Kinetic modeling of dissolution of salicylic acid with in situ ATR UV-vis spectroscopy

Chun H. Hsieh [a], Julien Billeter [a], Mary Ellen P. McNally [b], Ron M. Hoffman [b], Paul J. Gemperline [a]

[a] Department of Chemistry, East Carolina University, Greenville, NC 27858

[b] E.I. DuPont de Nemours and Co., Inc., Crop Protection Products and Engineering Technologies, Stine Haskell Research Center, Newark, DE 19711

E-mail: hsiehc07@students.ecu.edu

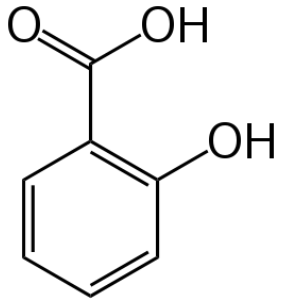
PROCESS ANALYTICAL TECHNOLGIES (PAT)

- **Food and Drug Administration (FDA)**
  - Design, control and monitoring of pharmaceutical manufacturing processes
- **Attenuated Total Reflectance Ultra-Violet visible (ATR UV-vis) spectroscopy**
  - Monitoring of concentration in liquid phase (e.g. reaction, dissolution, crystallization…)
- **Near-Infrared (NIR) diffuse reflectance spectroscopy**
  - Quantification of solid fraction (e.g. degree of saturation in dissolution and crystallization processes)

NIR transflectance probe

RESEARCH PROJECT

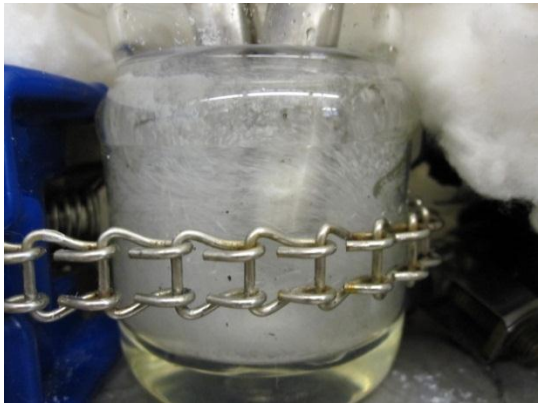
- Develop a kinetic model for the dissolution of salicylic acid in a solvent mixture (52% ethanol, 48% water), based on a power law equation



$$r = k(c_{sat} - c)^n$$

- Use ATR UV-vis and NIR diffuse reflectance spectroscopy to monitor liquid and solid phases

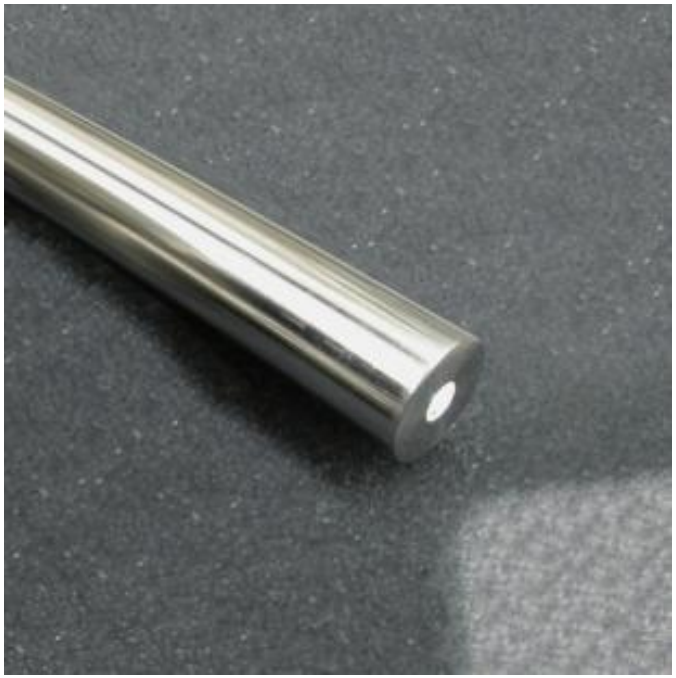
- Optimize the rate constant (*k*) and the exponent (*n*) of the power law equation



SPECTROSCOPIC PROBES

NIR Spectroscopy

Diffuse Reflectance Probe



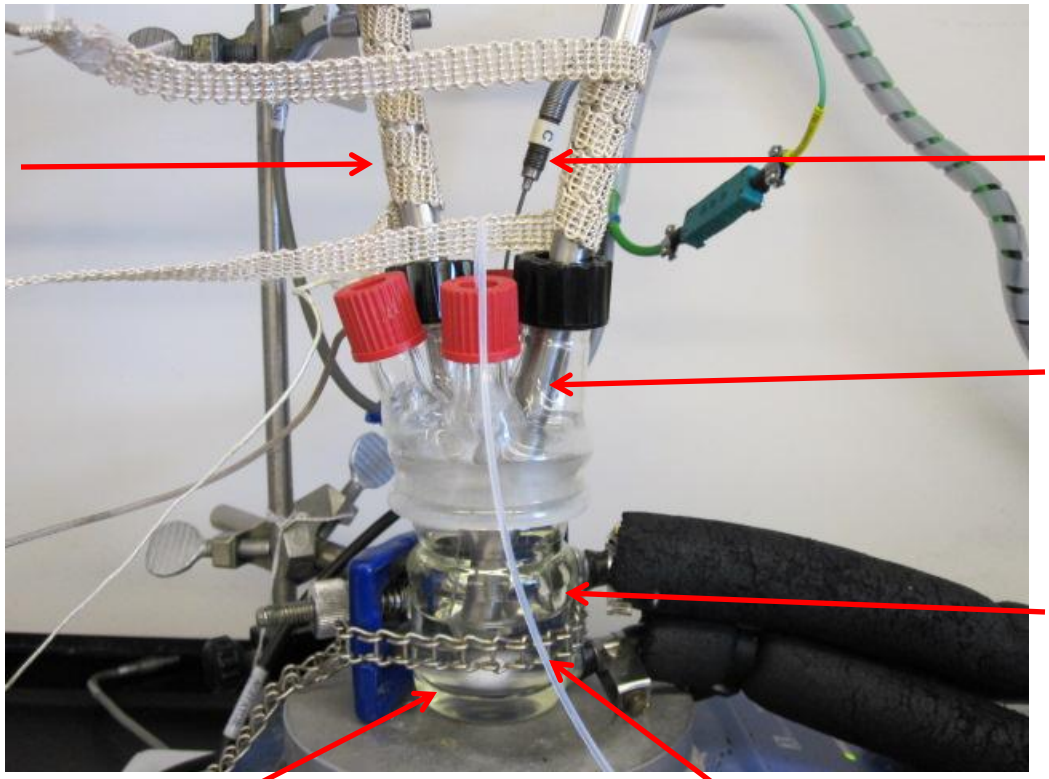
1100 nm - 2500 nm

ATR UV-vis Spectroscopy

ATR Probe (sapphire crystal)

200 nm - 1020 nm

IN-HOUSE MINIATURE SEMI-BATCH REACTOR



KINETIC MODELING & DATA ANALYSIS

Beer's Law

$$\mathbf{Y} = \mathbf{c}\,\mathbf{a}$$

Dissolution Power Law

$$\frac{\mathrm{d}c}{\mathrm{d}t} = r = k(c_{sat} - c)^n$$

Change of Mass

$$\frac{\mathrm{d}m}{\mathrm{d}t} = -MW \cdot v \cdot r$$

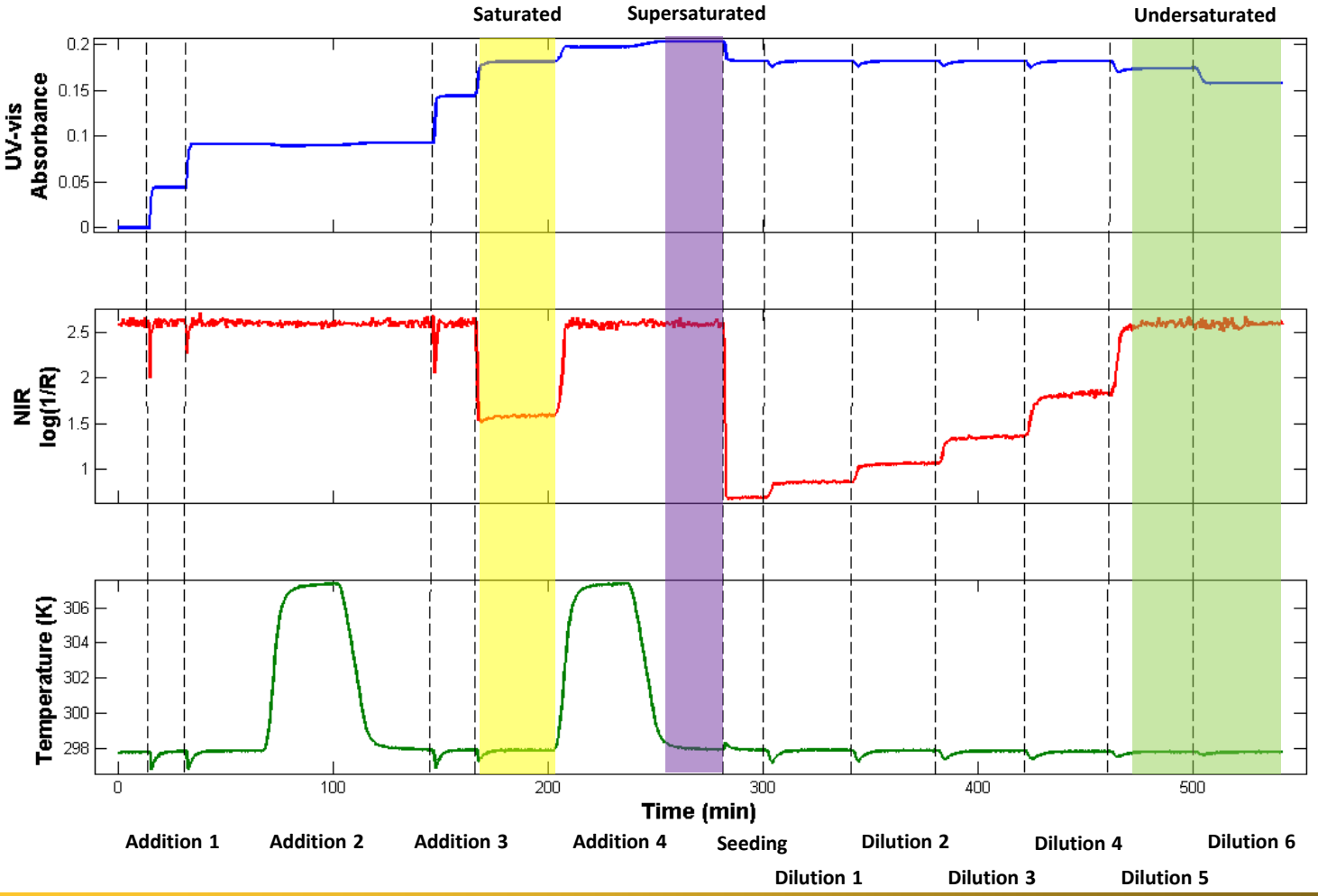
Least Squares Optimization

$$\min_{k,n} \sum_{i=1}^{nt} \sum_{j=1}^{nw} \left(y_{i,j} - \mathbf{C}\,\mathbf{C}^{+} y_{i,j}\right)^2$$

Kubelka-Munk Transformation

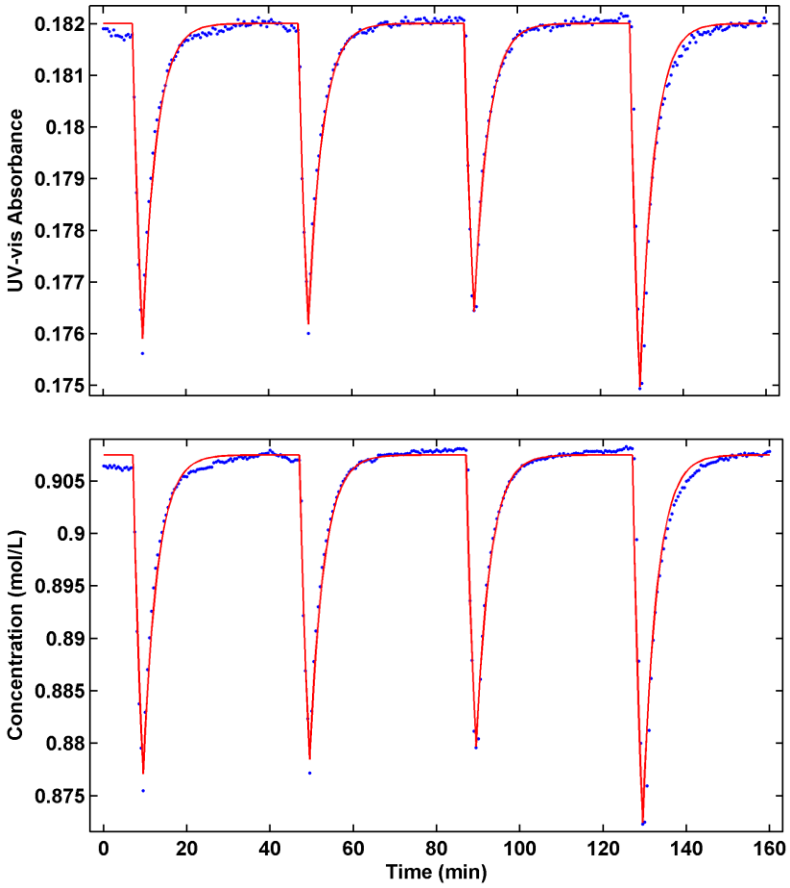
$$F(\mathbf{R}) = \frac{(\mathbf{1} - \mathbf{R})^2}{2\mathbf{R}}$$

DISSOLUTION OF SALICYLIC ACID

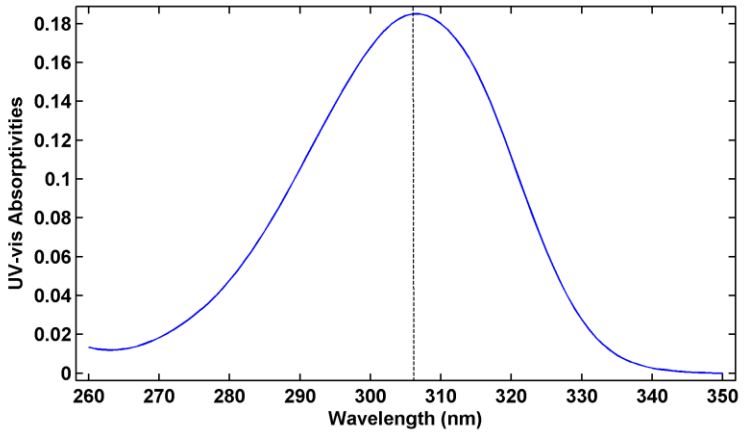


KINETIC MODELING OF LIQUID PHASE (UV-vis)

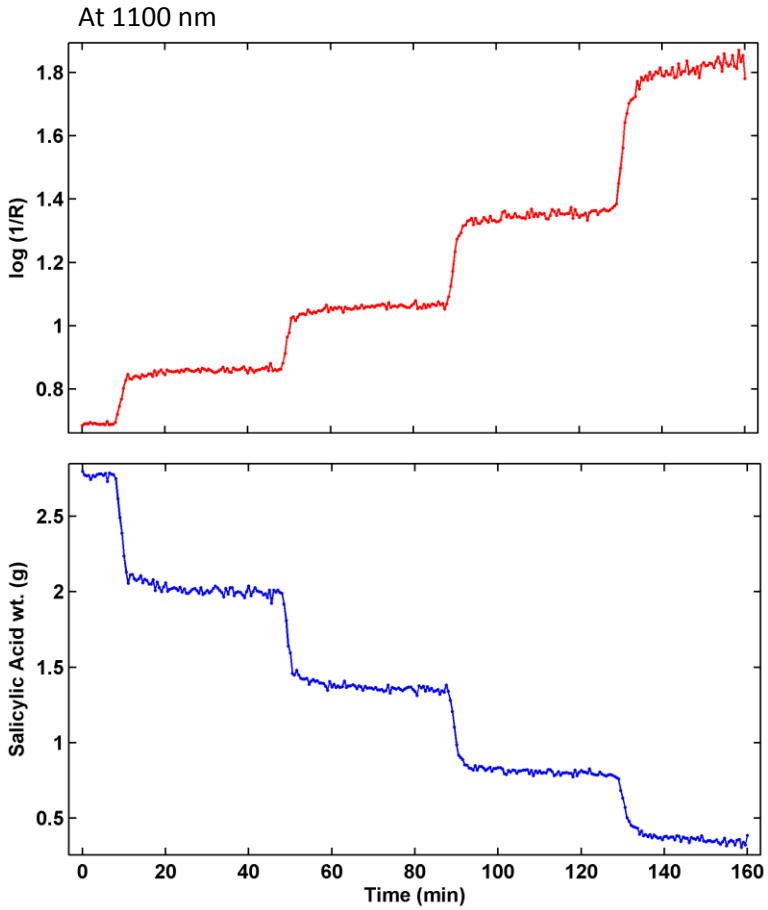
At 307 nm

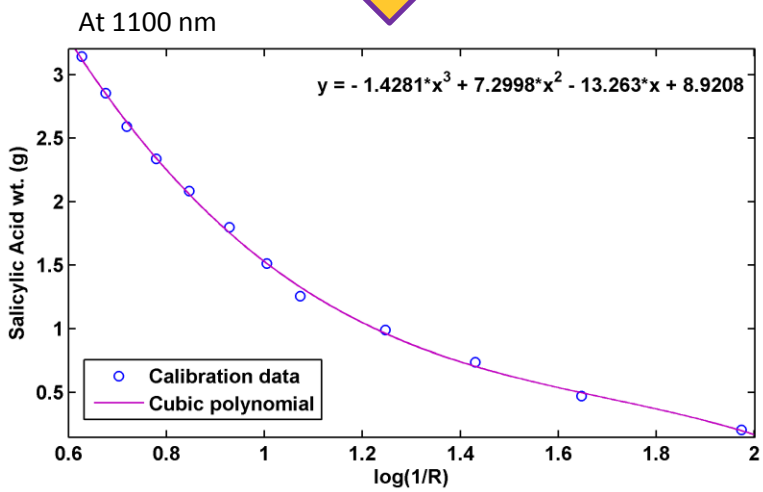


$k = 0.2811\ L^{n-1}/(mol^{n-1}min)$, $n = 0.99$



DISSOLUTION SEEN FROM SOLID PHASE (NIR)





CONCLUSION & FUTURE WORK

- ATR UV-vis and NIR diffuse reflectance spectroscopy were used to monitor liquid and solid fractions of the dissolution of salicylic acid in a solvent mixture
- A power law equation was successfully used to model the first four dissolution steps for the liquid phase, with k = 0.2811 $L^{n-1}/(mol^{n-1}min)$ and n = 0.99. This latter coefficient is in agreement with the range predicted by Fevotte et al.
- The solid phase still has to be modeled using the NIR diffuse reflectance data

* Fevotte G., International Journal of Pharmaceutics 241 (2002) 263-278

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