growth takes a steady hand!
  - re-dissolve the sample
  - knock off crystallites
- Avoid areas prone to mechanical vibration
- Don’t constantly “check in” on your samples

Time

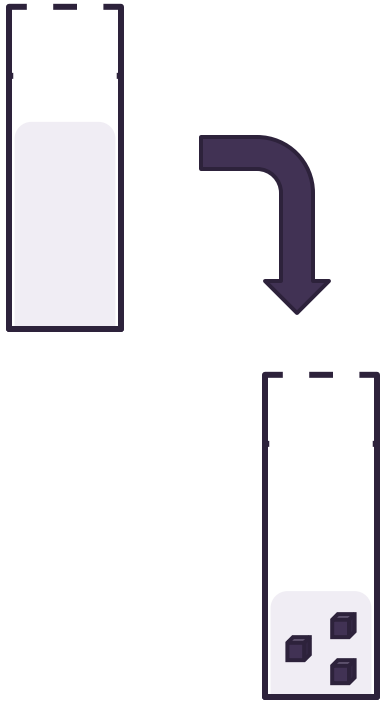
- Crystal growth takes time
  - reduces lattice defects and twins
  - results in larger crystals
- Best results appear within 2 days to 2 weeks
- Sometimes these “rules” are broken

Crystallization Techniques

- Many methods, easiest involve solvents
- Prepare to use a lot of material
- Develop a solubility profile

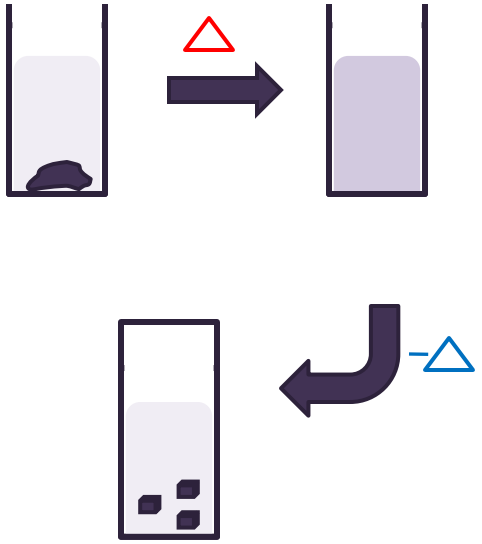
Slow Evaporation

- Dissolve sample to near saturation
  - use solvents in which sample is only moderately soluble
- Loosely cover vial
  - 1 dram vials with holes poked in a plastic cap
- Wait
  - depends on vapor pressure of solvent
  - 2 days to 2 weeks.



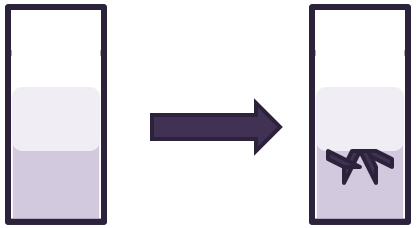
Slow Cooling

- Dissolve sample in hot solvent
  - good for material that is insoluble at room temperature
- Cap off and allow to cool slowly
  - moderate temperature with oven, heating pad, cotton wool, water bath, or a warm spot in the lab



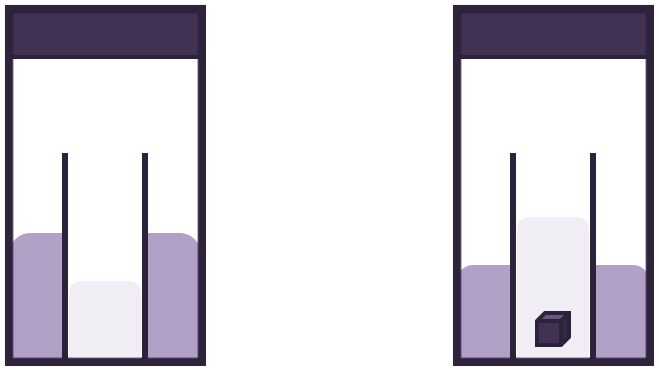
Layering/Solvent Diffusion

- Use two solvents, S1 and S2
  - material is soluble in S1 but not S2
  - S2 is less dense than S1
- Dissolve in S1 in vial, slowly add S2 to form a layer on top
- Crystals grow at the S1-S2 interface as solvents diffuse slowly.
- $MeCl_2/Et_2O$ popular combination



Vapor Diffusion

- similar to solvent diffusion, but uses separate vials for S1 and S2
  - dissolve material in S1, in open small vial
  - place small vial in larger vial with S2 and cap off
- must choose solvents carefully



Other Techniques

- Sublimation
  - Sample loaded into tube under vacuum.
  - Thermal gradient applied
- Hydrothermal / Solvothermal
  - Materials dissolved in solvent, sealed in container
  - Subjected to moderate heat for a period of time
- “Protein” methods
  - Hanging drop
  - Use of precipitant

How to coax the crystals out

- Try many different solvents
  - run recrystallizations in parallel
  - build a solubility profile
- Combine methods
  - combinations or trios of solvents
  - slow cooling + evaporation
- Alter environmental conditions
  - leave in the fridge or on a windowsill
  - use a different vial
  - set up a thermal gradient
- Functionalize