In-line prediction of drug release profile for pH-sensitive coated pellets

A.L. Pomerantsev, O.Ye. Rodionova

M. Melichar, A.J. Wigmore,

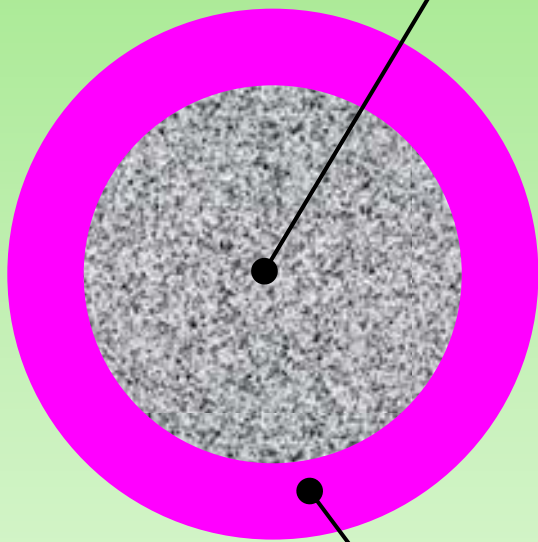**A. Bogomolov**

Institute of Chemical Physics

GEA Pharma Systems

J&M Analytik
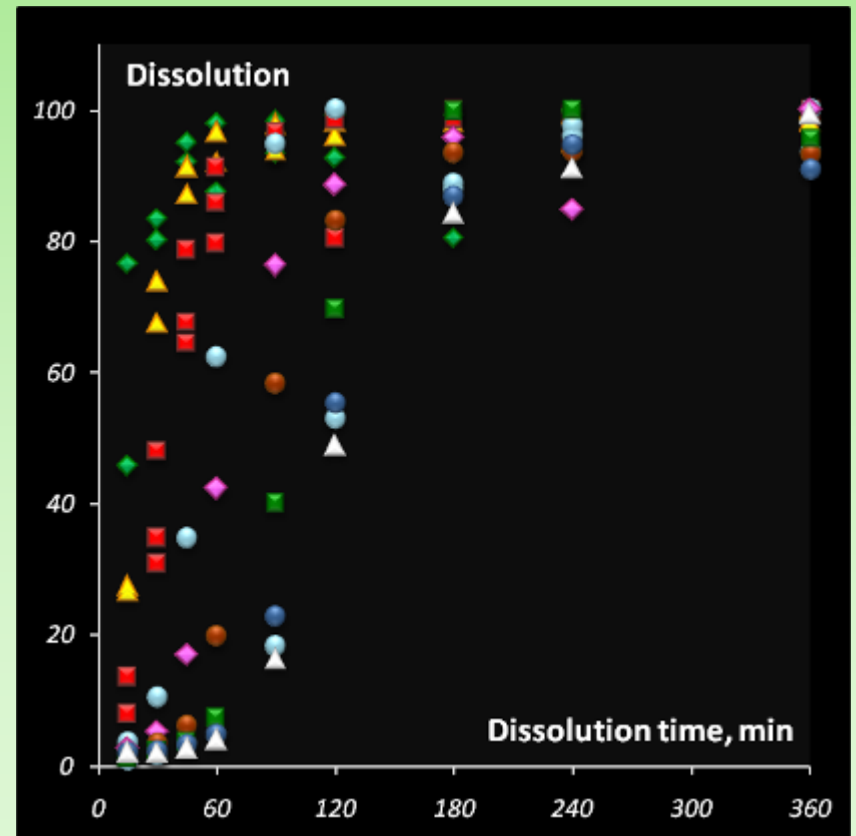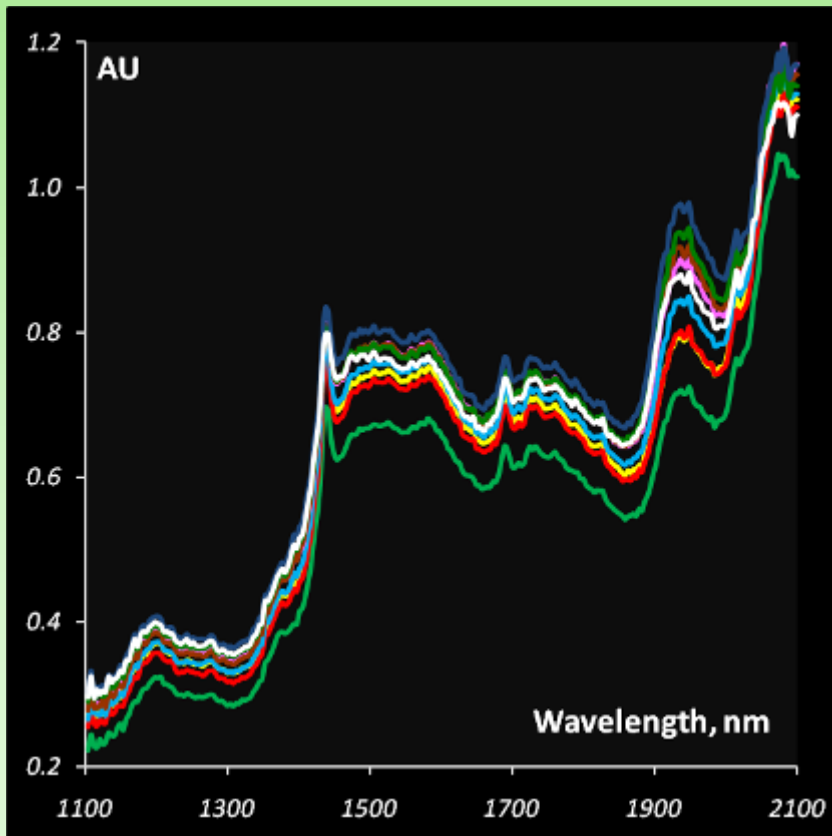
Objects: Pellets

Sugar +API

Coating: Acryl EZE

CAC 2010

Fluid bed coating

CAC 2010

Experiment

NIR Spectra

Dissolution Profiles

t = 105

Our goal

NIR Spectrum

Wavelength, nm

Prediction

Dissolution Profile
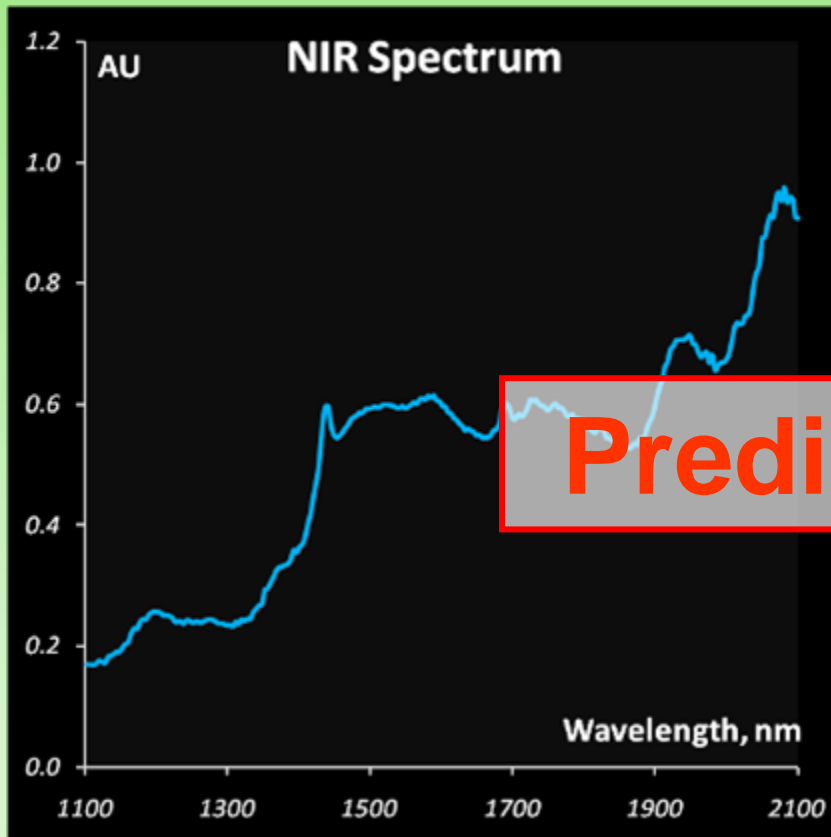
Dissolution time, min
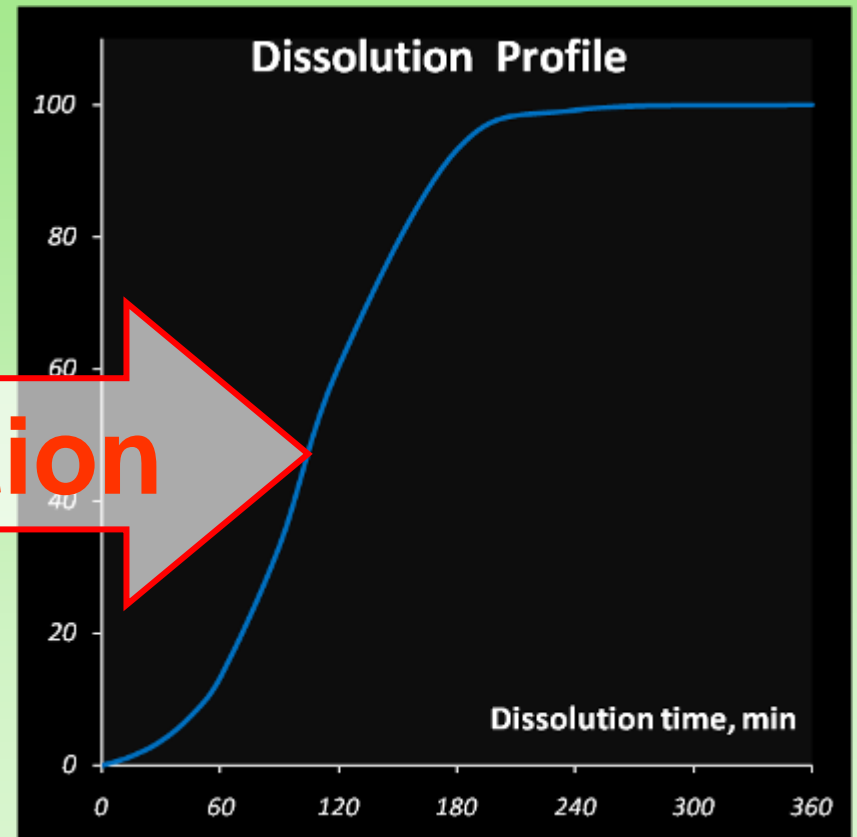
Data overview

	Samples								
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
W1	25	44	62	82	99	117	136	154	171
W2	22	37	52	67	81	98	110	124	142
W3	18	30	41	52	62	73	85	97	114
W4	19	36	52	67	83	98	114	129	137
W5				51		70			105
W6	39	70	98	127	156	188	215	246	260
W7	19	34	48	64	79	95	111	125	140
Y1	21	40	59	77	96	115	133	152	168
Y2	20	30	43	55	67	82	92	105	121
Y3	24	46	70	89	111	133	155	176	191
Y4	26	50	74	98	122	150	171	194	209
Y5	18	31	42	52	63	73	83	94	110
Y6	19	34	49	64	79	94	109	124	140

Batches

Process time, min

Conventional approach
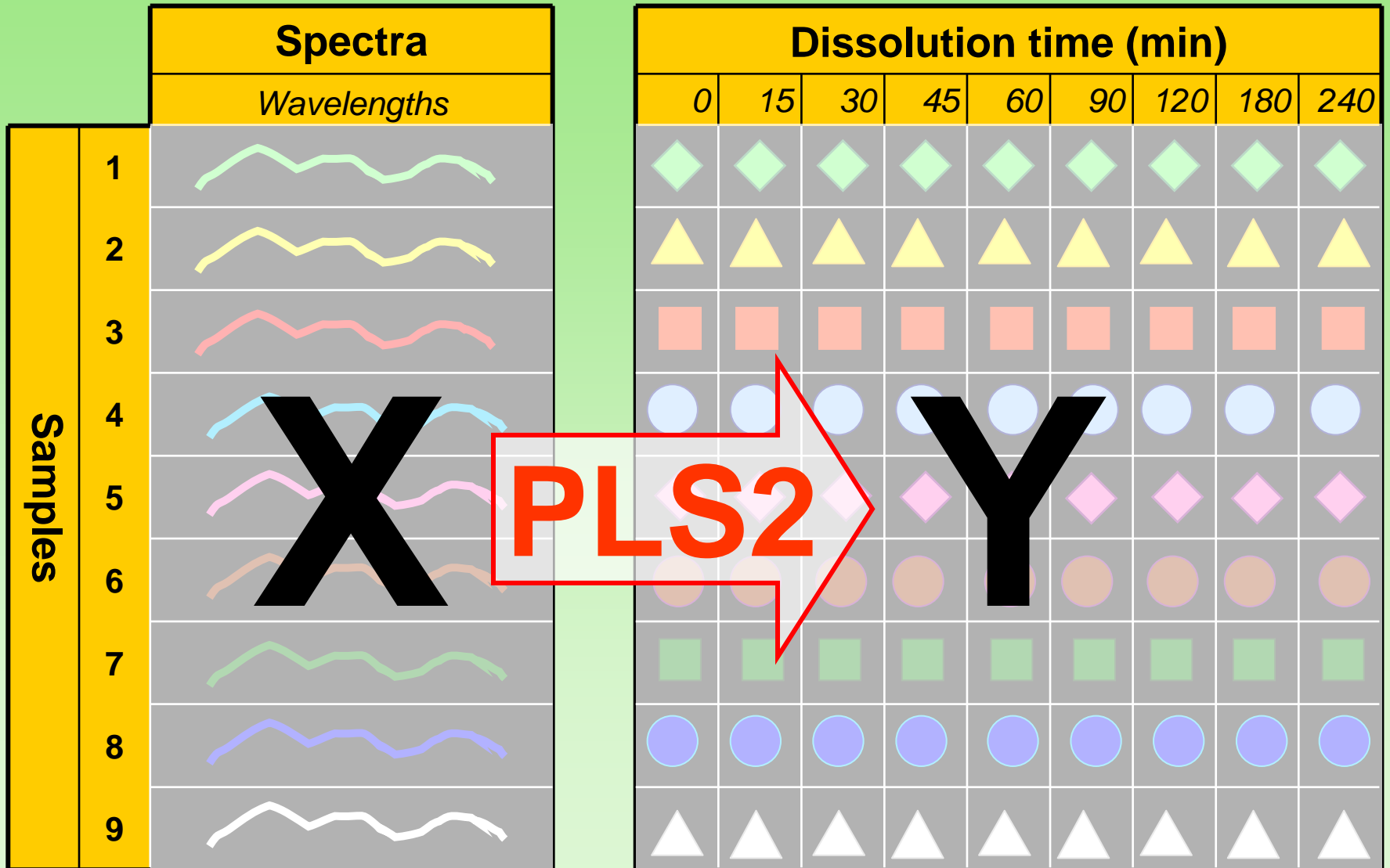
PLS2 results
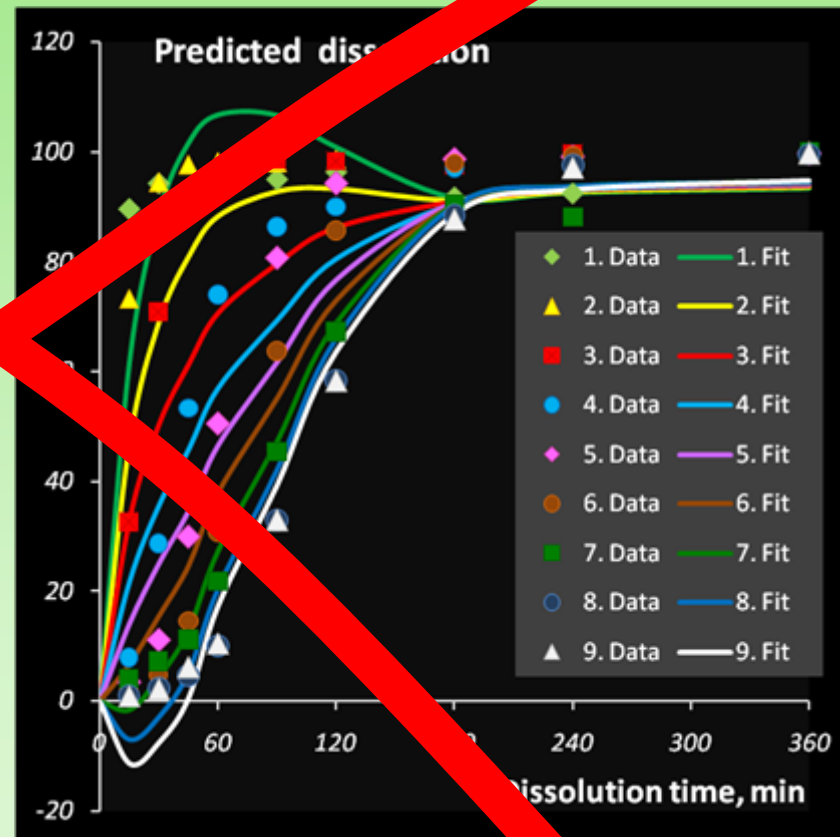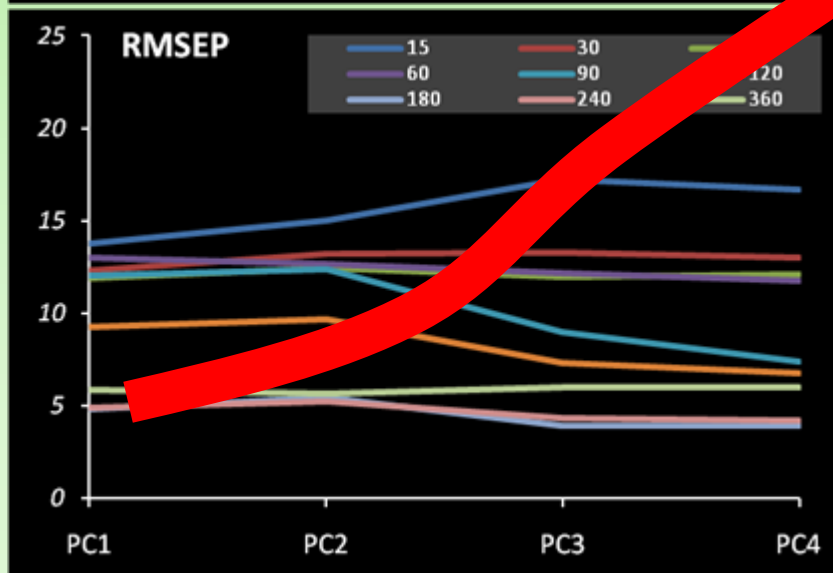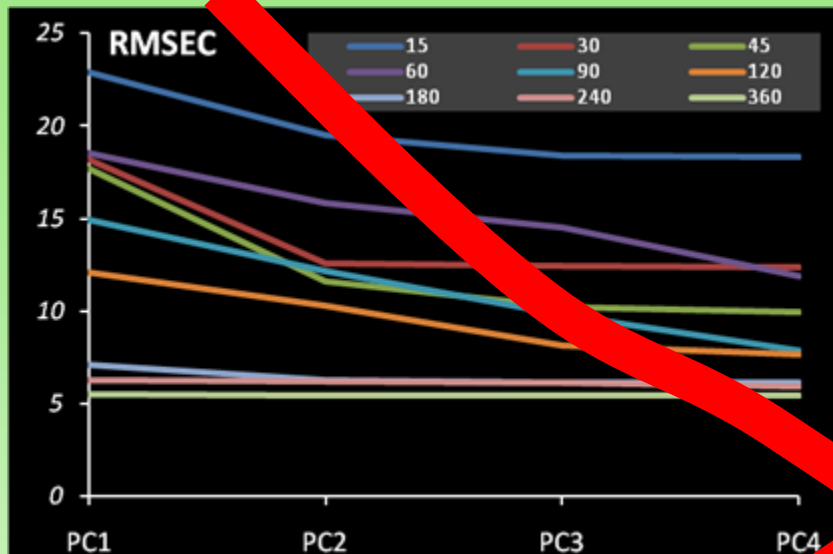
Kinetic approach
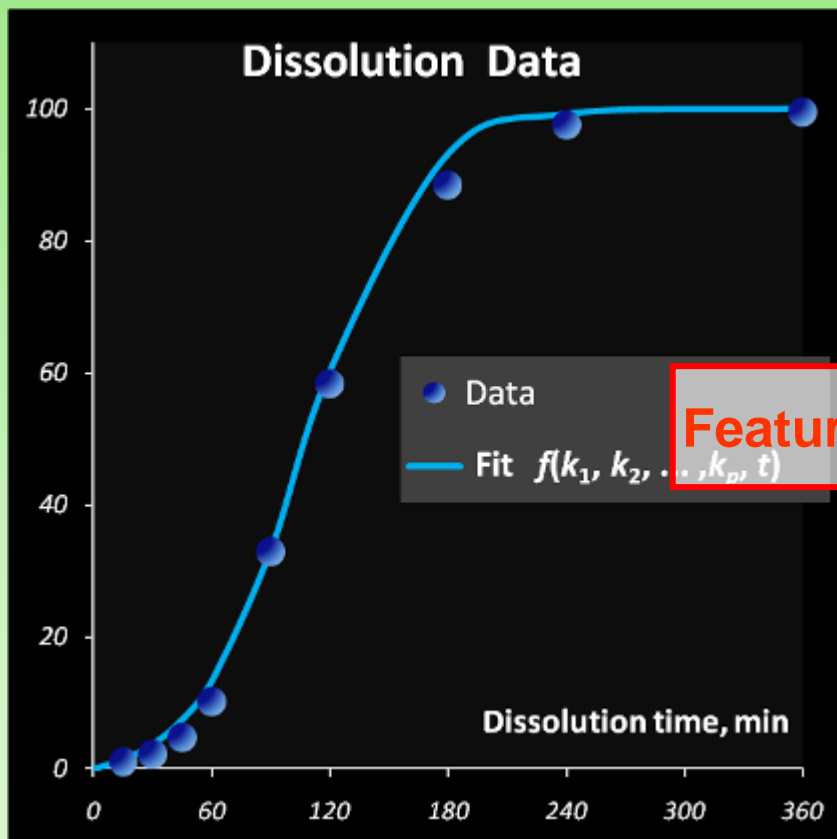
		k_1	k_2	...	k_p
	1	3.56	0.10	...	0.33
	2	4.03	0.09	...	0.66
	3	4.99	0.10	...	0.98
Samples	4	6.13	5		1.28
	5	6.84	0.2	...	1.62
	6	7.81	0.25	...	1.93
	7	8.66	0.30	...	2.23
	8	9.49	0.33	...	2.54
	9	9.82	0.35	...	2.54

Features extraction

Autocatalysis

$$\varphi(t,m,k) = 100k\,\frac{\exp[(m+k)t]-1}{m+k\exp[(m+k)t]}$$
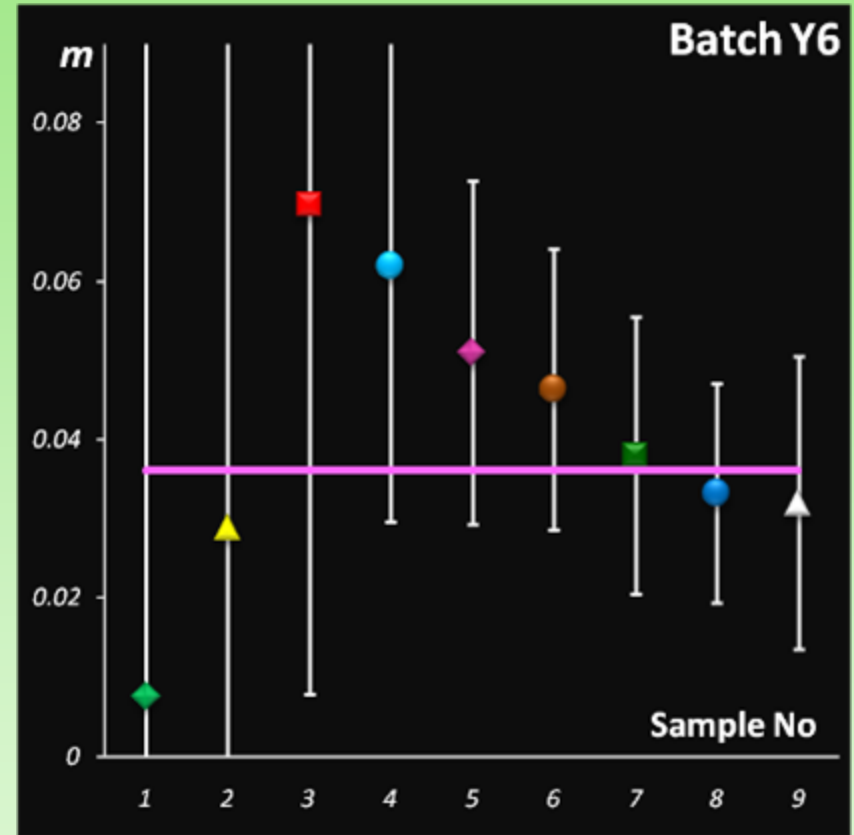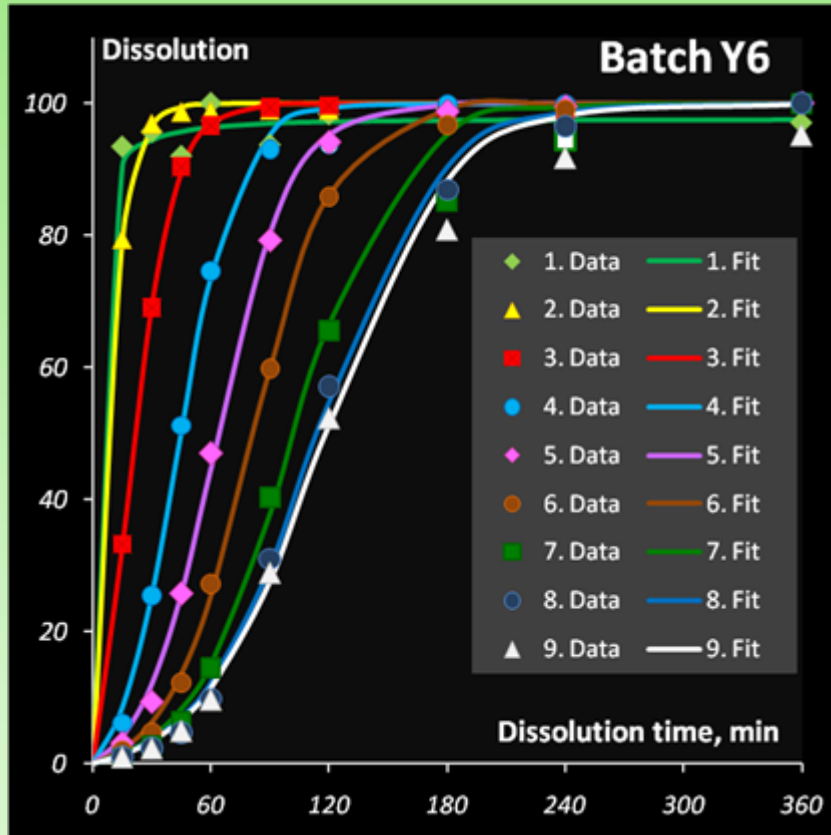
$$A + B \xrightarrow{\;m\;} 2B$$

$$A \xrightarrow{\;k\;} B$$
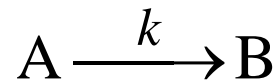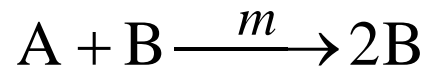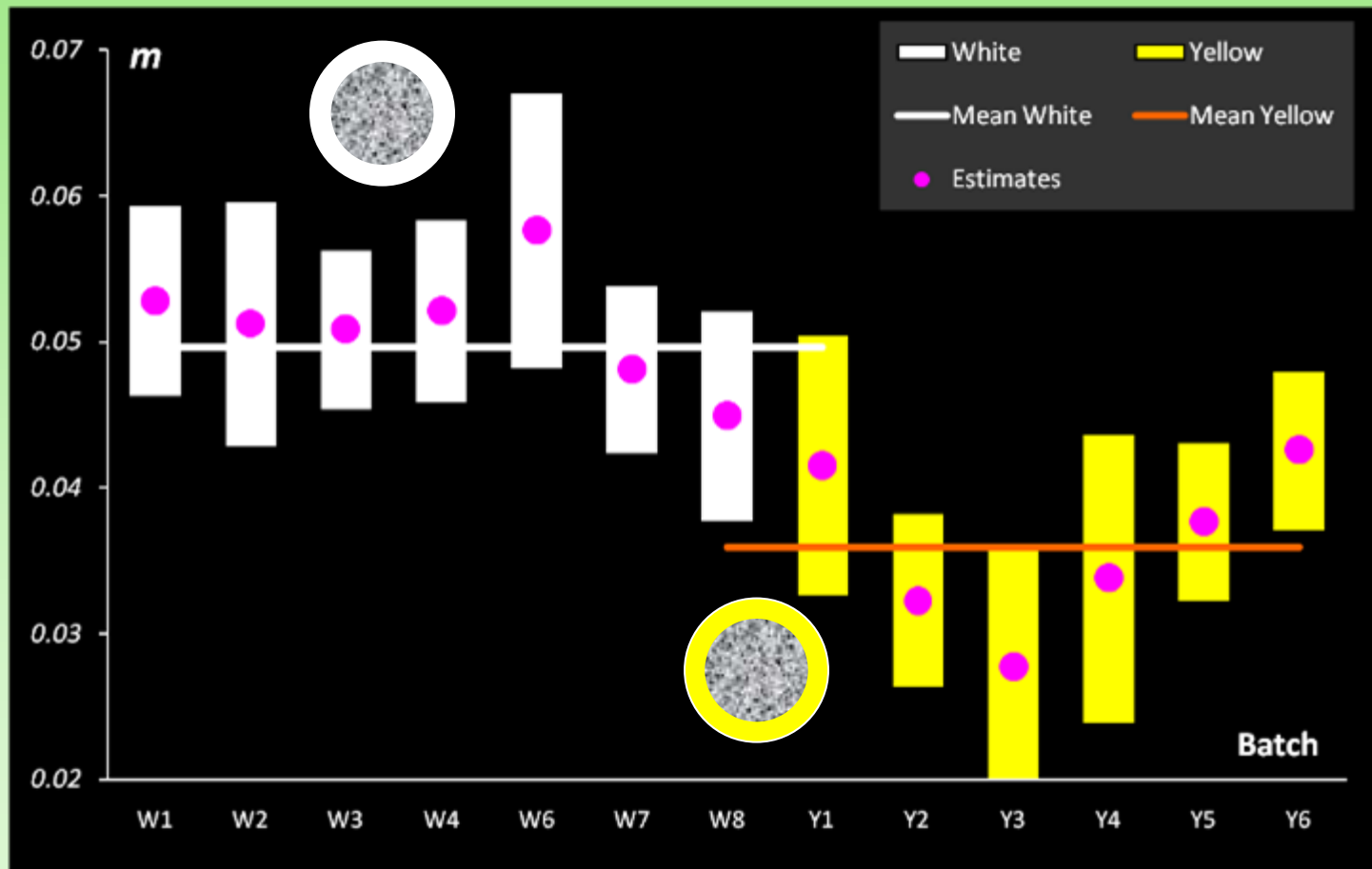
$$[A] + [B] = 100$$

$$[B](0) = 0$$

$$\varphi = [B]$$
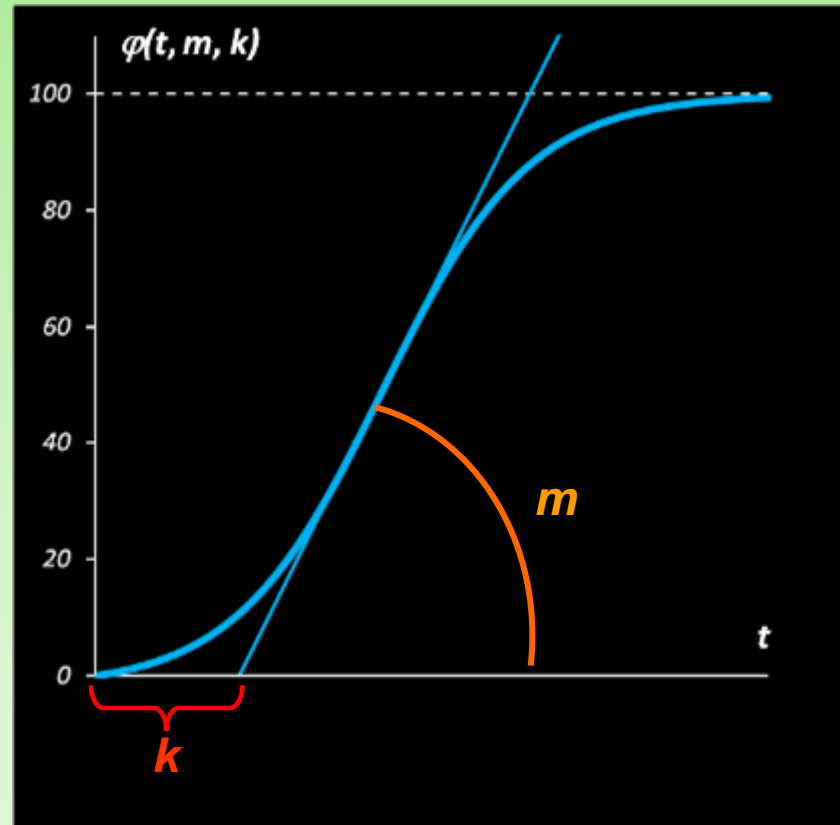
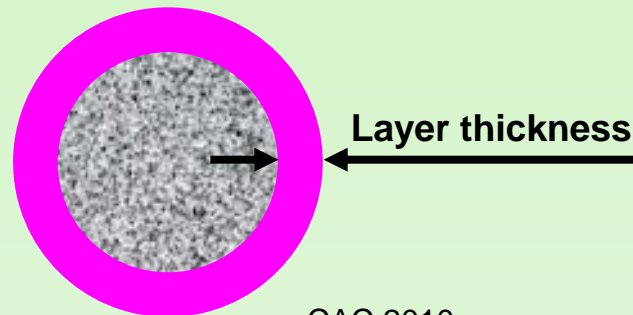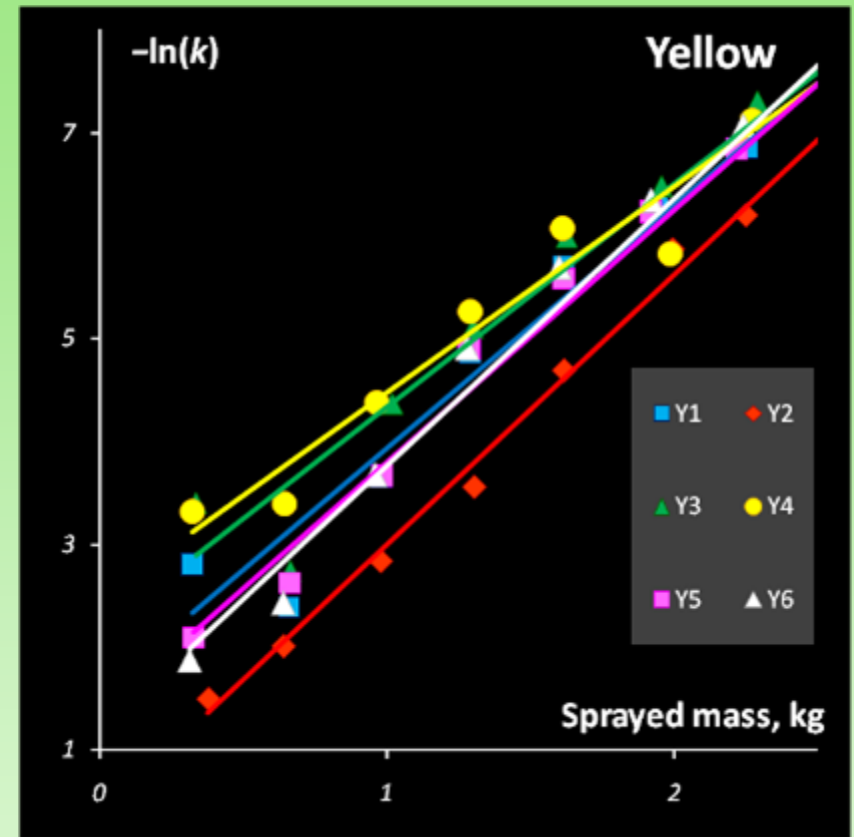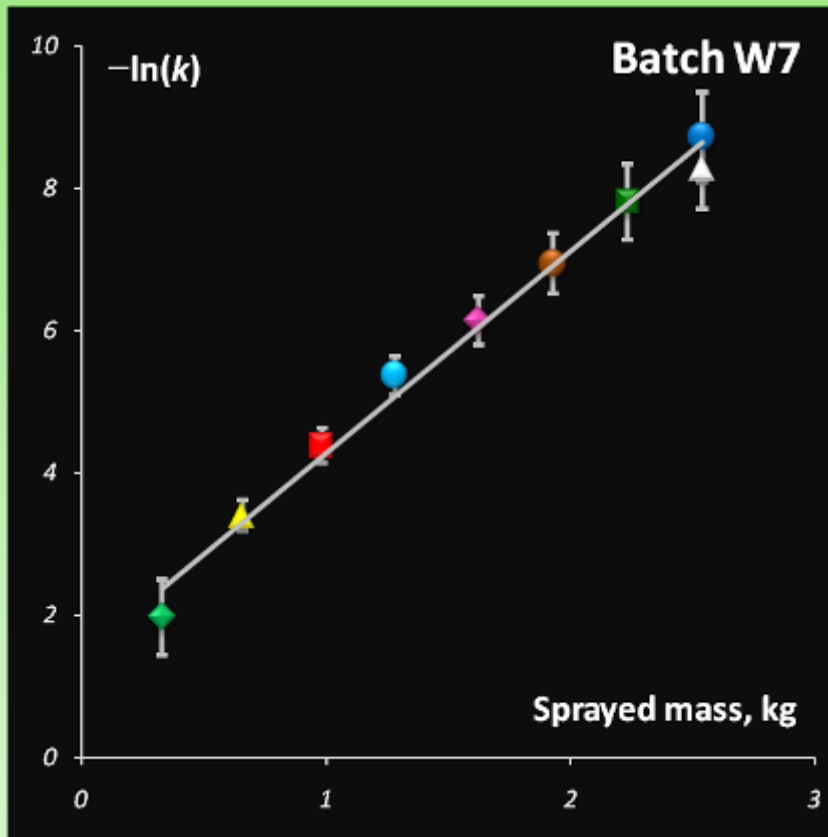# Parameter *m* is common within a batch

Parameter *m* and the layer grade

Parameter *k* and the layer thickness
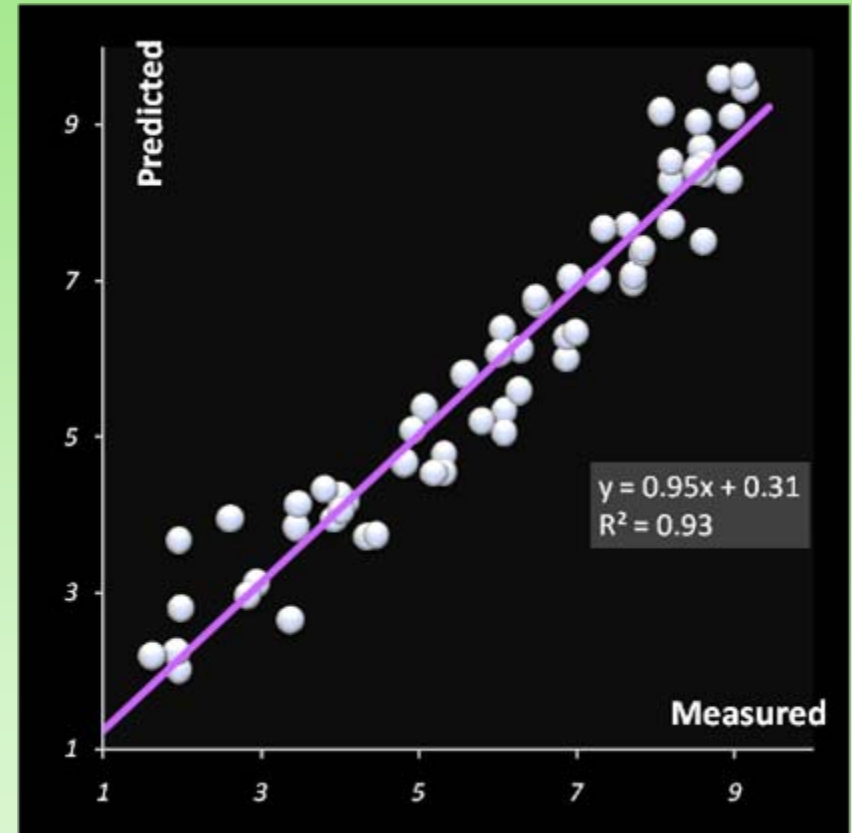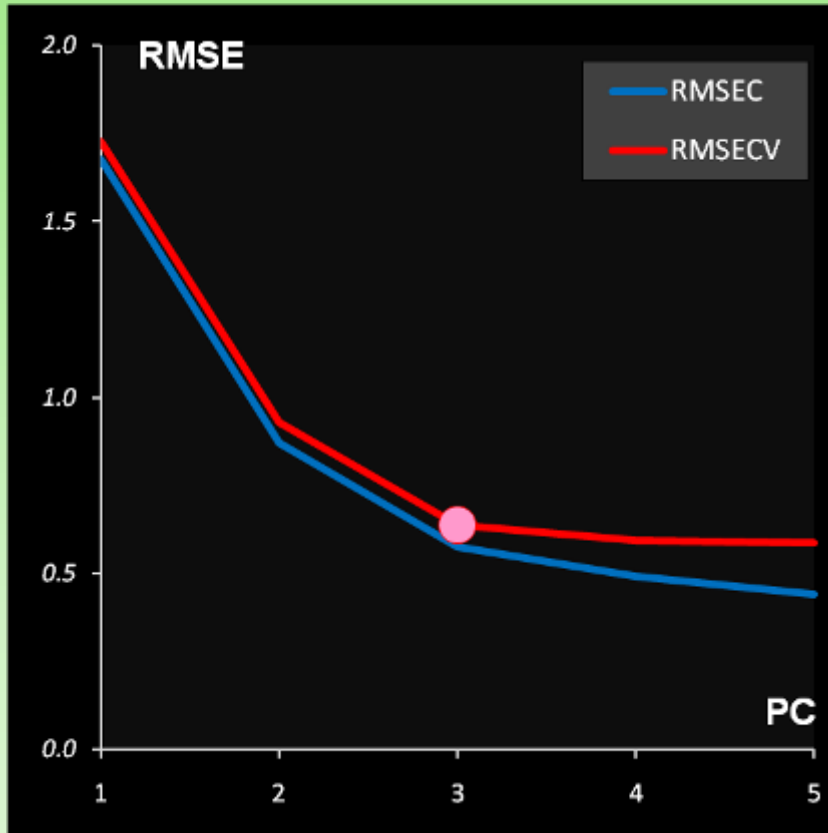

Layer thickness

Intermediate conclusions
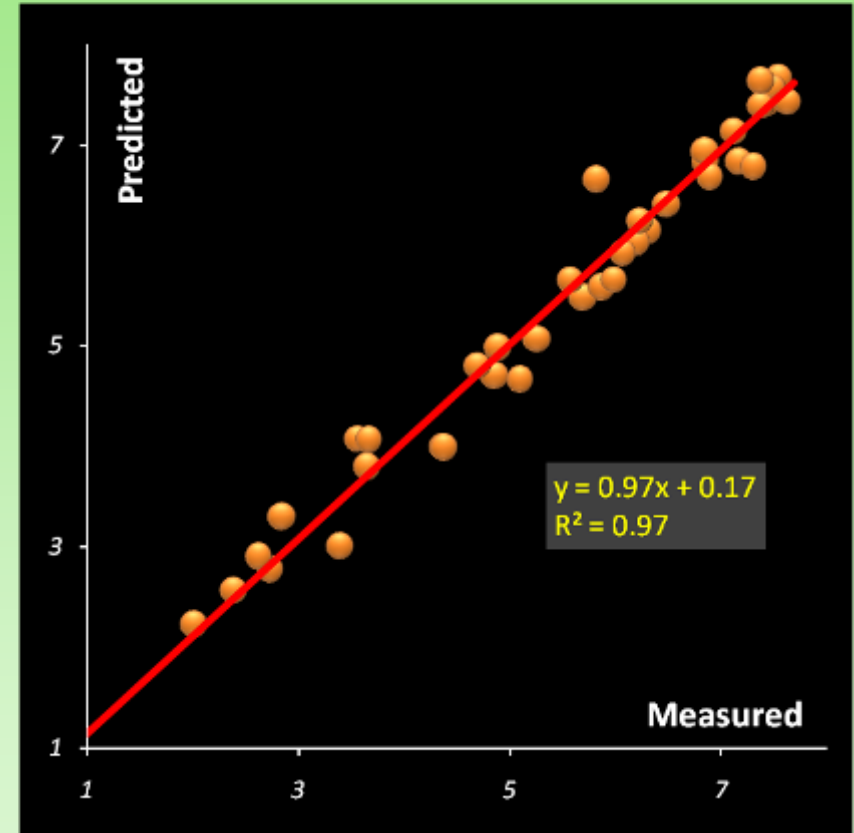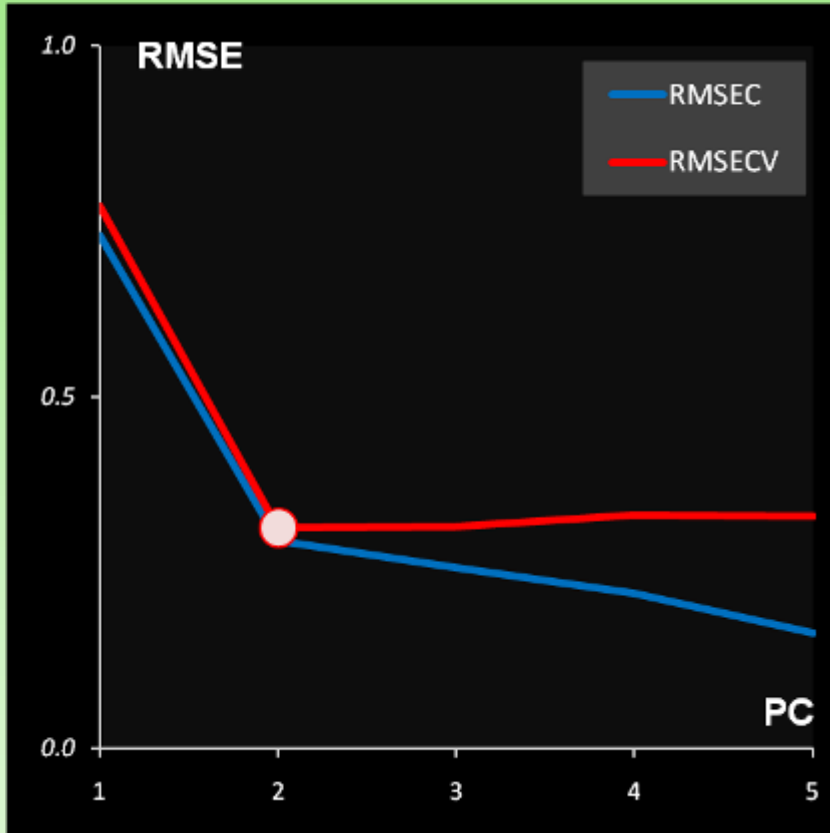
**parameter *m*
reflects the material grade**

**parameter *k*
depends on the layer thickness**
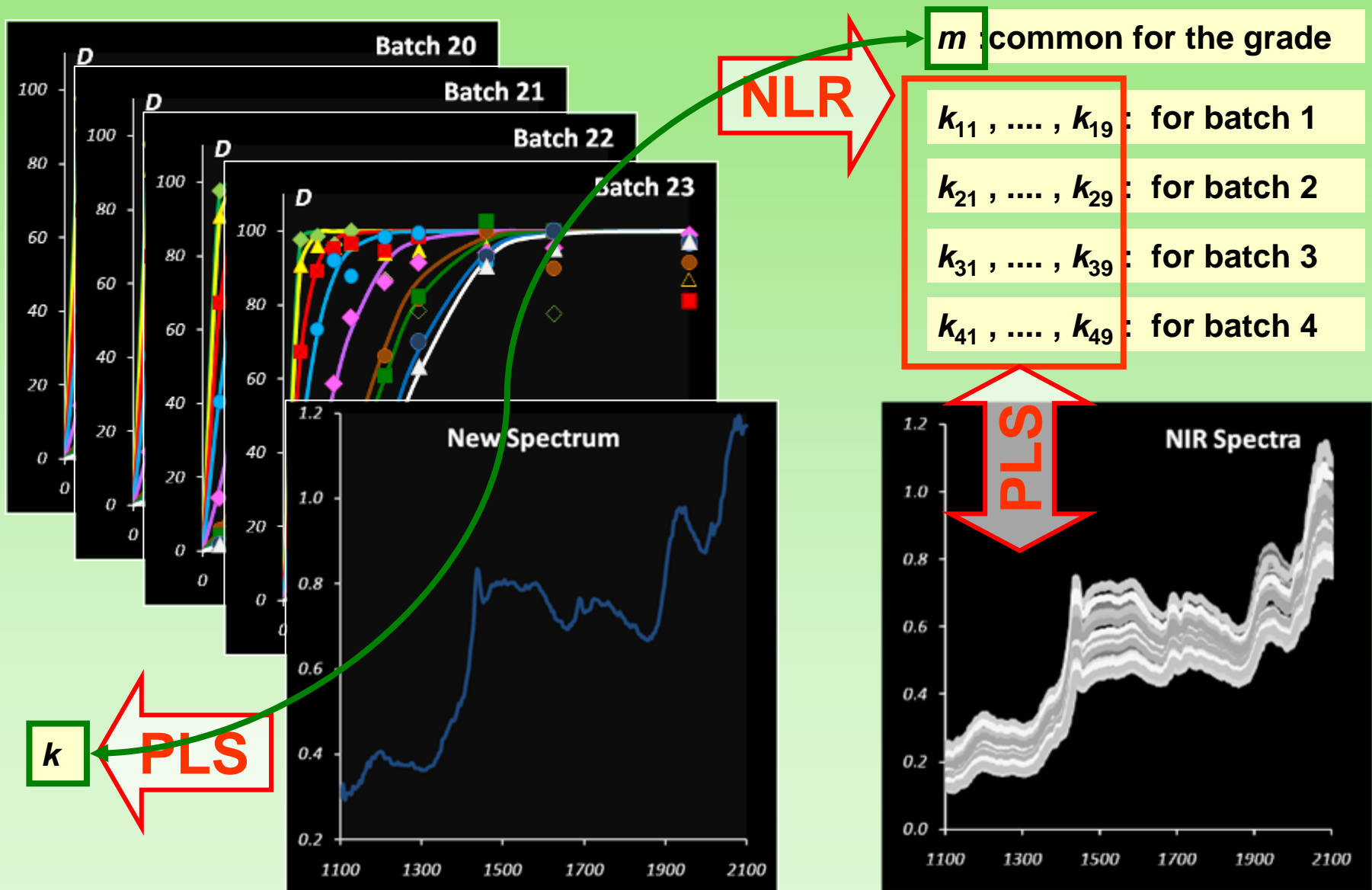
**parameter *k*
keeps track of batch variations**
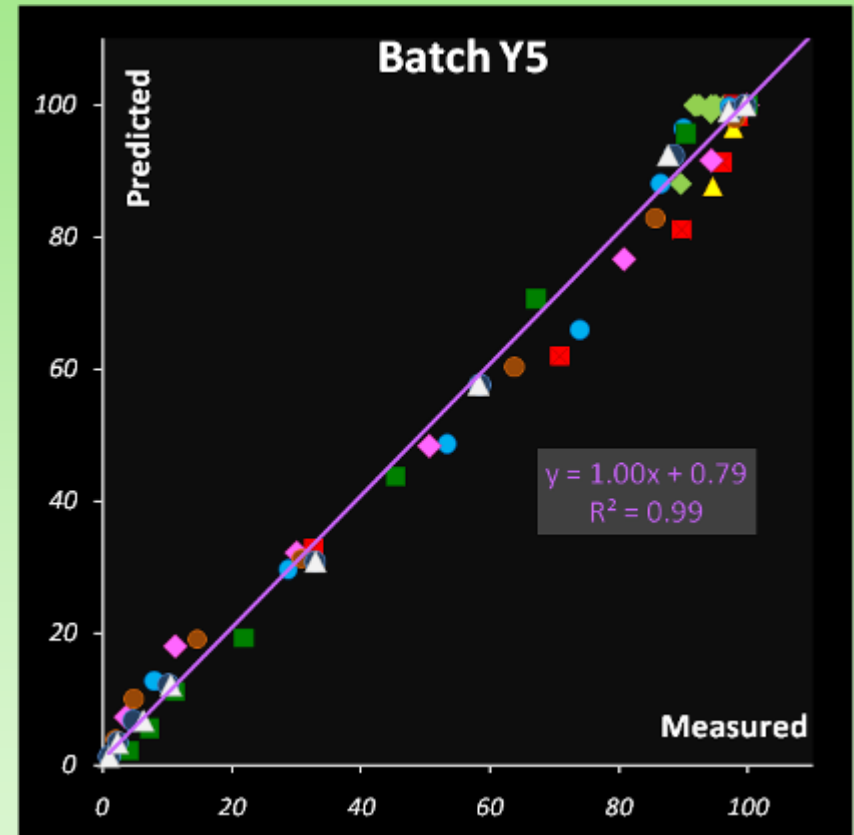
Prediction of *k*: NLR – NIR (White subset)

Prediction of *k*: NLR – NIR (Yellow subset)

Prediction technique

m : common for the grade

NLR

k_{11} , ... , k_{19} : for batch 1

k_{21} , ... , k_{29} : for batch 2

k_{31} , ... , k_{39} : for batch 3

k_{41} , ... , k_{49} : for batch 4

PLS

k

PLS

Test set validation: W2 and Y5 prediction
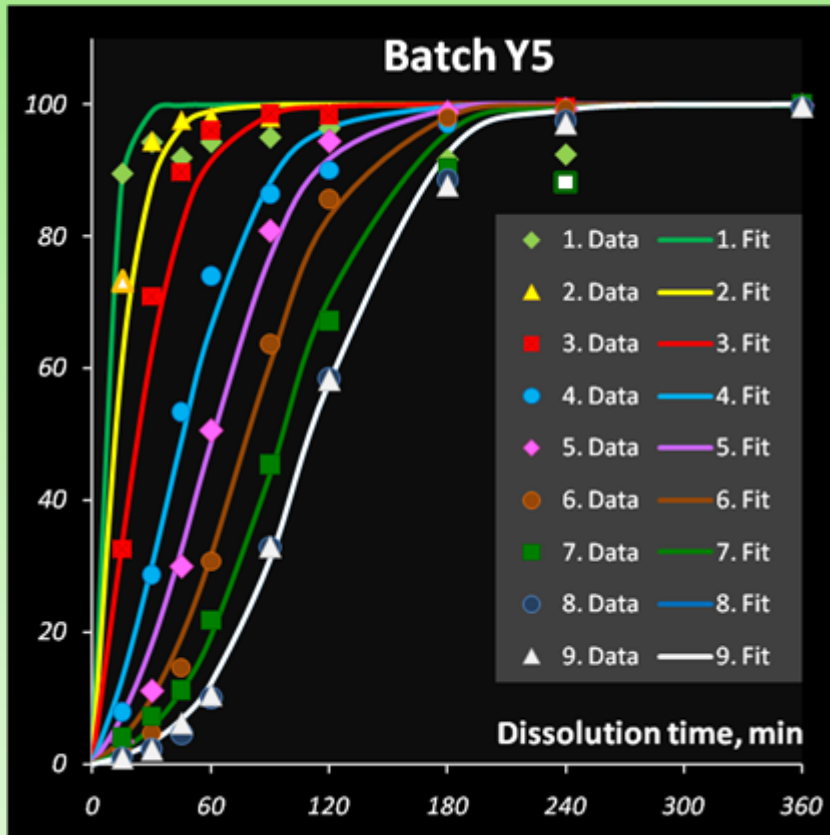
Conclusions

- PAT solution for the in-line release profile prediction

- novel "curve to curve" calibration approach via NLR

- autocatalytic model for the drug release

Project PANOPOD- II (25304/02) sponsor