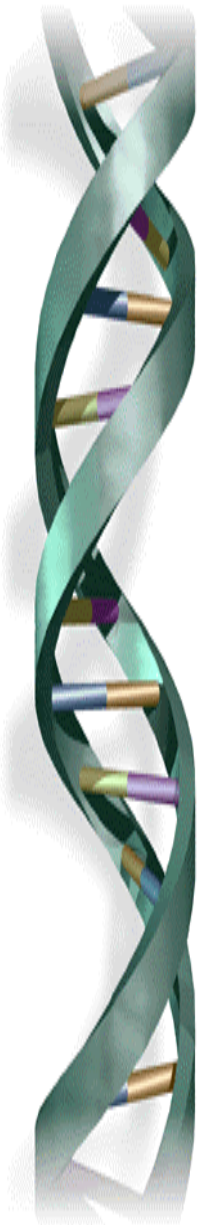
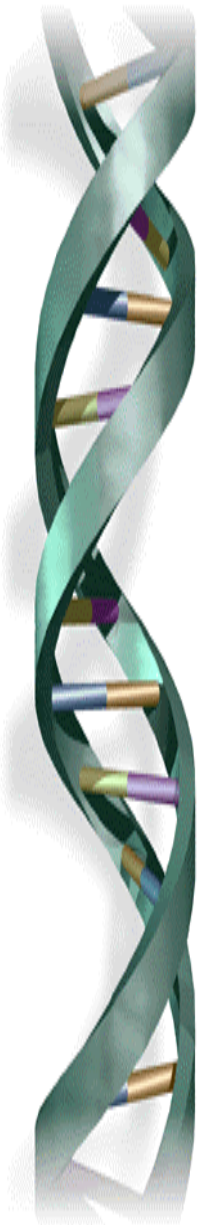


Technology Overview of PAT in Biochemical Manufacturing

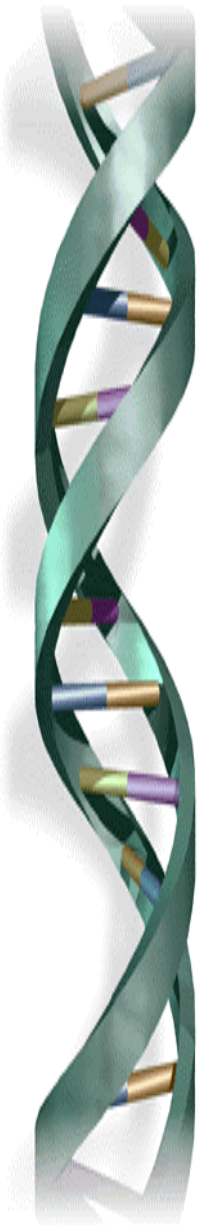
Tina M. Larson
Genentech, Inc.

PPAR 2004



Summary of Current Measurements

- Optical Density
- Temperature
- Pressure
- Volume
- pH
- Dissolved O_2
- O_2 and CO_2 flow
- Conductivity
- Flowrate (air & liquid)
- Turbidity



Future Areas for Growth

Sensors that could be implemented now

- Capacitance (viable cell density)
- NIR (moisture & vacuum detection in lyophilized vials)

Sensors for the near future

- Biosensors

Sensors for the more distant future

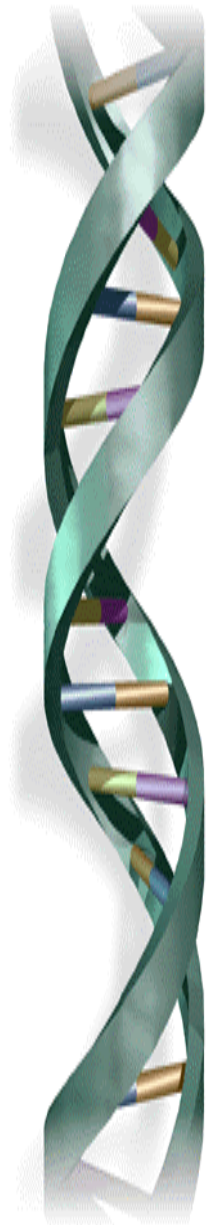
- NIR in aqueous streams
- Fluorescence
- Raman

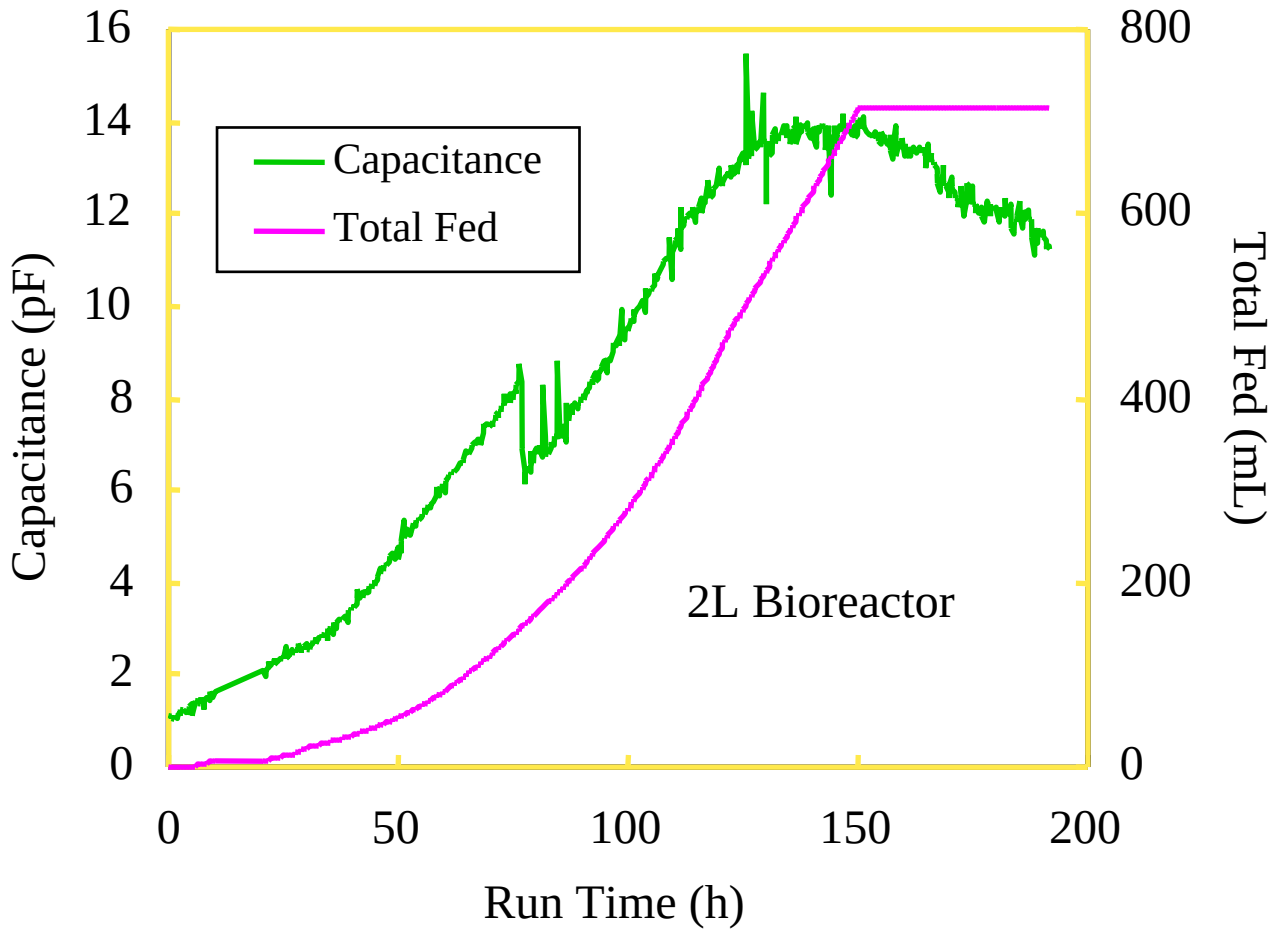
Future Areas for Growth

Technologies other than sensors

- Data technology
- Raw Material Characterization
  - NIR, Raman, ICP, etc.
- Rapid Microbial Detection

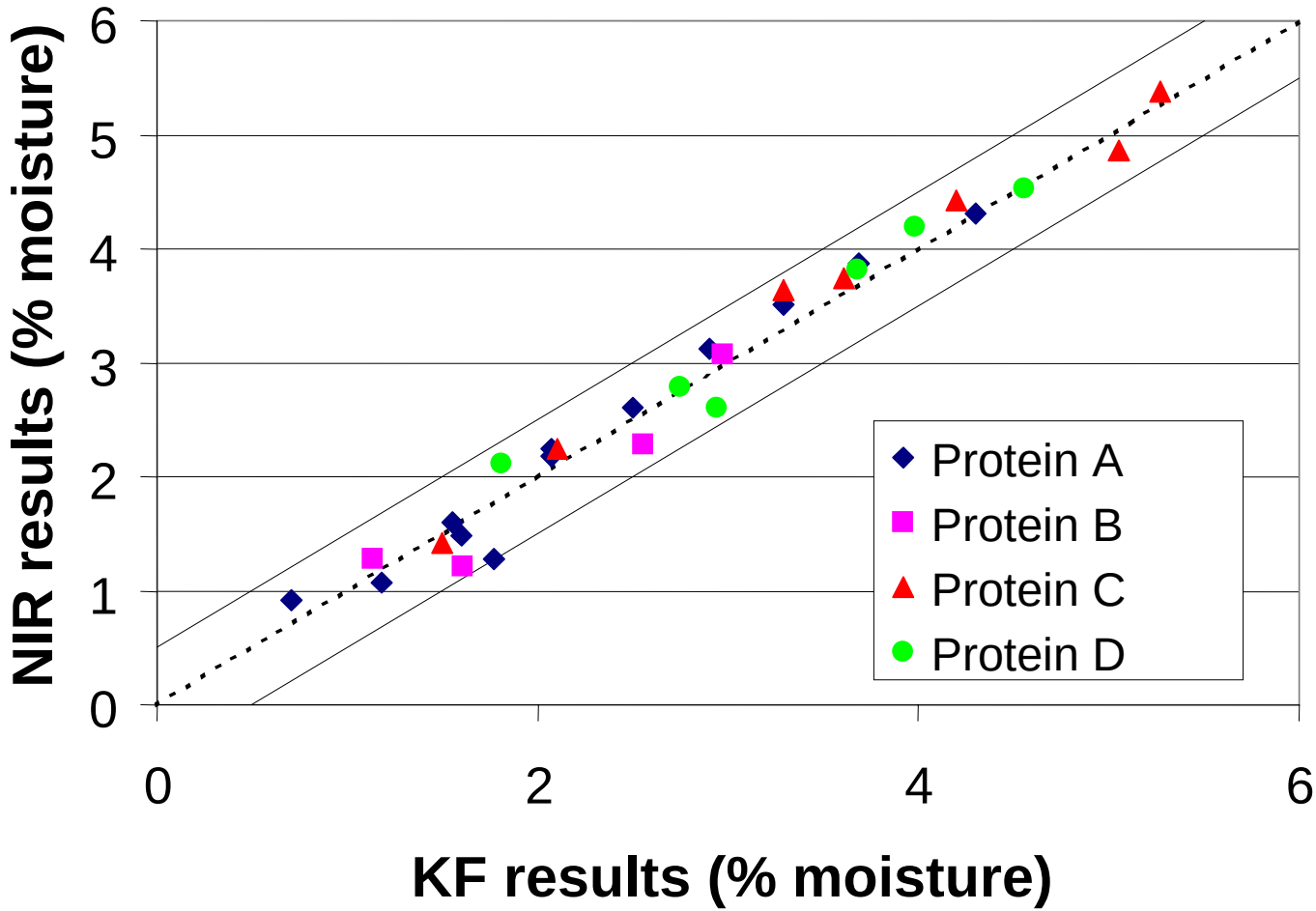
Capacitance probes can measure viable cell count



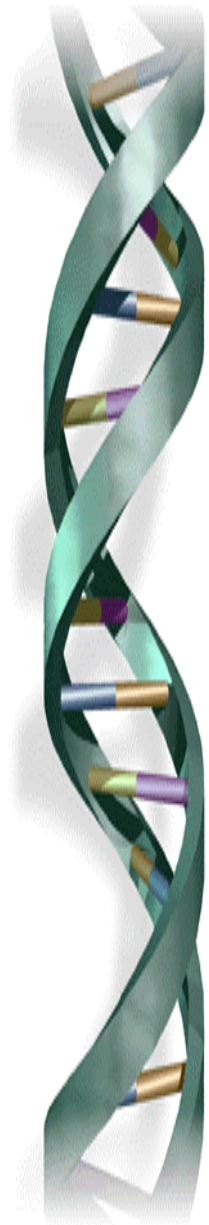


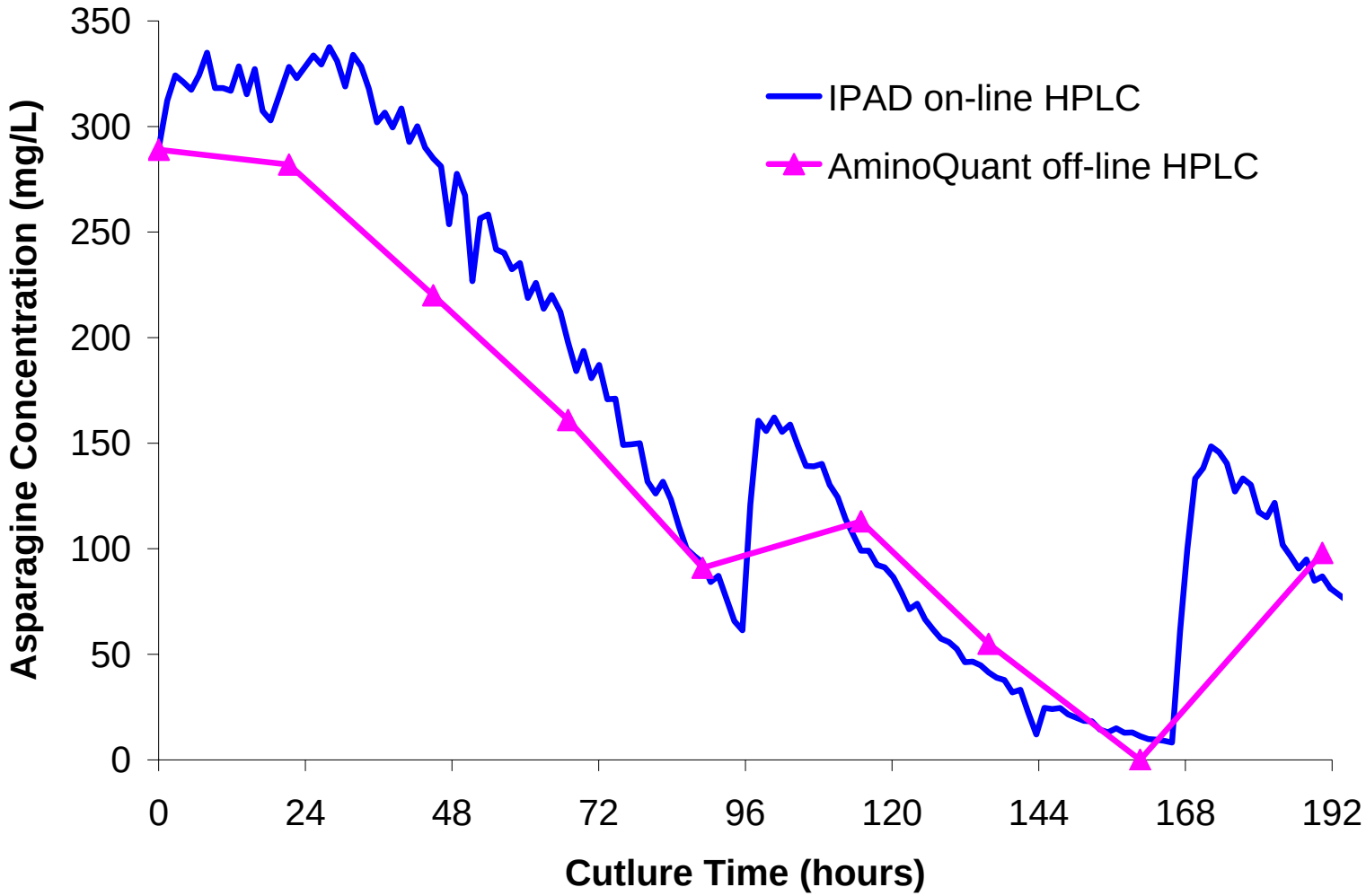
Data courtesy of Bob Kiss and Paul Magreta

NIR to replace destructive moisture detection in lyophilized vials

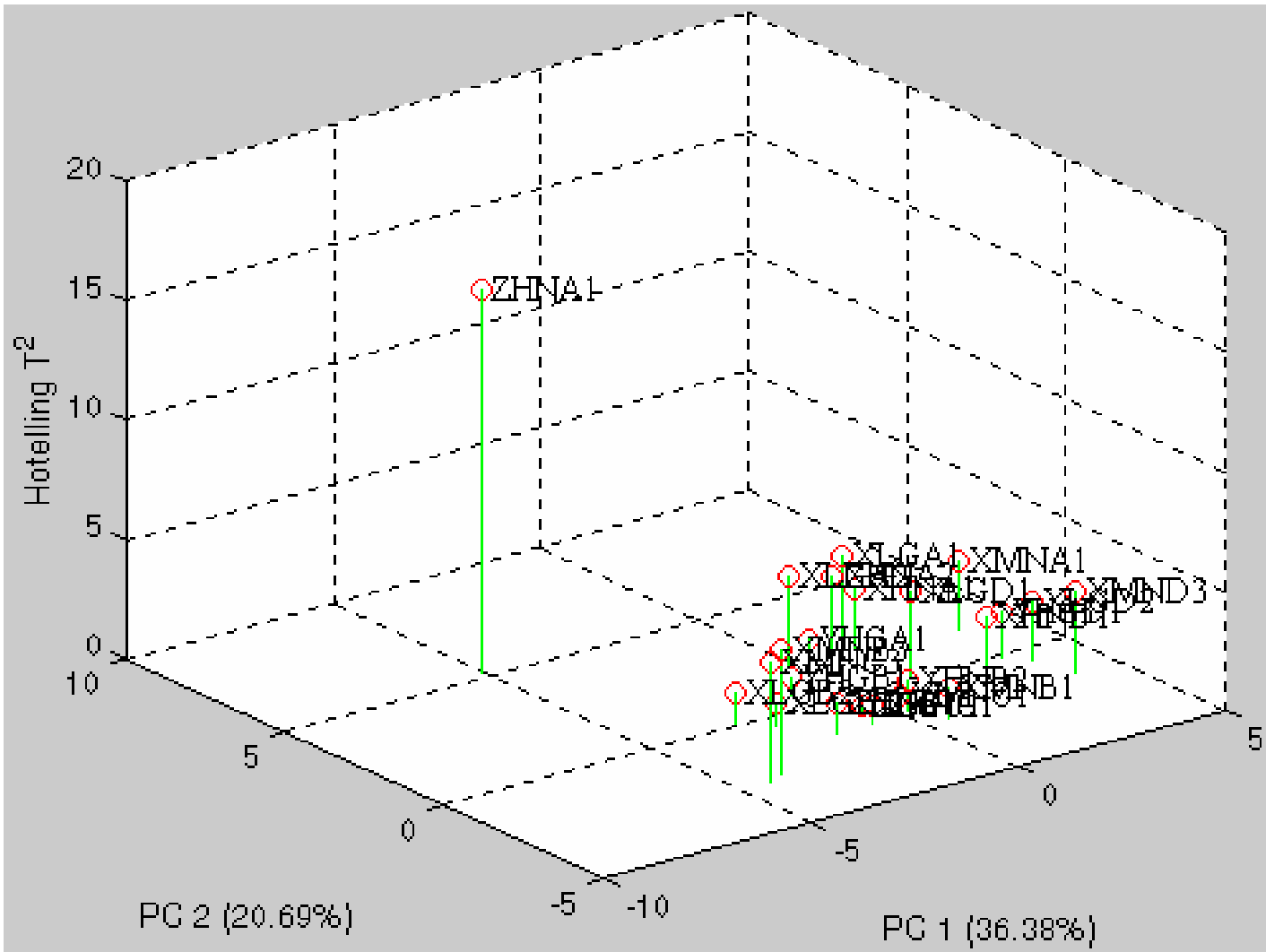


Amino acid & sugar analysis (HPLC shown, biosensor better)

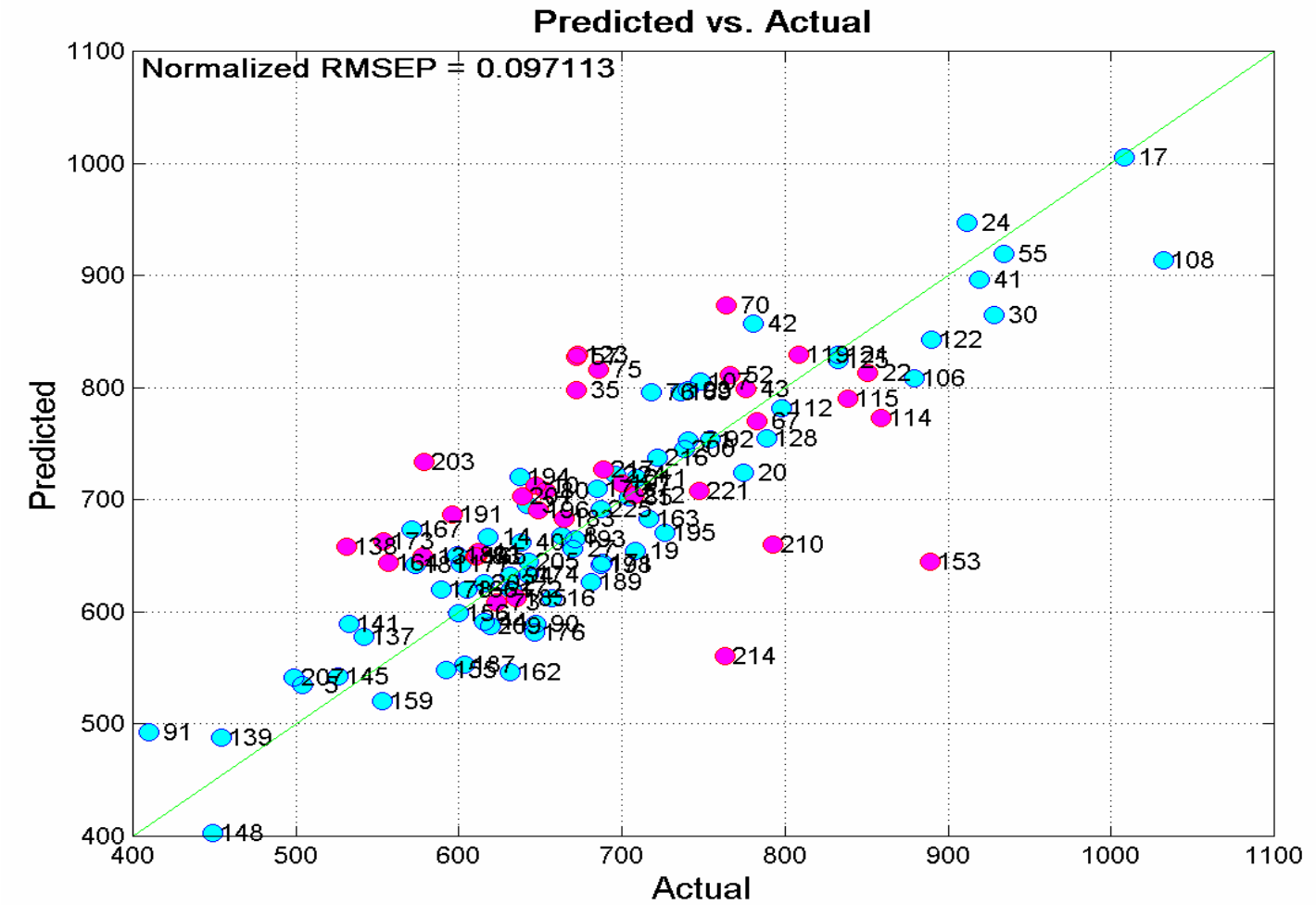




Product Z exhibits variation inside of the model



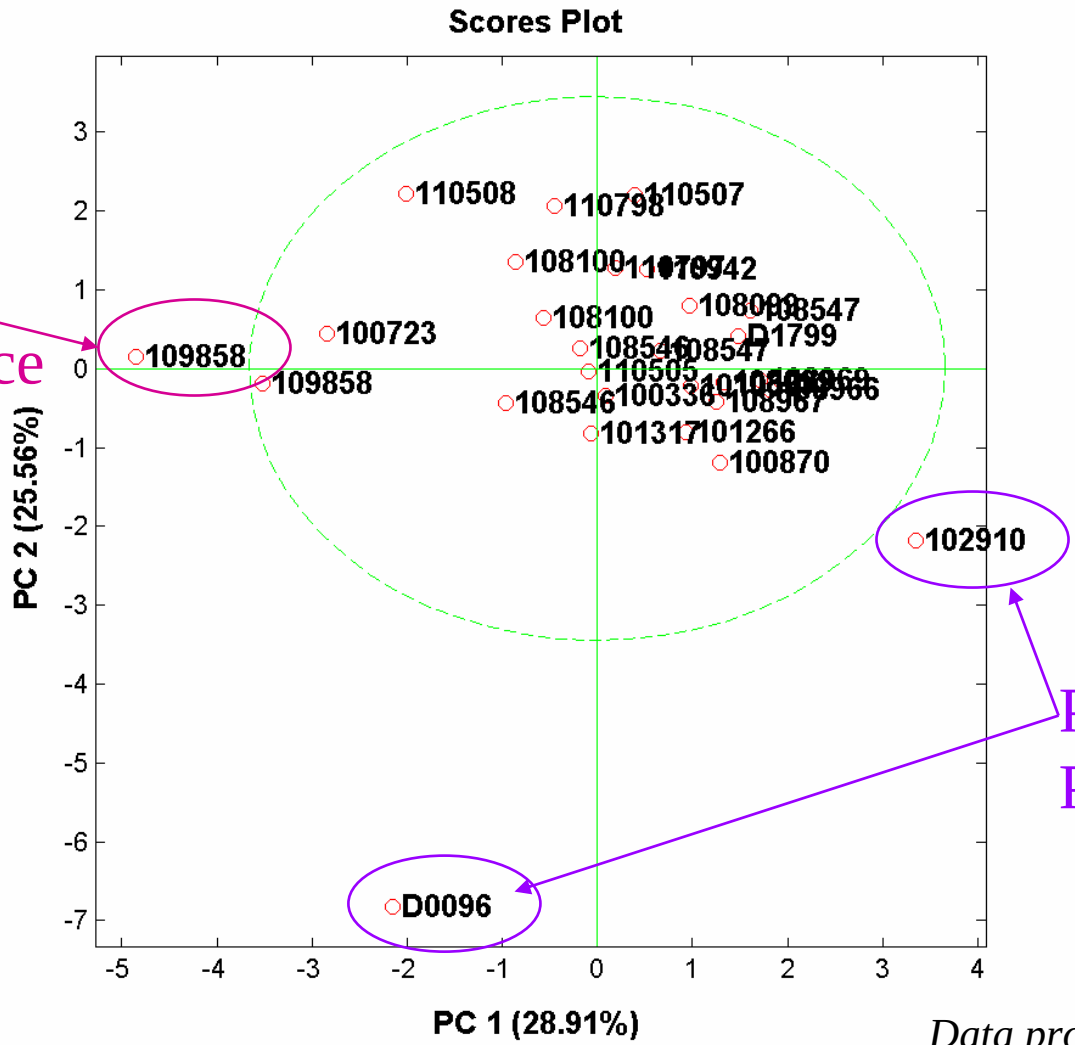
PLS model to predict titer based on 1695 variables



Data courtesy of Kirin Malik

Correlating raw material ICP results to process performance

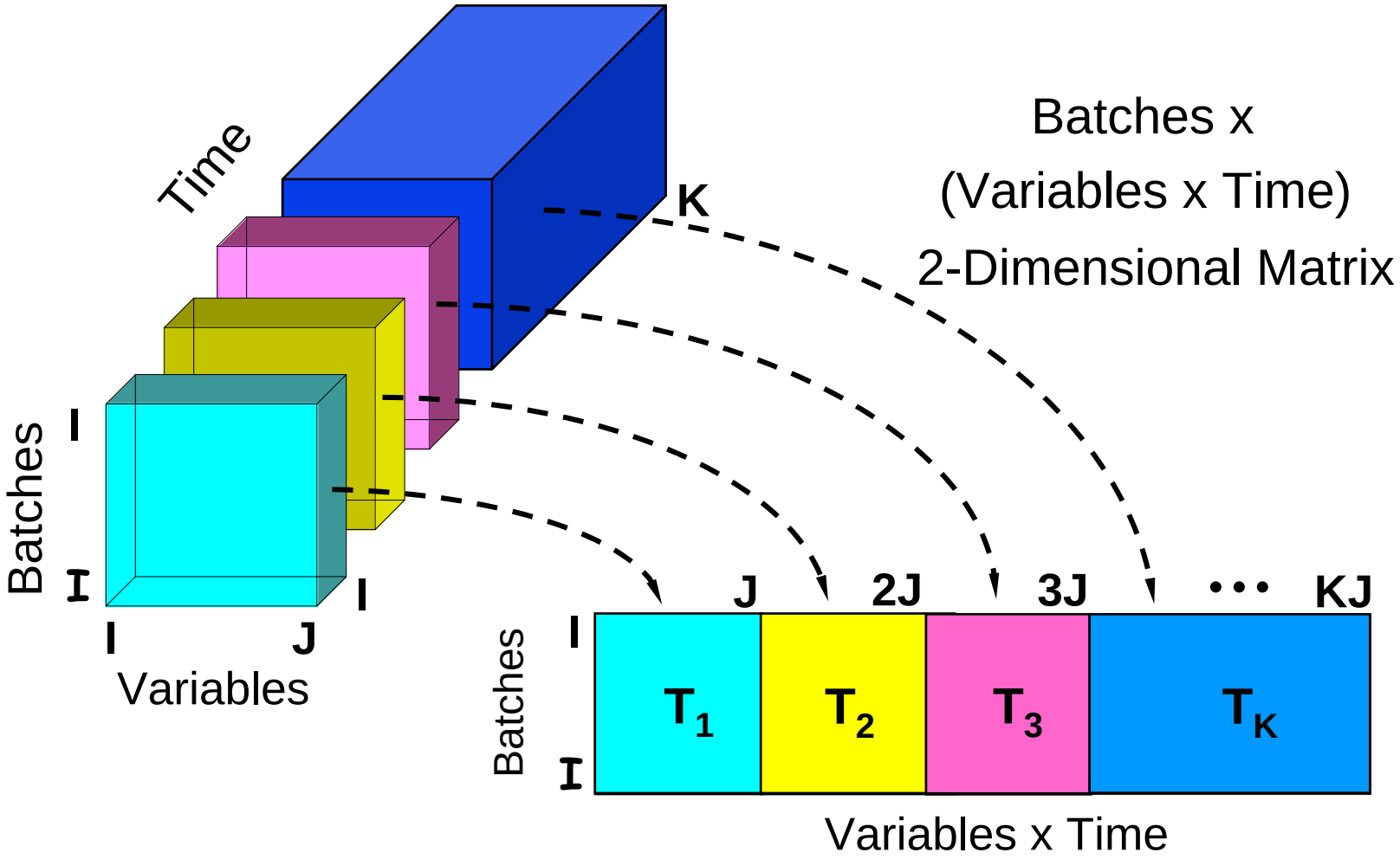
Good Performance



Poor Performance

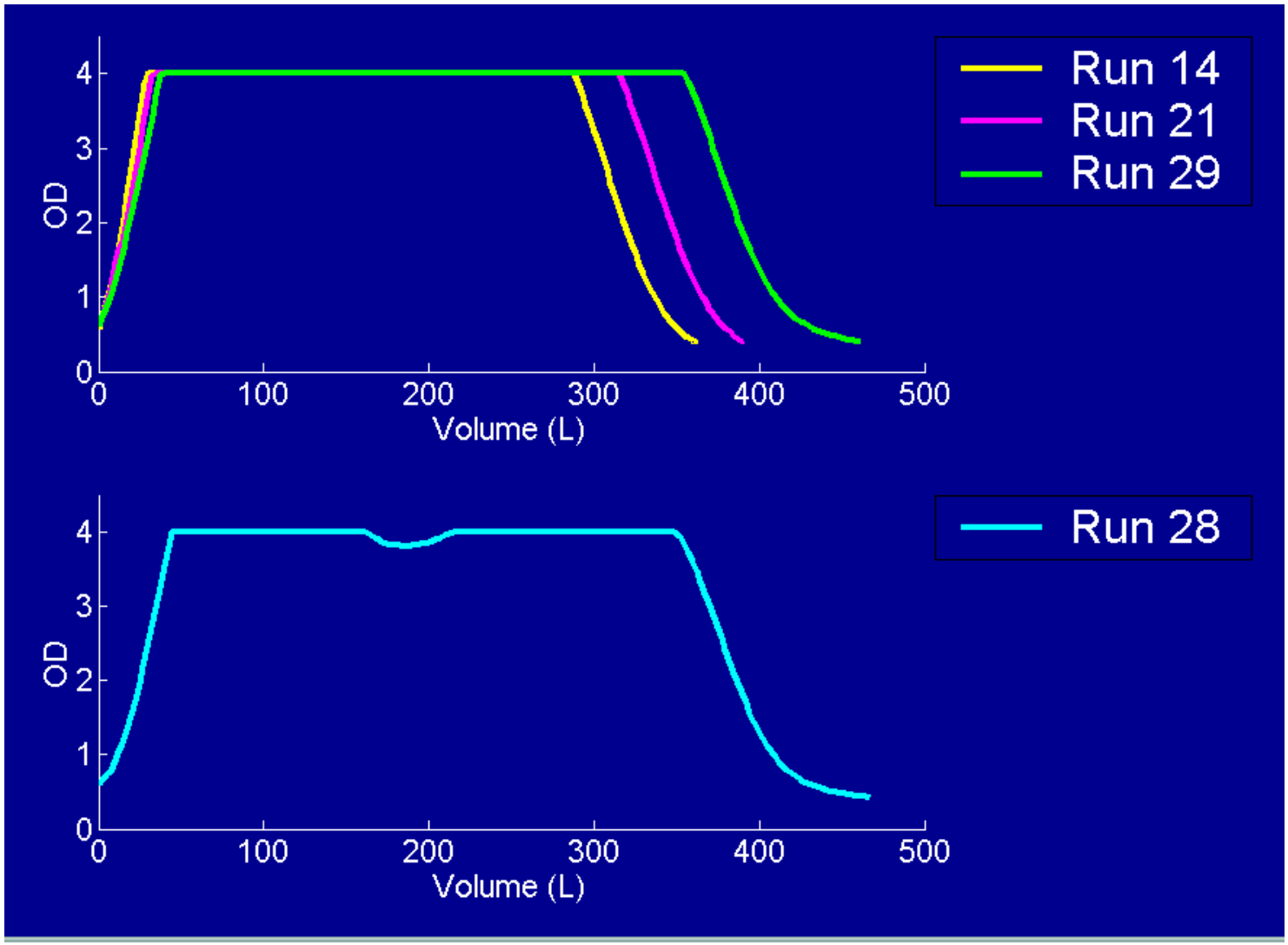
Data provided by Kirin Malik

Multi-way PCA



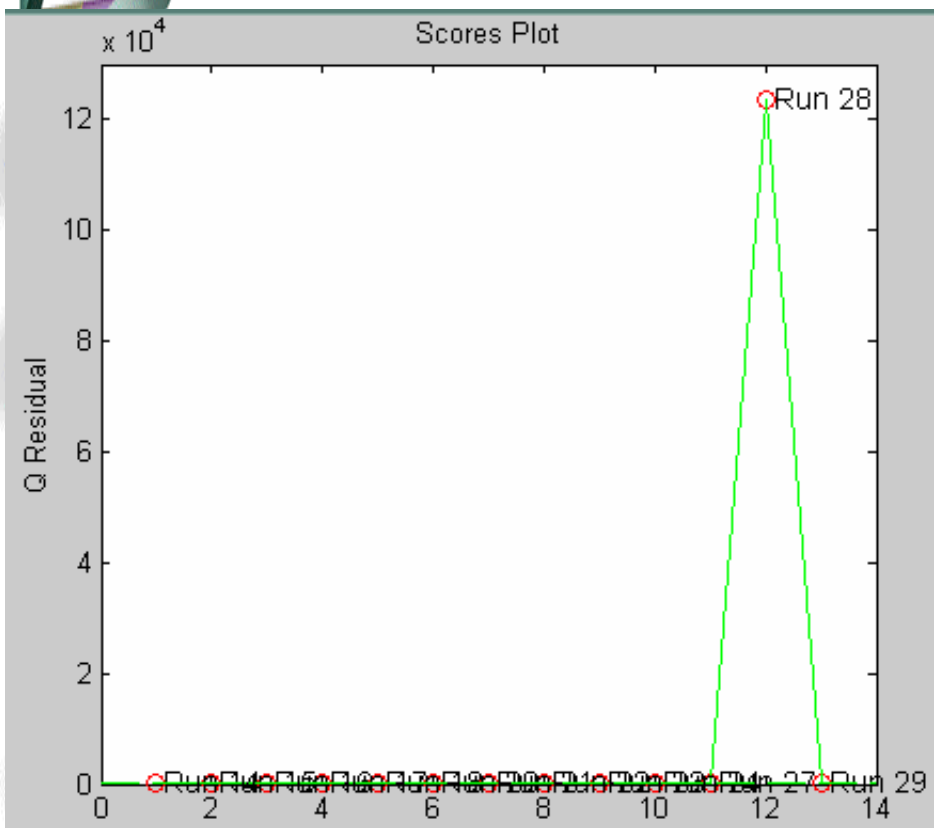
 Adapted from work by Barry Wise, Graphic by Michelle Mostajo

MPCA for chromatogram review



PCA analysis easily picks up change in peak shape

$Q_{residual}$



Hotelling's T^2