



# Electrochemical Calibration (ECC) of Dissolution Testing Apparatus

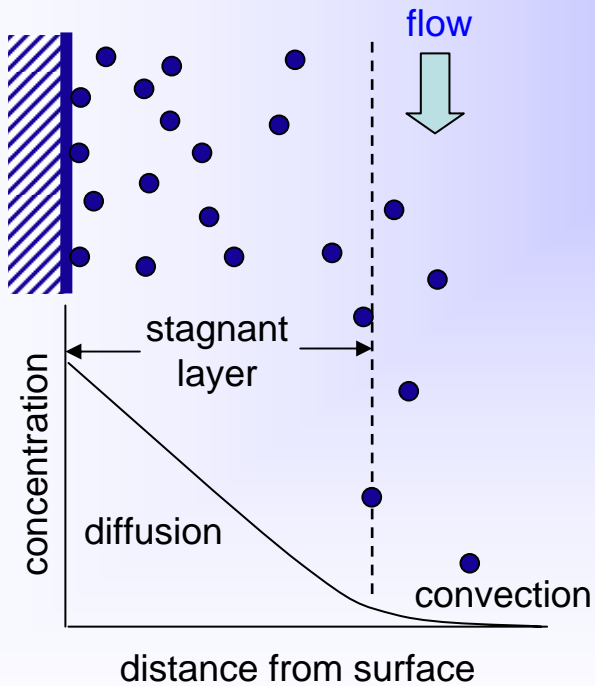
CVG-TPD Convention  
October 6, 2006

# ● ● ● Features of Electrochemical Calibrator

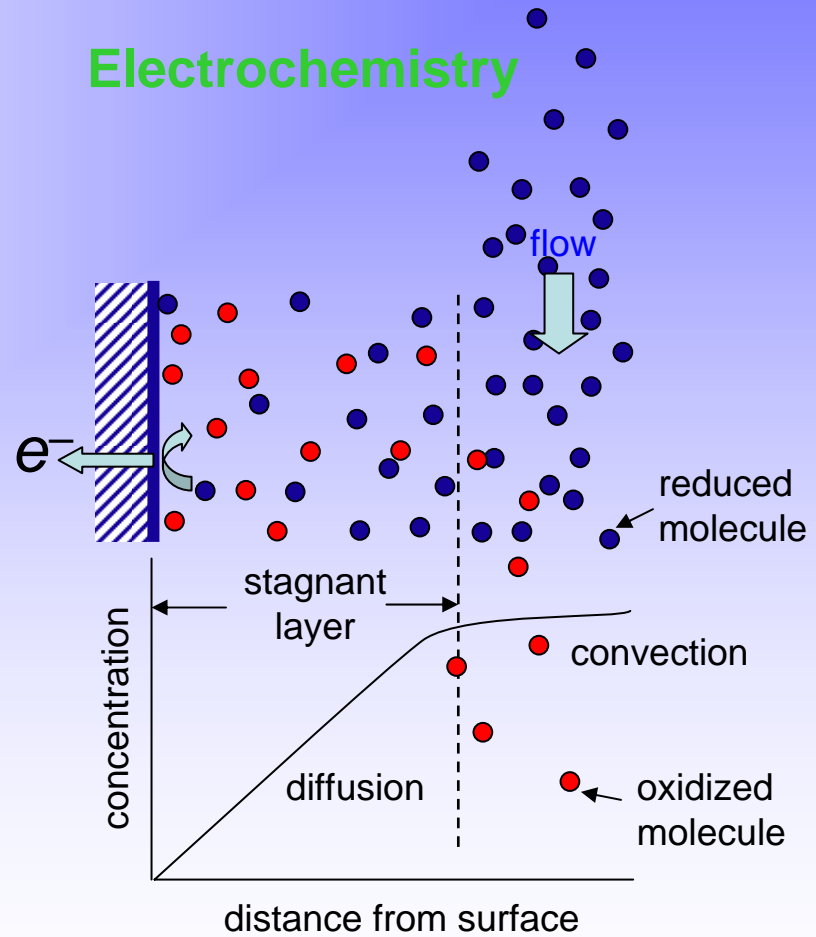
- Reusable
  - Long term cost reduction.
  - Calibrator variability is eliminated.
- Reproducible
- Diagnostic

# Principles - Same factors affect dissolution and electrochemistry.

## Dissolution



## Electrochemistry





# Principles

Electric Current  $\propto \sqrt{\text{Flow Rate}}$

Dissolution Rate  $\propto \sqrt{\text{Flow Rate}}$

# Electrochemical Calibrator (ECC)

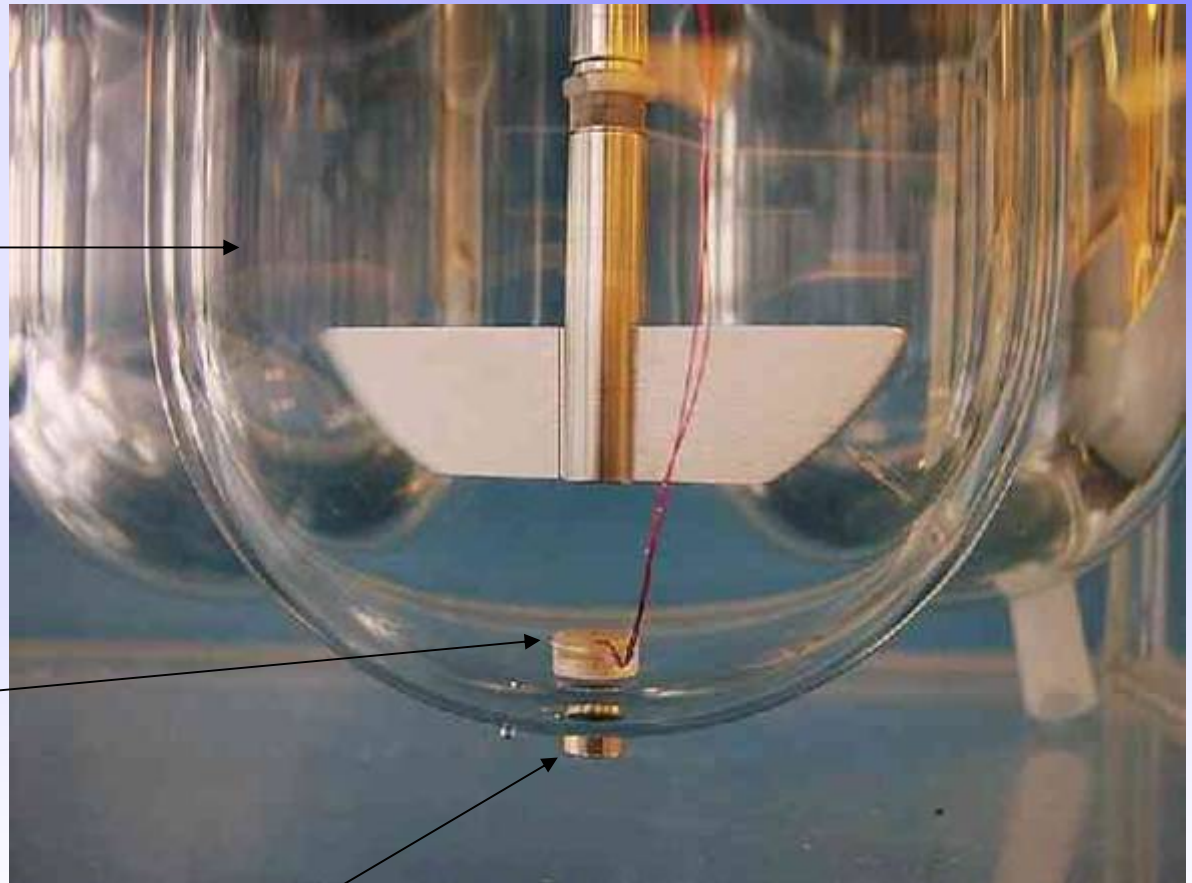
0.001 M Sodium Iodide  
(electrochemically active)

0.1 M Potassium Chloride (supporting electrolyte increases solution conductivity)

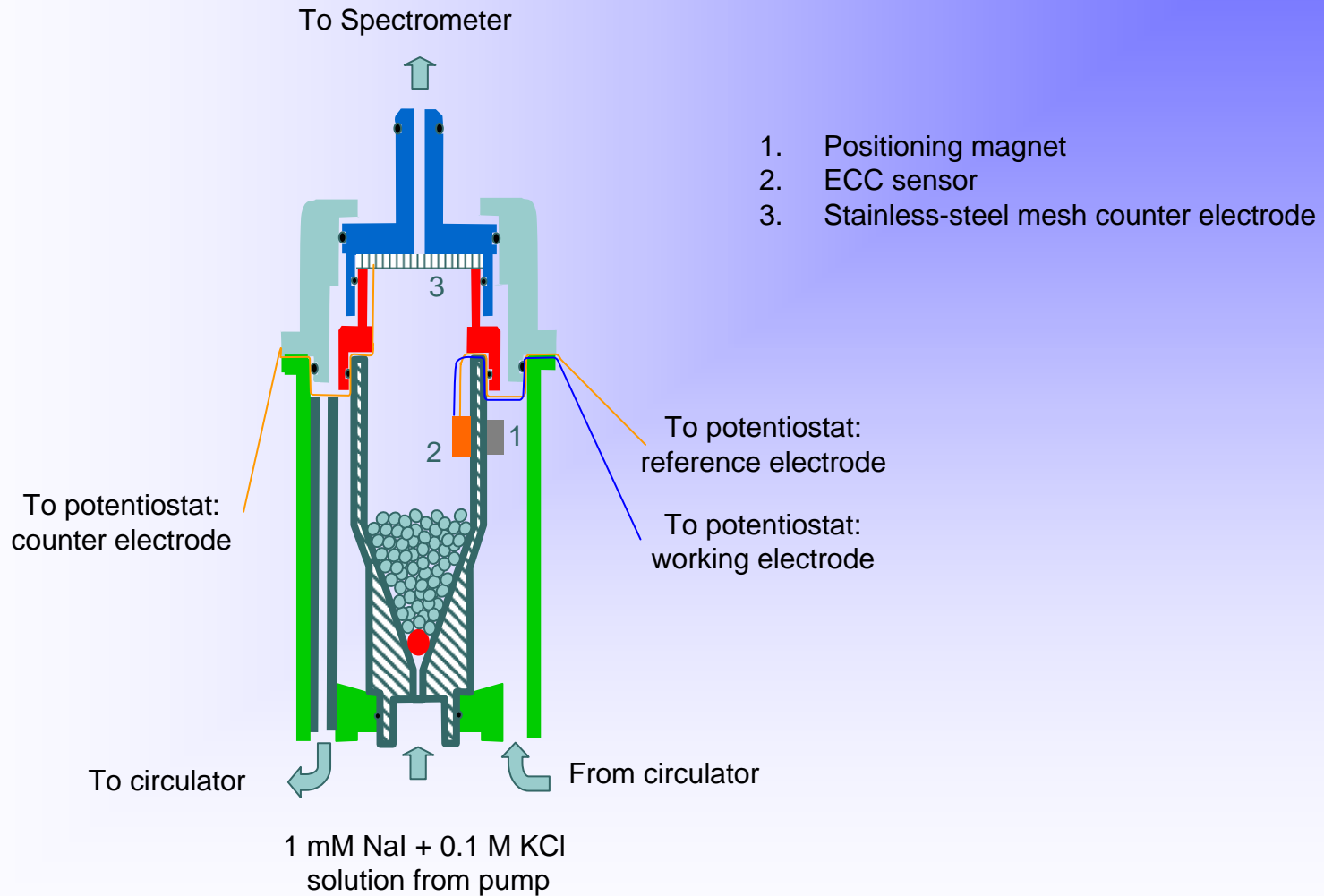
Electrode/Sensor

Positioning Magnet

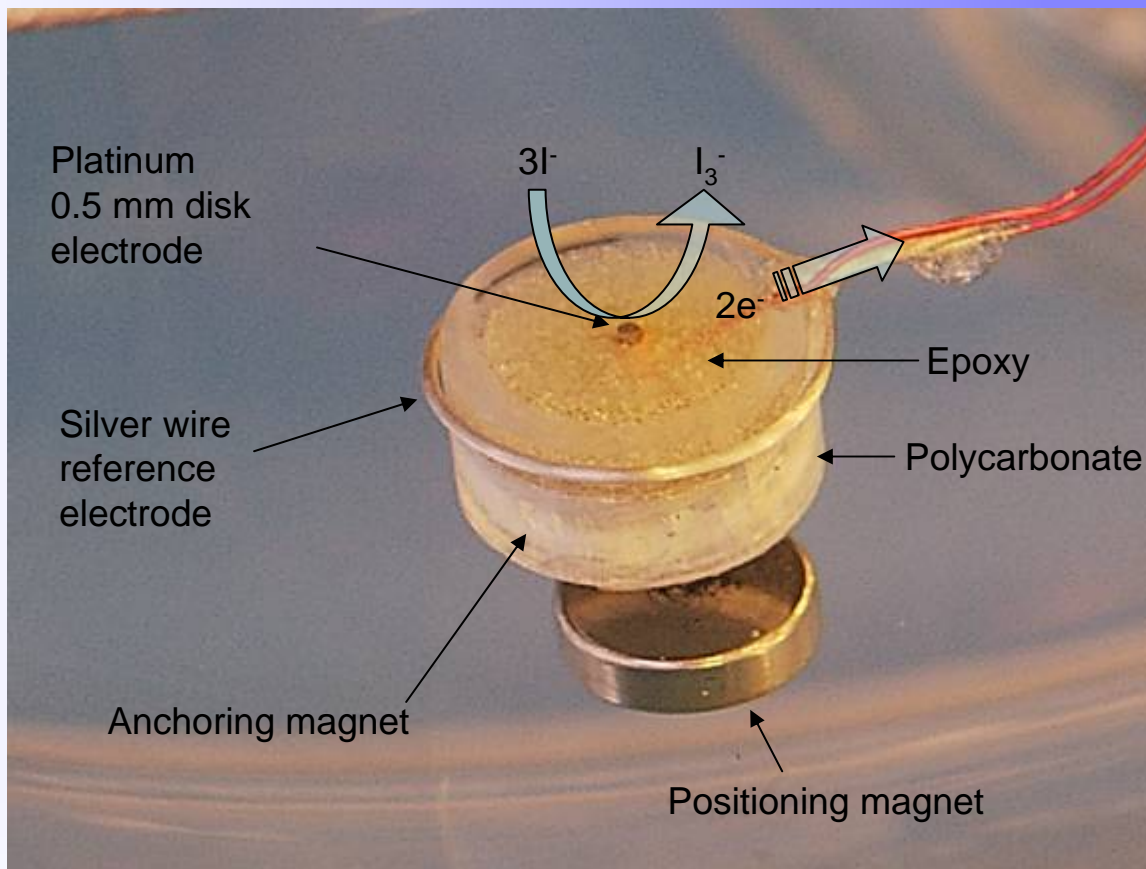
5



# ECC & Flow Through Apparatus



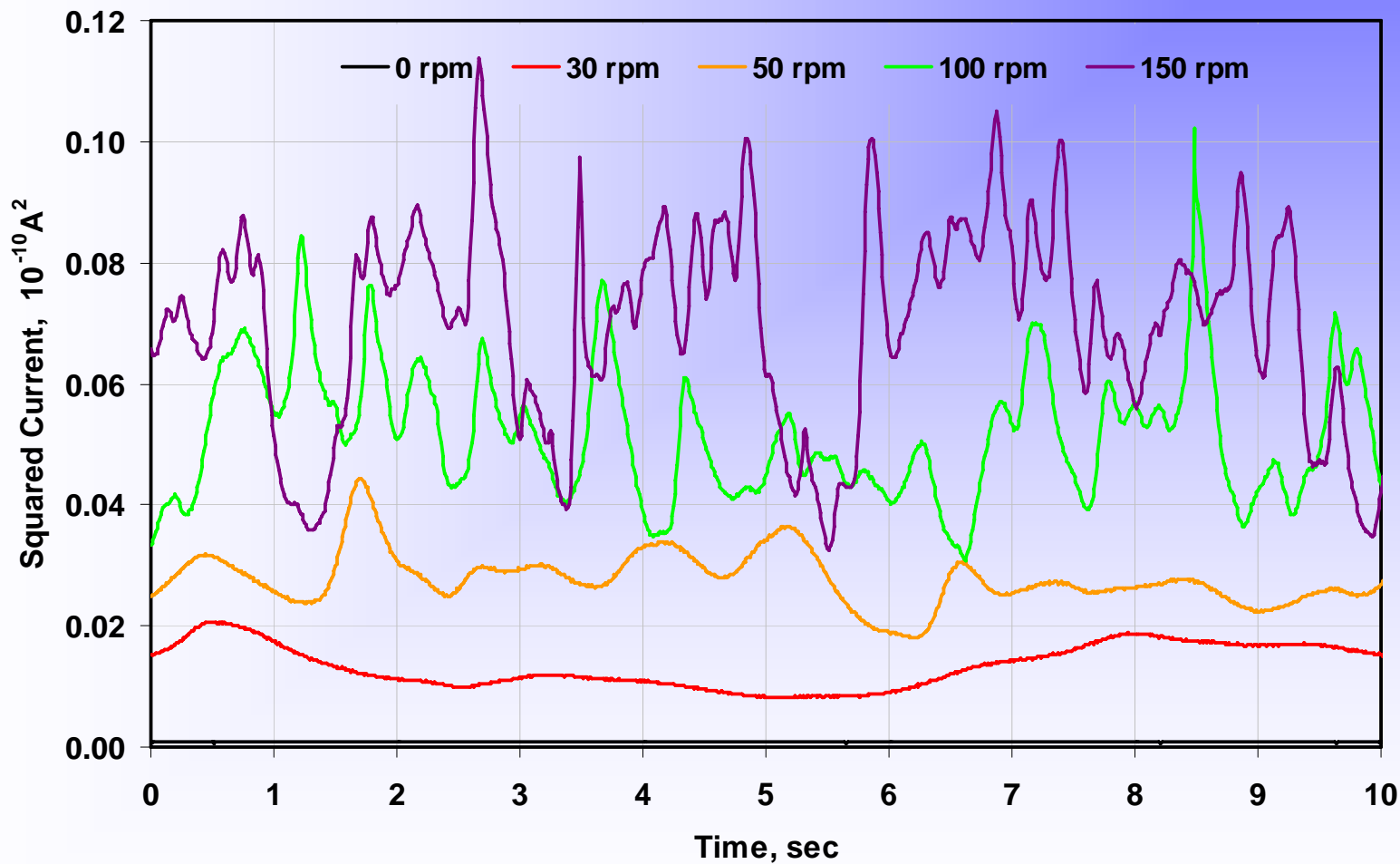
# ● ● ● Electrochemical Calibrator (ECC)



# ● ● ● ECC Signal and Diagnostics

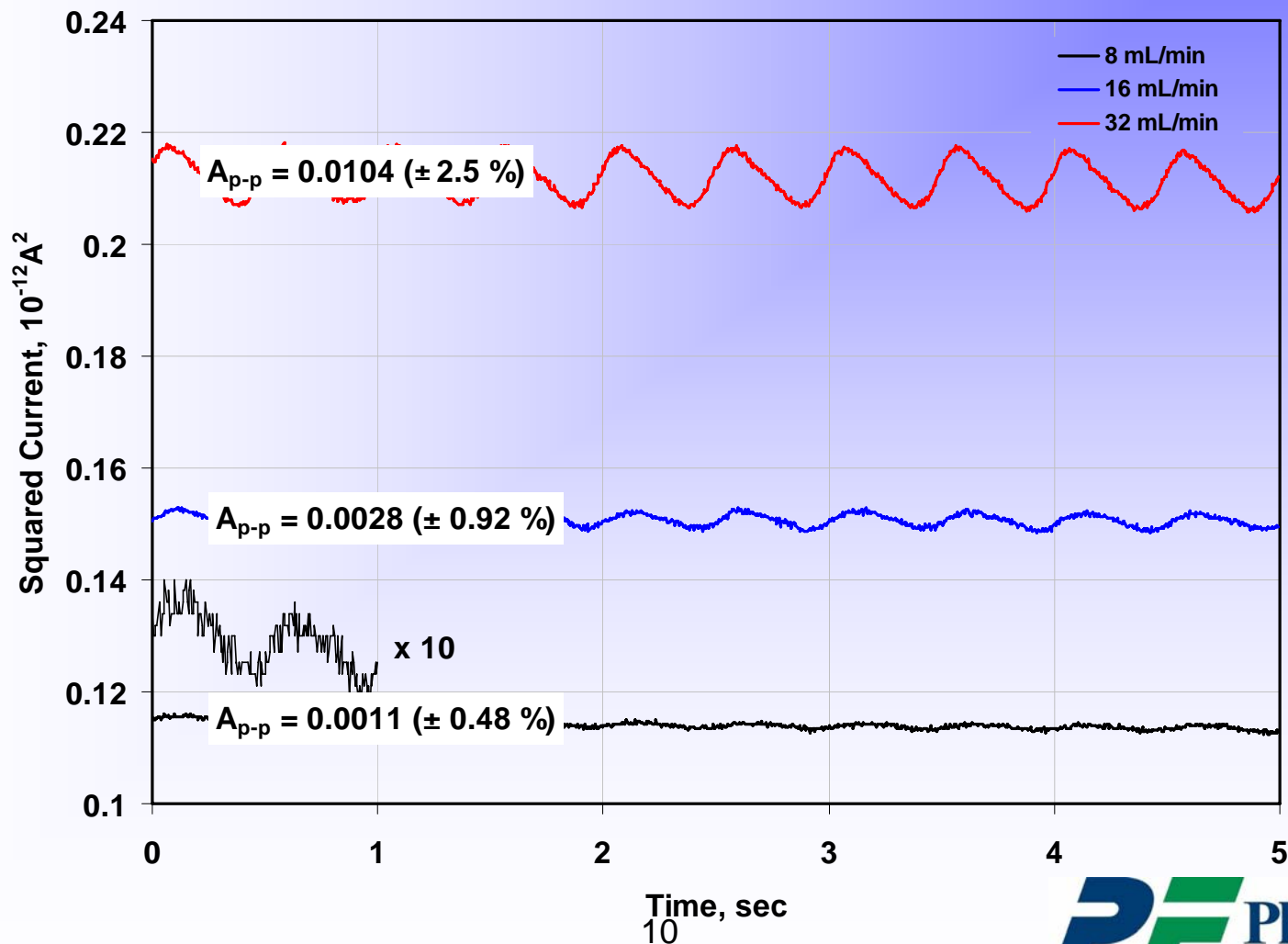
How can the signal be used to diagnose a malfunctioning dissolution apparatus?

# Electrochemical Signature

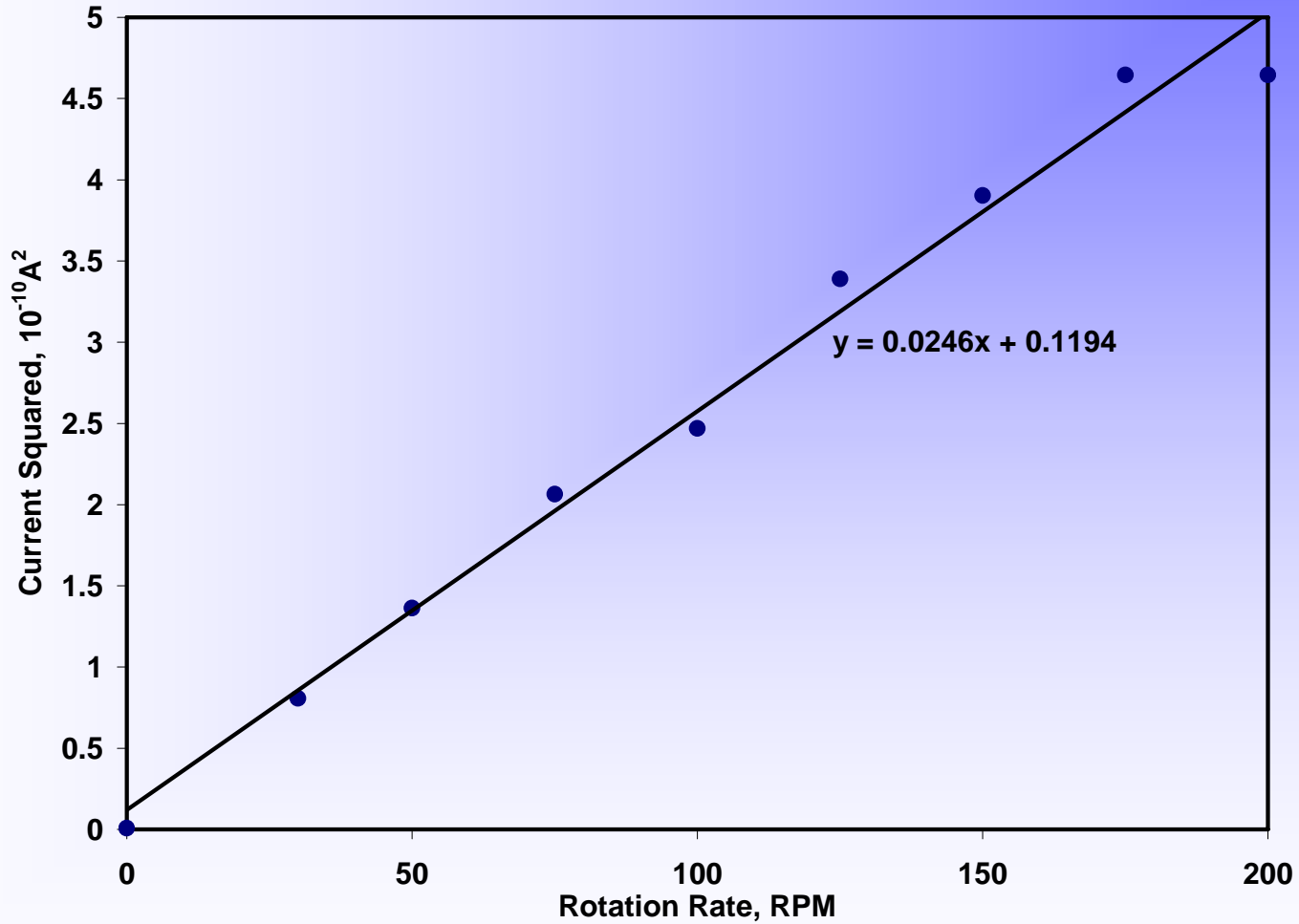


# Electrochemical Signature

## ECC Signature in USP Apparatus 4

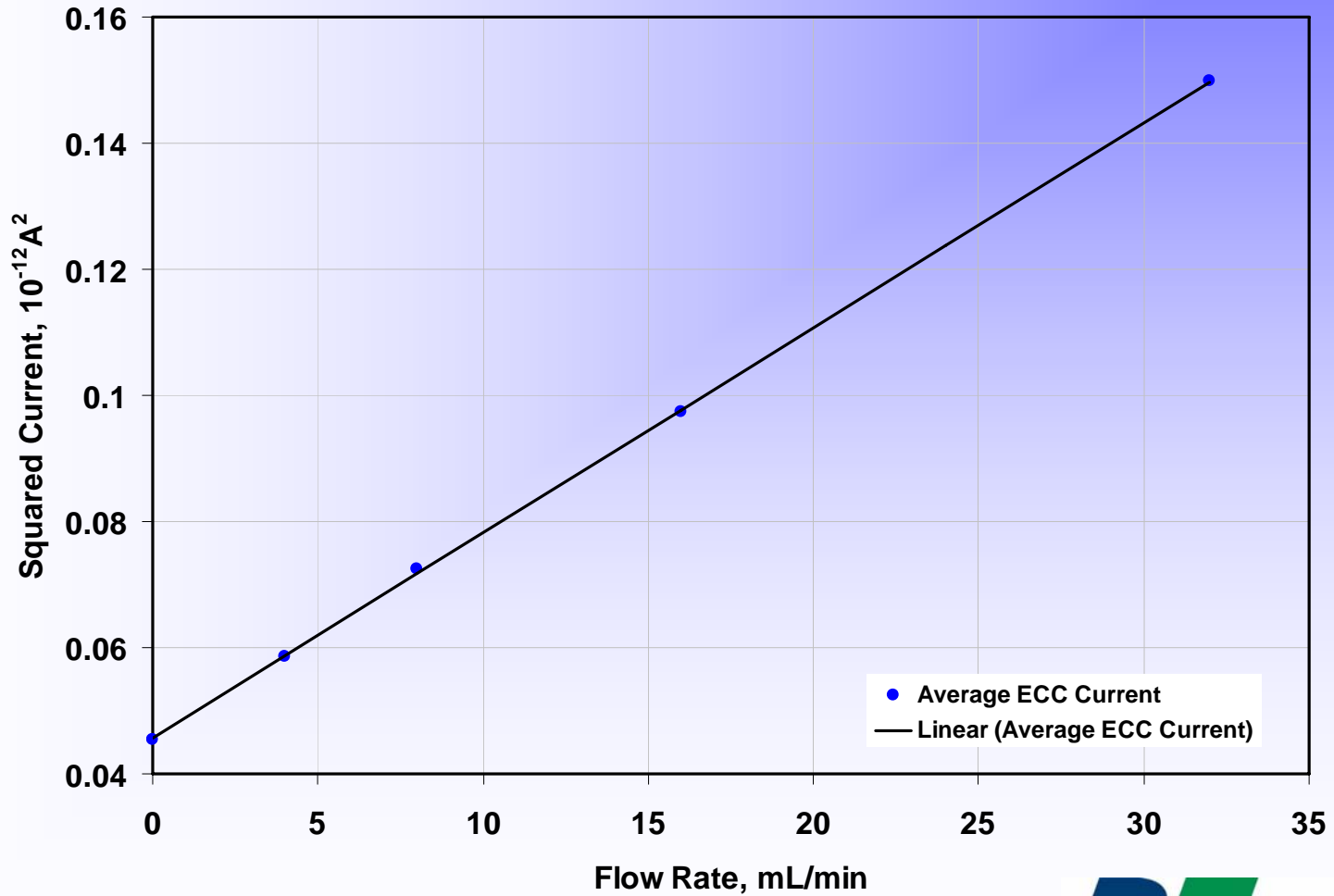


# Average Current vs. Rotation Rate



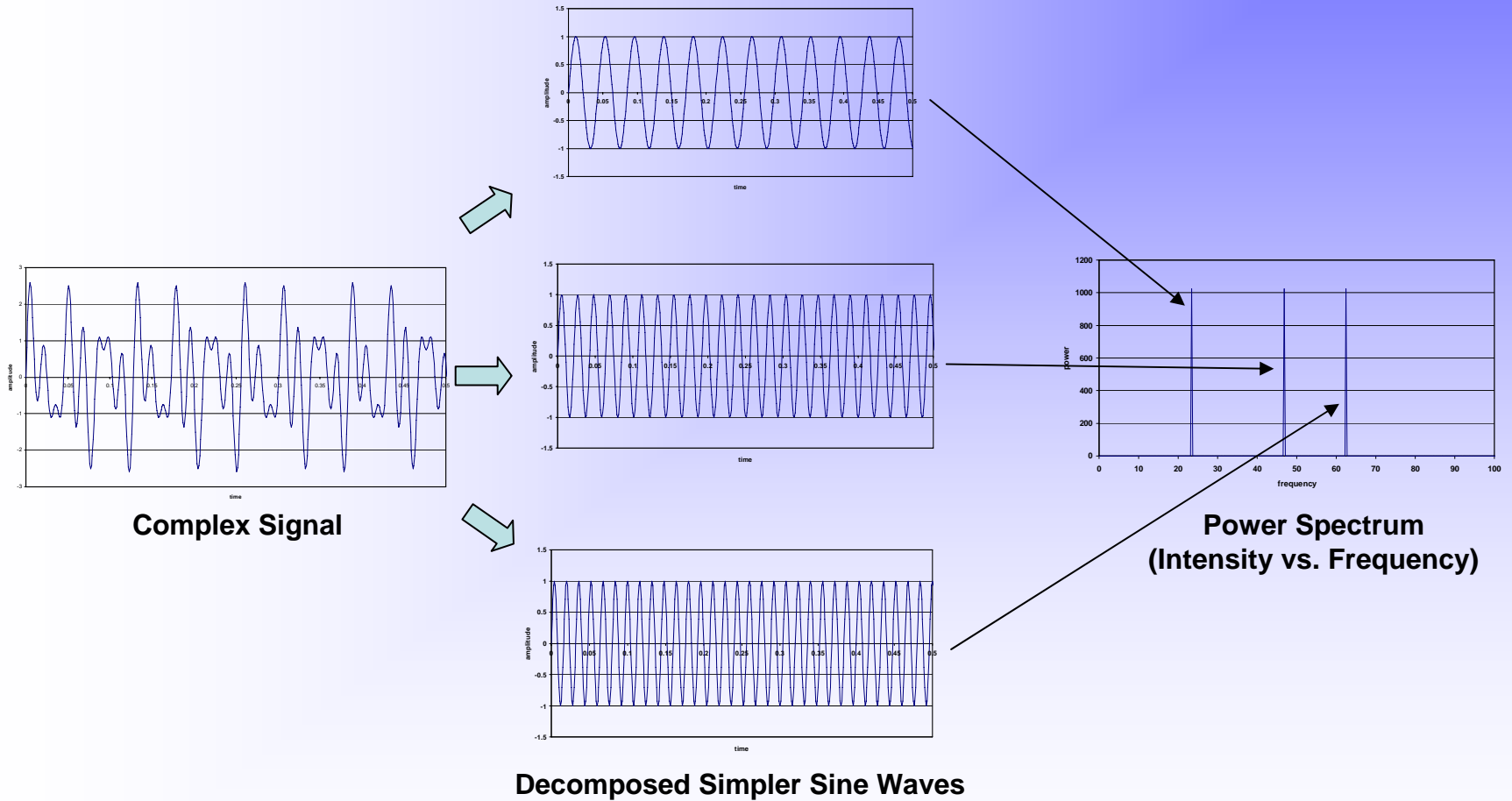


### Dependence of ECC Average Current on Flow Rate in USP Apparatus 4

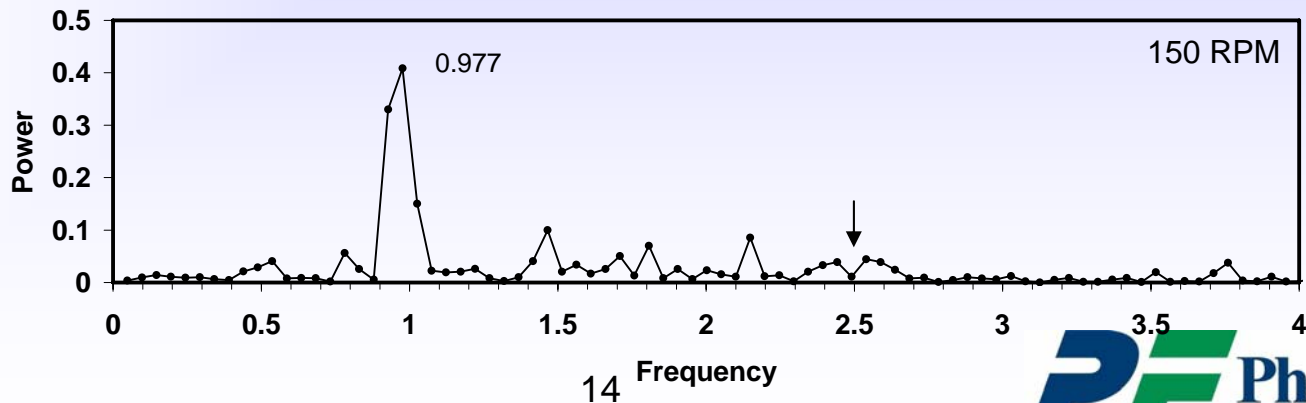
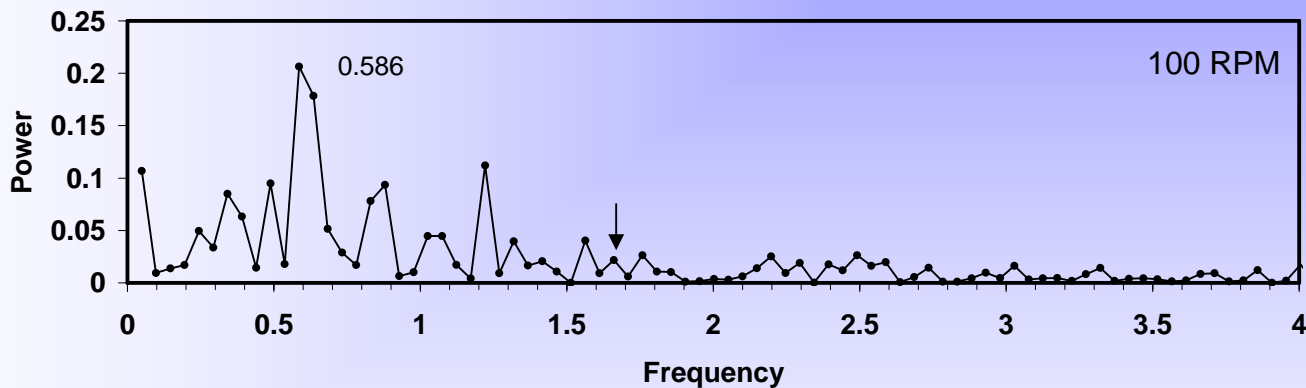
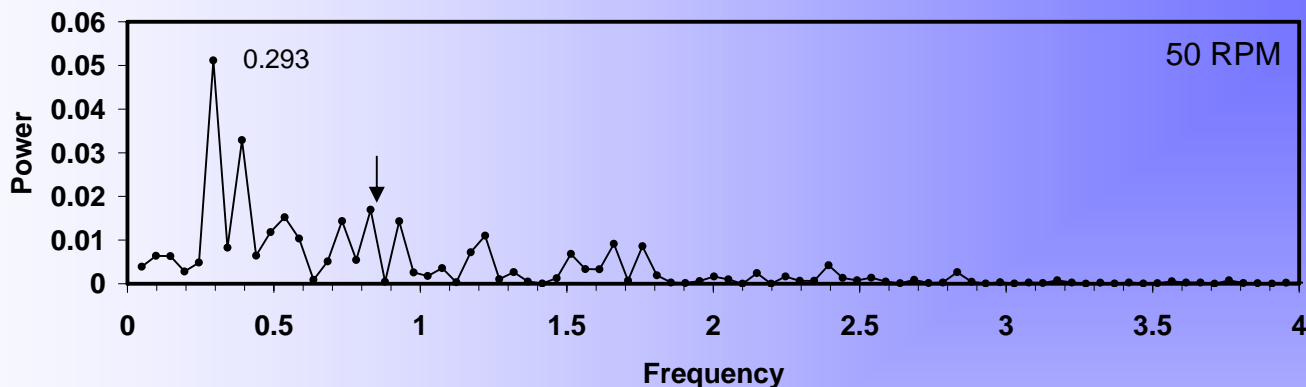




# Fourier Transformation



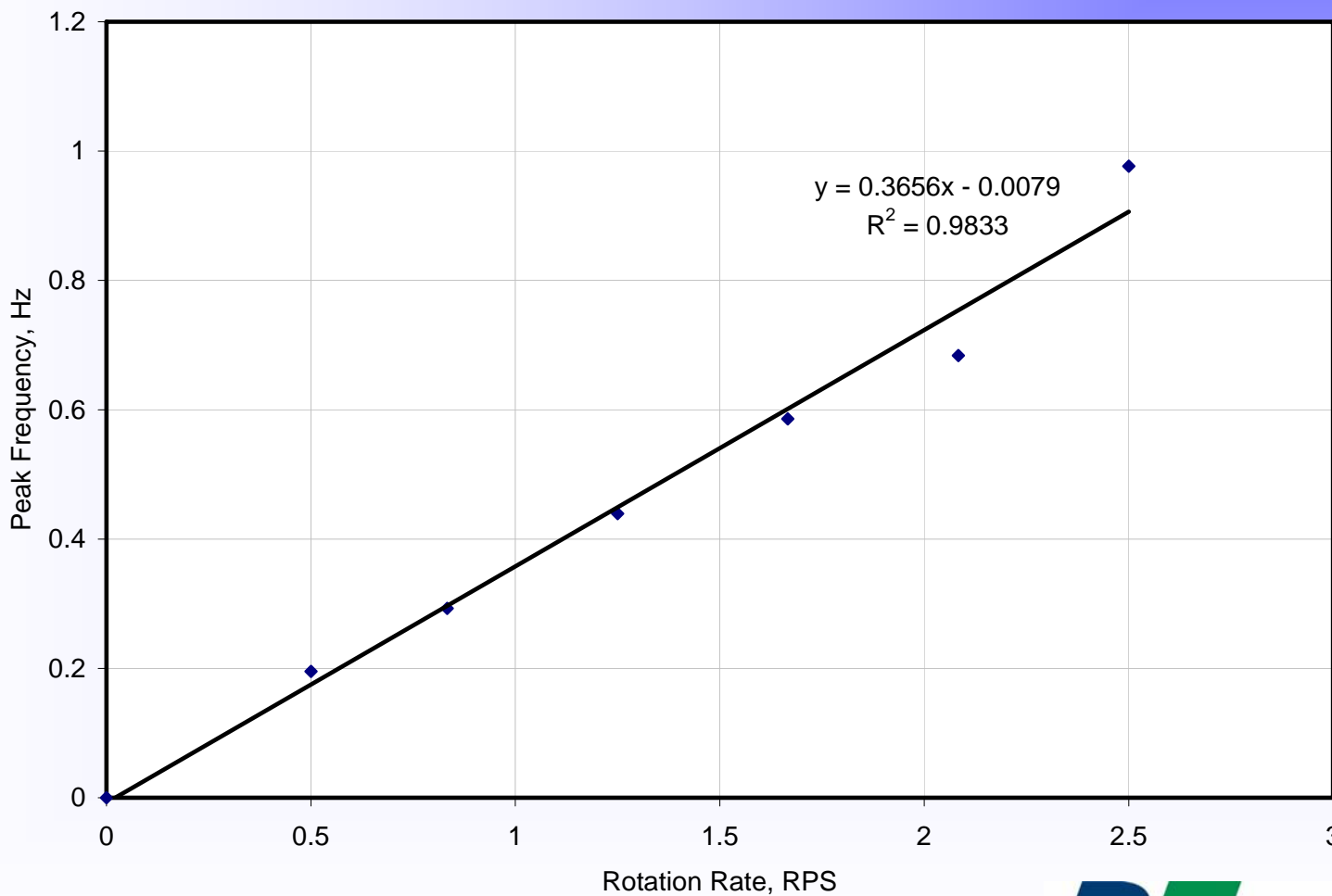
# “Spectrum” of a Dissolution Vessel



14 Frequency

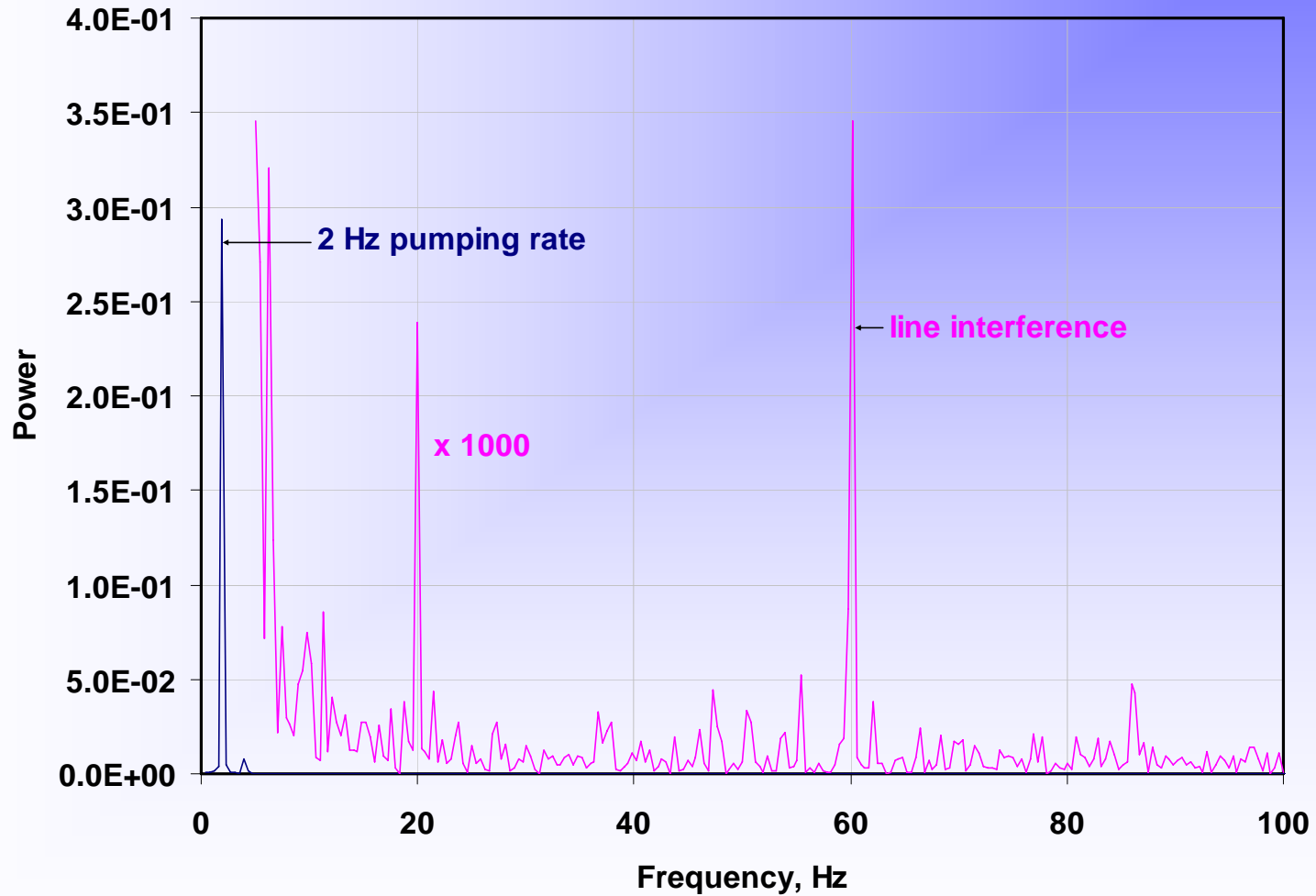
# Spectral Frequency vs. Rotation Rate

Effect of Rotation Rate on Peak Frequency

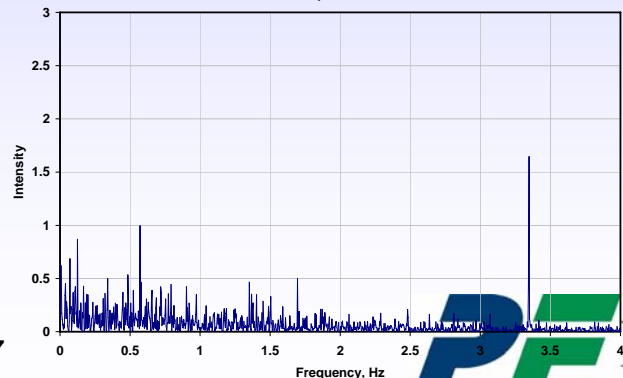
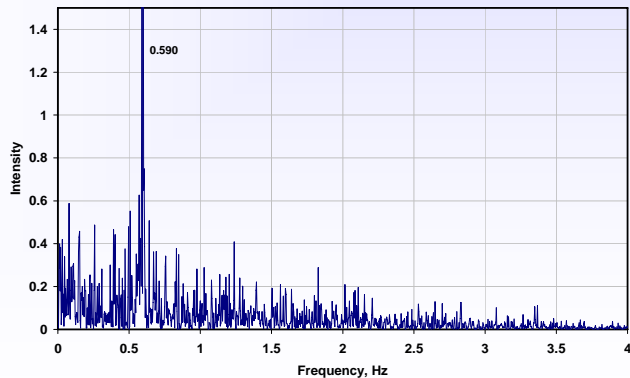
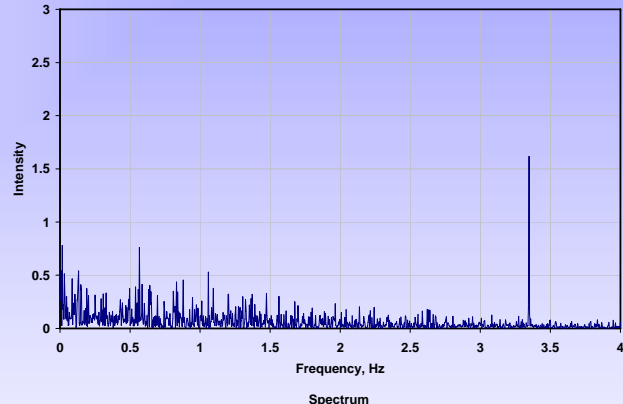
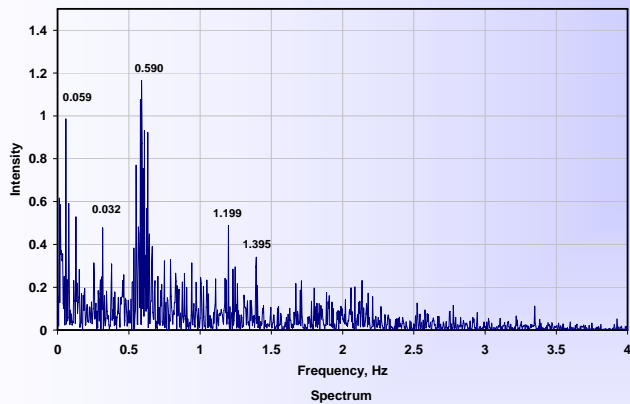
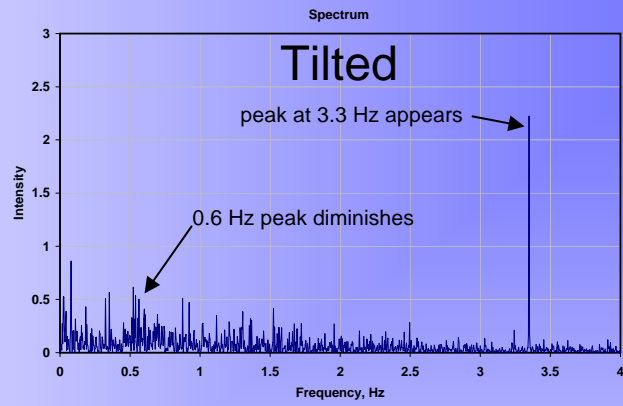
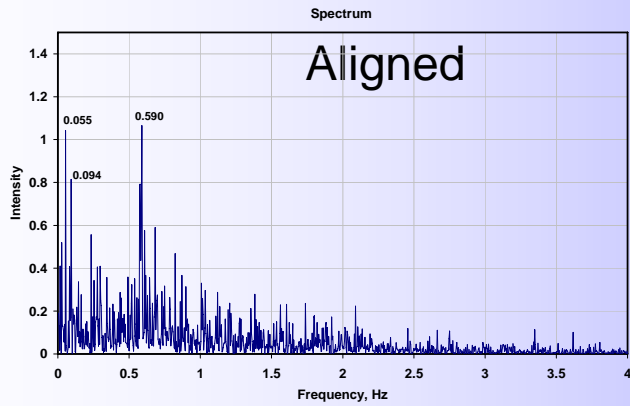




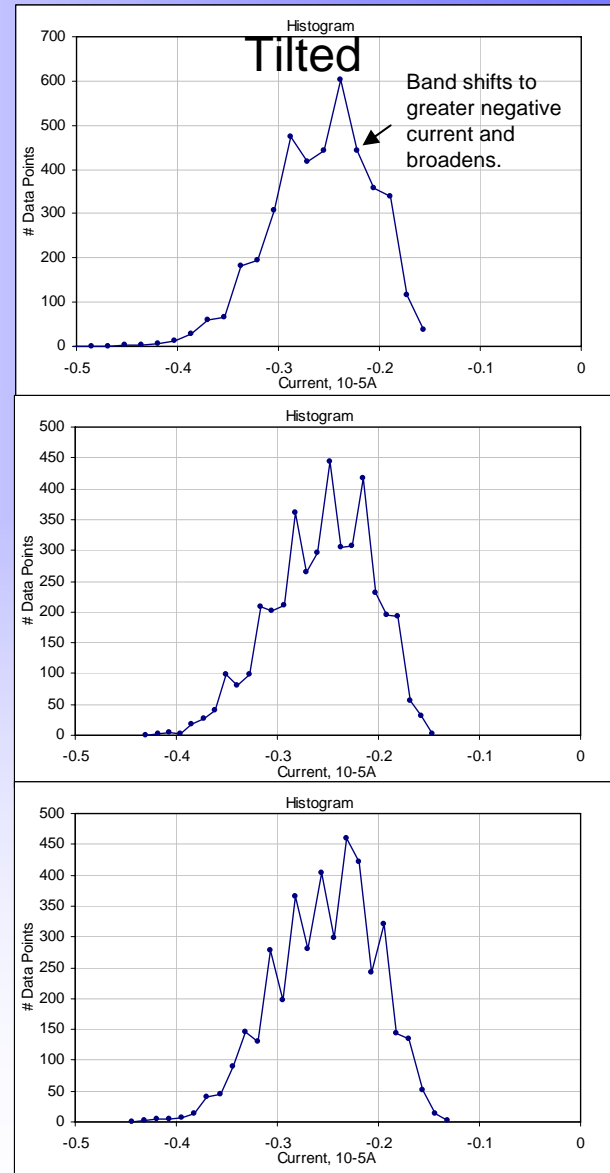
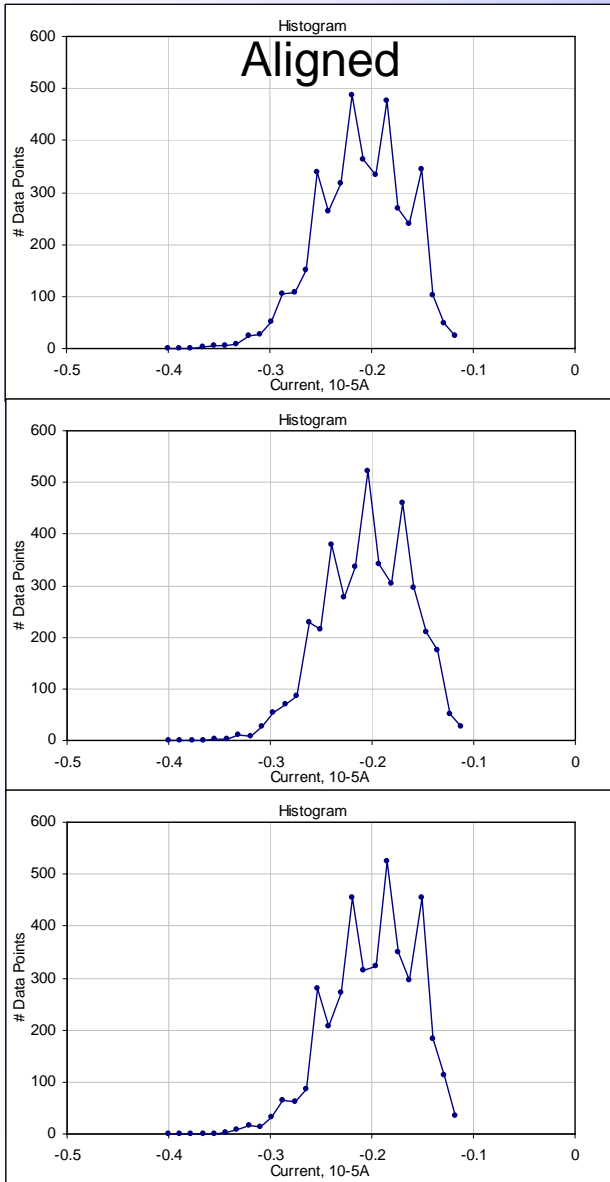
# “Spectrum” of a Flow-Through Cell



# Tilted Vessel

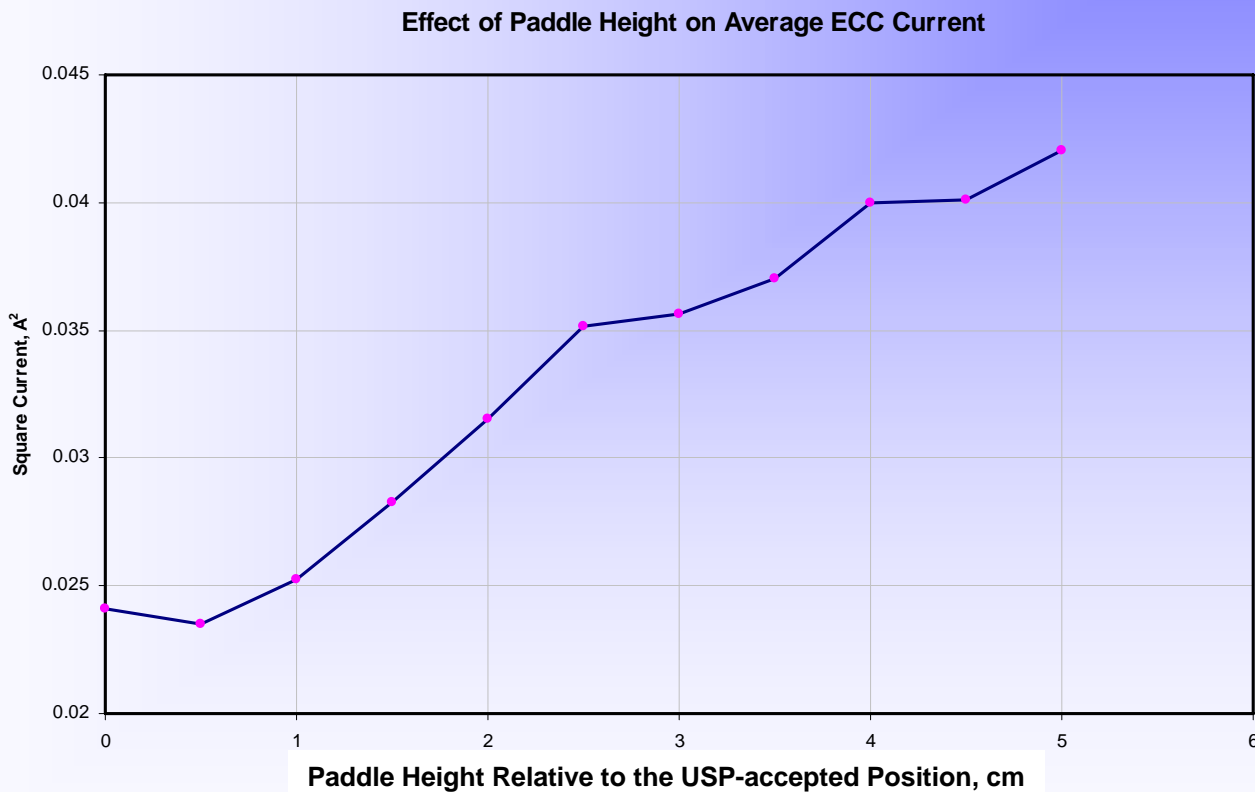


# Tilted Vessel

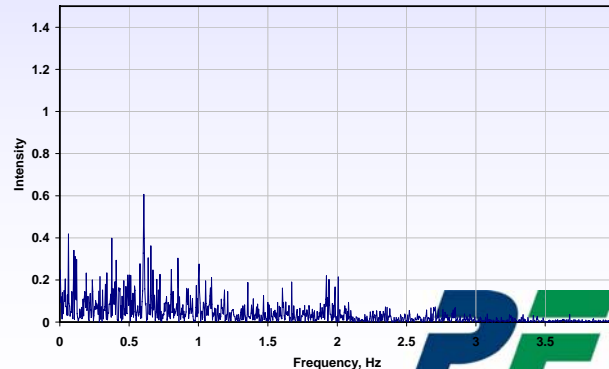
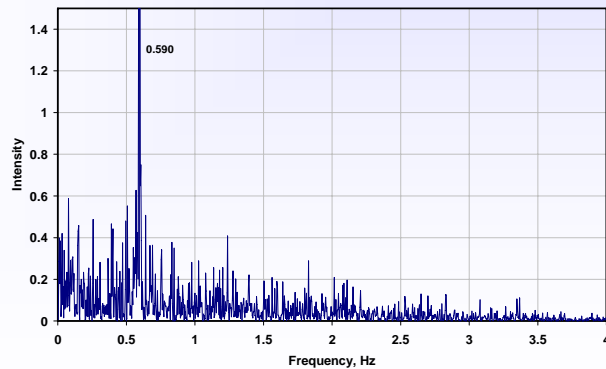
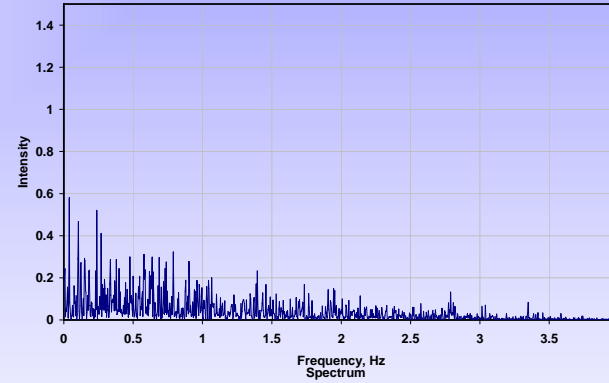
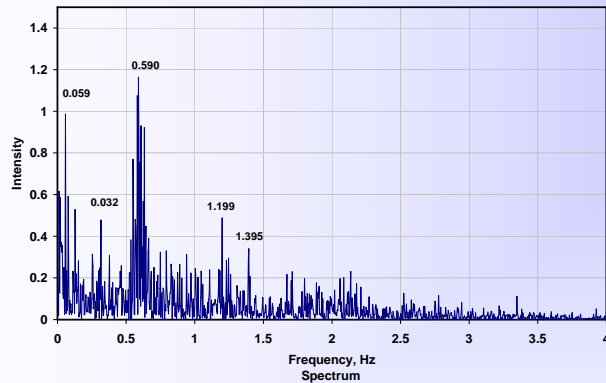
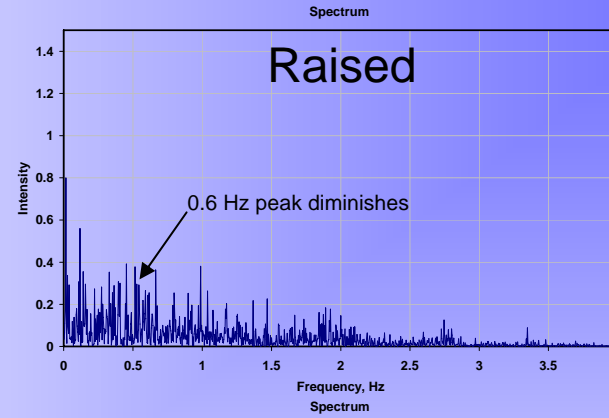
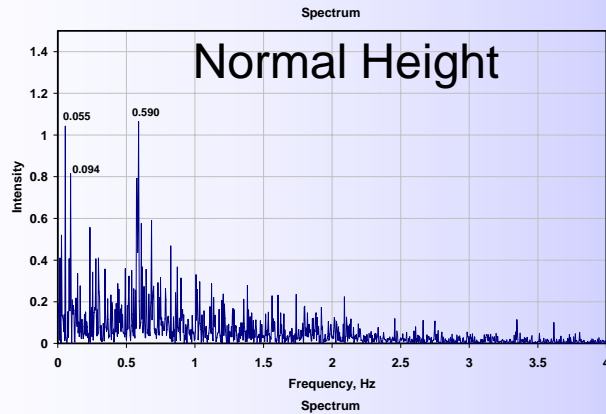


# Effect of Raised Paddle

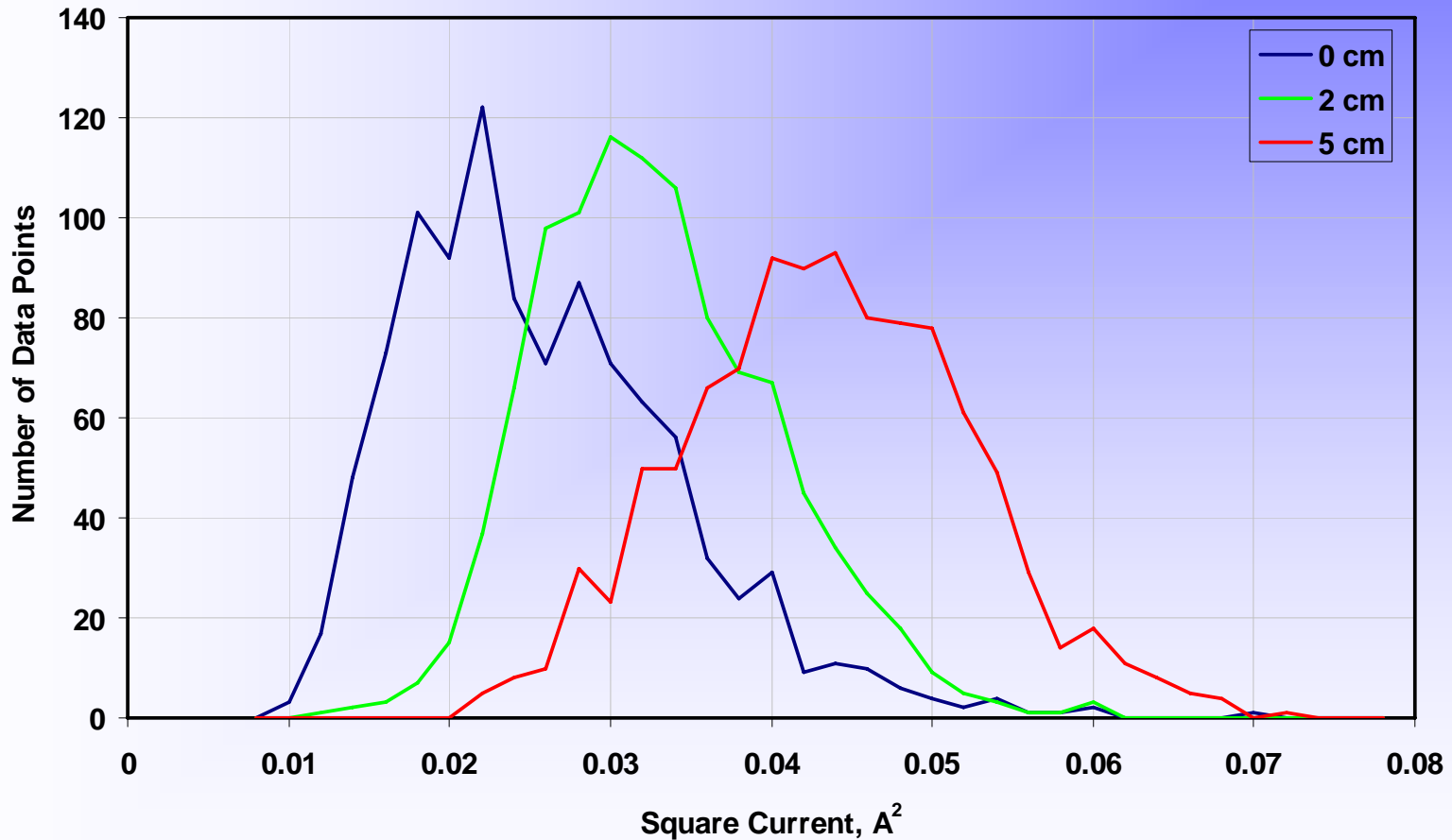
(Paddle Rotation Rate = 100 RPM)



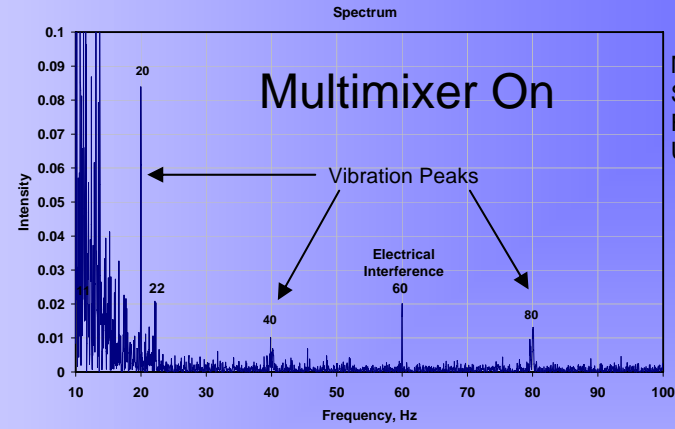
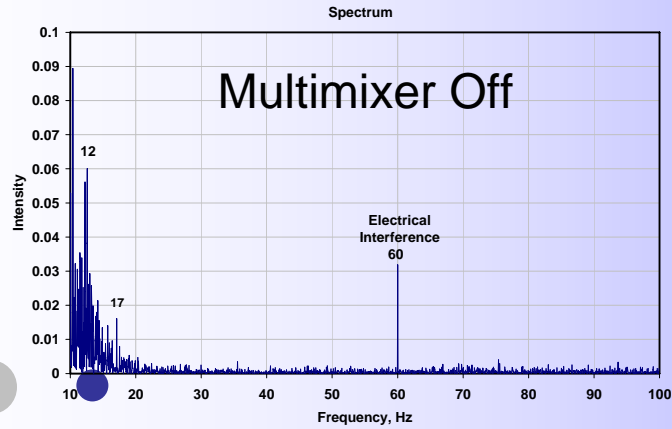
# Raised Paddle



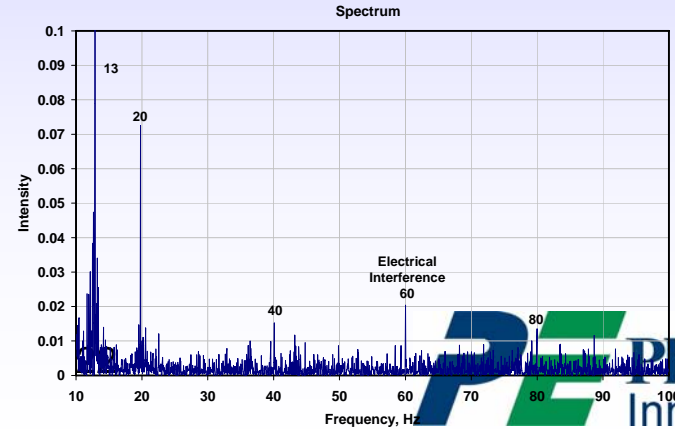
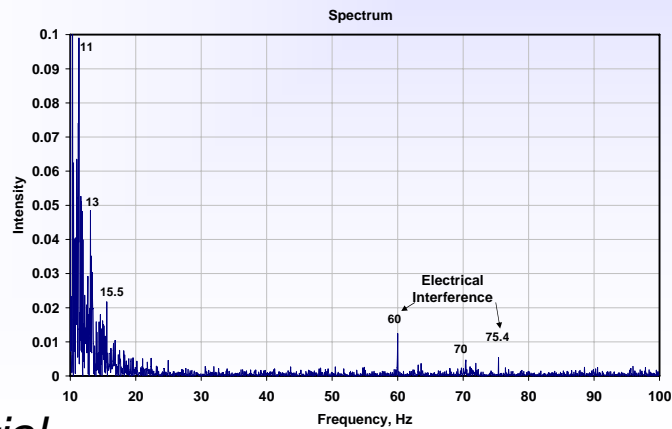
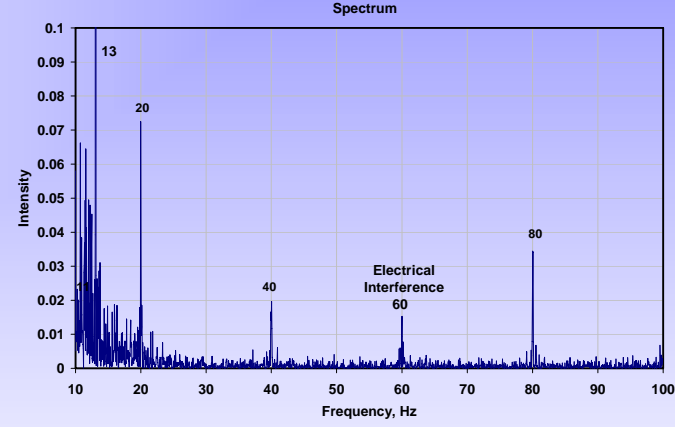
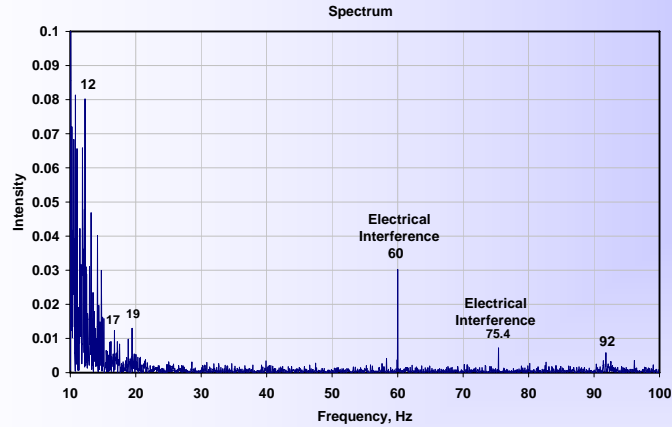
# Effect of Paddle Height on Current Distribution



# Multimixer Vibration

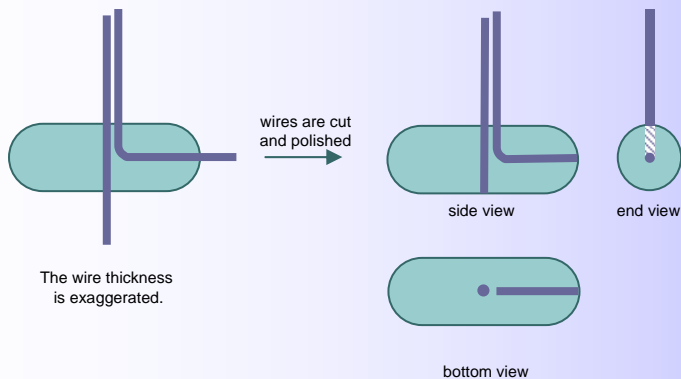


Multimixer Vibrations:  
Side-to-side: 22 – 31Hz  
Front-to-back: 70 - 116 Hz  
Up-Down: 34 - 42 Hz



# Other Forms of the ECC Technology

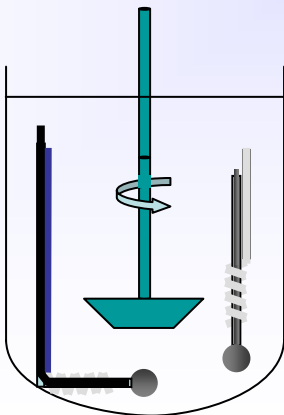
**Inlaid Disk Electrodes for Assessing Dissolution Rates at Specific Points on a Caplet**



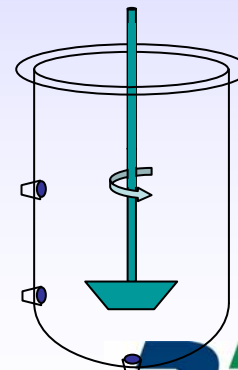
**Drug-shaped Electrodes for Predicting Initial Dissolution Rates**



**Platinum Bead Electrodes for Mapping Local Flow Rates in the Cell/Vessel**



**Embedded Inlaid-disk Electrodes for Self-Calibrating Dissolution Vessels/Cells**



# ● ● ● Current ECC Research Initiatives

- Field testing in other pharmaceutical laboratories
  - Different vendors, different dissolution baths
- Obtain ECC signatures simultaneously at different positions within the vessel
  - ECC signature mapping
- Compare sensitivity to detect perturbations by using current USP calibrators and ECC (collaboration with USP)

# ● ● ● Acknowledgement

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