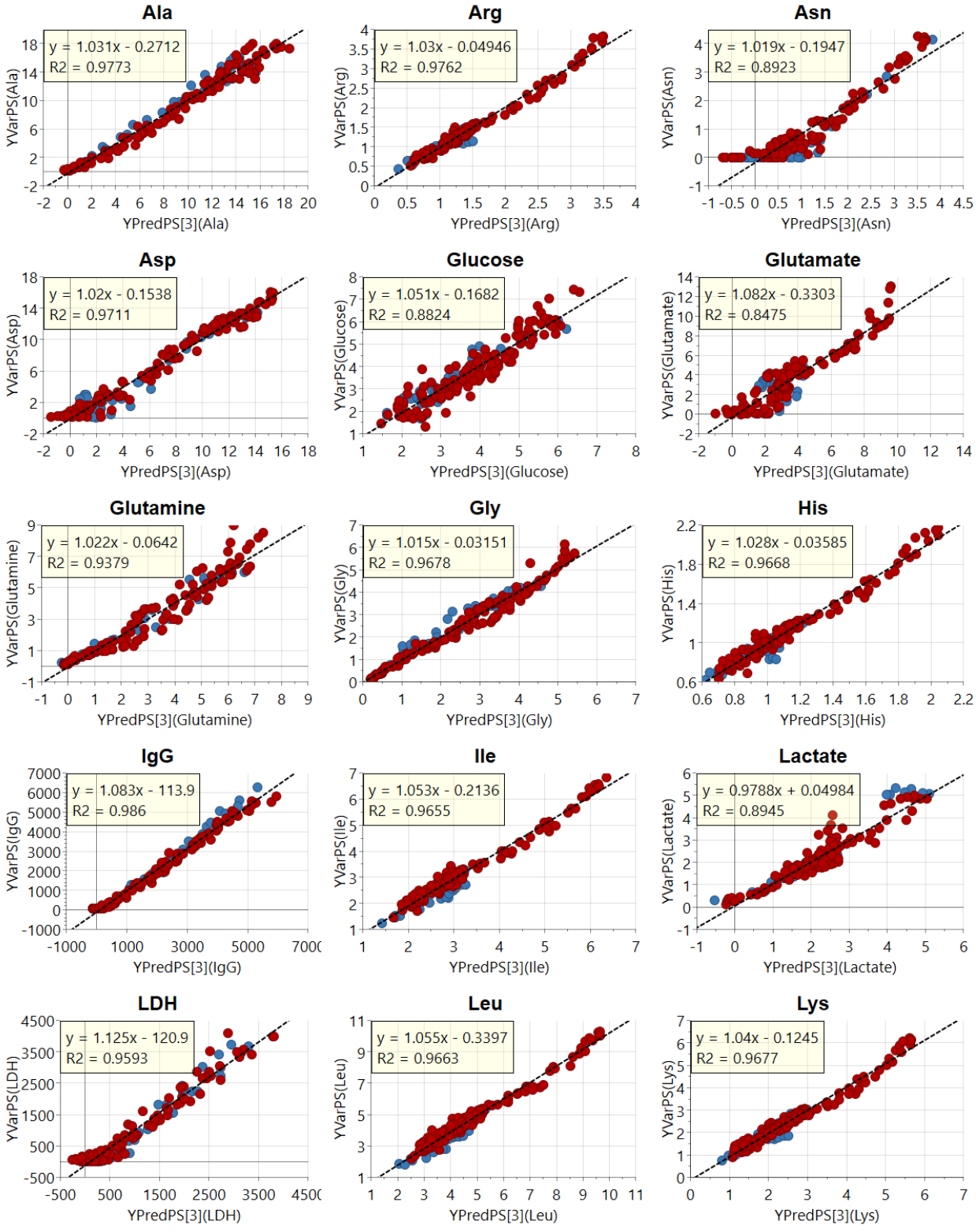
A hierarchical model combining process and Raman spectroscopic data for real-time monitoring of cell culture process

Pei Yin, Jing Tong, Liwei Zhang, Weihua Tang, Pei Jiang, Xun Wan, Meijin Guo

Supplementary information

Table S1: Summary of OPLS2 model calibration and prediction results

Attribute	Abbreviation	Unit	Range	Calibration and cross-validation			Prediction	
				R2Y	Q2	RMSECV	RMSEP	$RMSEP_{percent}$ (%)
Alanine	Ala	mM	0.15 - 18.04	0.979	0.976	0.8983	1.0052	12.0
Arginine	Arg	mM	0.43 - 3.83	0.980	0.977	0.1135	0.1195	8.4
Asparagine	Asn	mM	0.00 - 4.27	0.892	0.903	0.4117	0.5200	54.2
Aspartic acid	Asp	mM	0.00 - 16.06	0.978	0.975	0.7900	1.2318	17.1
Glucose		g/L	1.32 - 7.45	0.878	0.873	0.5074	0.4141	11.0
Glutamate		mM	0.00 - 13.05	0.885	0.876	1.0064	1.2765	36.8
Glutamine		mM	0.08 - 8.98	0.931	0.927	0.6272	0.3852	13.4
Glycine	Gly	mM	0.12 - 6.16	0.973	0.970	0.2679	0.3157	12.5
Histidine	His	mM	0.62 - 2.17	0.973	0.968	0.0618	0.0690	6.3
IgG titer	IgG	mg/L	50 - 6264	0.987	0.986	205.6540	395.3710	20.7
Isoleucine	Ile	mM	1.25 - 6.82	0.975	0.971	0.1966	0.3090	10.1
Lactate		g/L	0.11 - 5.38	0.885	0.880	0.3760	0.4260	19.5
Lactate dehydrogenase	LDH	U/L	0.7 - 4091.2	0.951	0.948	255.2220	318.1660	35.7
Leucine	Leu	mM	1.80 - 10.29	0.975	0.970	0.3133	0.5014	10.7
Lysine	Lys	mM	0.76 - 6.21	0.972	0.968	0.2143	0.2364	9.5
Methionine	Met	mM	0.69 - 1.88	0.968	0.962	0.0533	0.0645	5.8
Ammonium	NH4	mM	0.16 - 5.83	0.815	0.805	0.6308	0.4718	21.0
Osmolality	osmo	mosm/kg	255 - 508	0.971	0.970	11.8327	10.3538	3.0
Phenylalanine	Phe	mM	1.02 - 3.75	0.973	0.968	0.1093	0.1107	6.1
Proline	Pro	mM	0.45 - 4.34	0.980	0.976	0.1412	0.1741	9.2
Serine	Ser	mM	1.04 - 9.91	0.980	0.976	0.3285	0.4065	9.7
Threonine	Thr	mM	1.03 - 5.78	0.973	0.969	0.1884	0.2403	9.2
Tryptophan	Trp	mM	0.21 - 1.14	0.974	0.969	0.0382	0.0521	8.7
Tyrosine	Tyr	mM	0.00 - 2.54	0.973	0.970	0.0998	0.0902	8.8
Valine	Val	mM	1.29 - 8.24	0.980	0.977	0.2350	0.3170	9.6
Viable cell density	VCD	E6 cell/mL	0.415 - 23.80	0.921	0.918	1.9604	2.3267	21.5


Ala
y = 1.031x - 0.2712
R2 = 0.9773
YVarPS(Ala)
YPredPS[3](Ala)
Arg
y = 1.03x - 0.04946
R2 = 0.9762
YVarPS(Arg)
YPredPS[3](Arg)
Asn
y = 1.019x - 0.1947
R2 = 0.8923
YVarPS(Asn)
YPredPS[3](Asn)
Asp
y = 1.02x - 0.1538
R2 = 0.9711
YVarPS(Asp)
YPredPS[3](Asp)
Glucose
y = 1.051x - 0.1682
R2 = 0.8824
YVarPS(Glucose)
YPredPS[3](Glucose)
Glutamate
y = 1.082x - 0.3303
R2 = 0.8475
YVarPS(Glutamate)
YPredPS[3](Glutamate)
Glutamine
y = 1.022x - 0.0642
R2 = 0.9379
YVarPS(Glutamine)
YPredPS[3](Glutamine)
Gly
y = 1.015x - 0.03151
R2 = 0.9678
YVarPS(Gly)
YPredPS[3](Gly)
His
y = 1.028x - 0.03585
R2 = 0.9668
YVarPS(His)
YPredPS[3](His)
IgG
y = 1.083x - 113.9
R2 = 0.986
YVarPS(IgG)
YPredPS[3](IgG)
Ile
y = 1.053x - 0.2136
R2 = 0.9655
YVarPS(Ile)
YPredPS[3](Ile)
Lactate
y = 0.9788x + 0.04984
R2 = 0.8945
YVarPS(Lactate)
YPredPS[3](Lactate)
LDH
y = 1.125x - 120.9
R2 = 0.9593
YVarPS(LDH)
YPredPS[3](LDH)
Leu
y = 1.055x - 0.3397
R2 = 0.9663
YVarPS(Leu)
YPredPS[3](Leu)
Lys
y = 1.04x - 0.1245
R2 = 0.9677
YVarPS(Lys)
YPredPS[3](Lys)

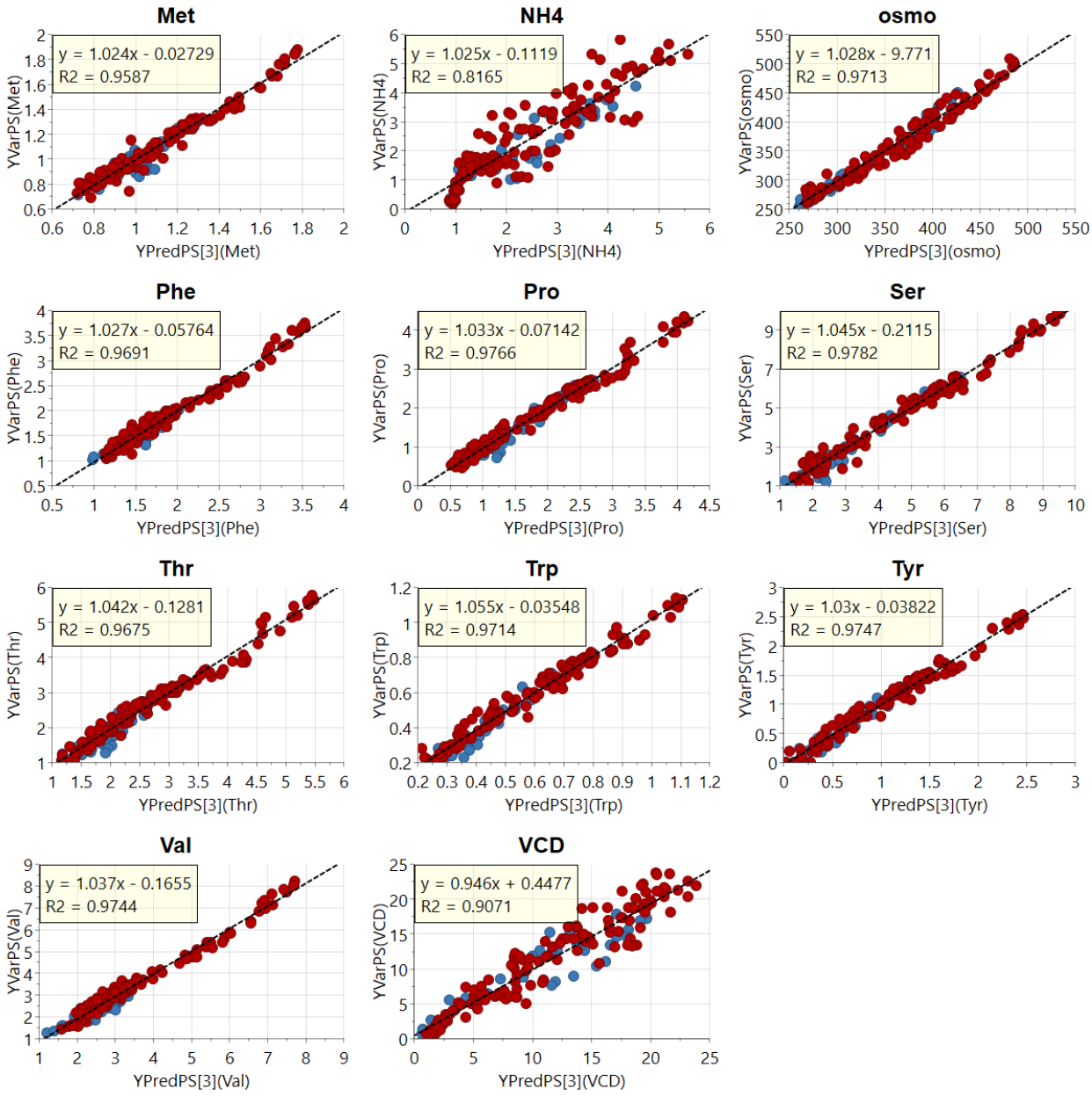


Figure S1: Measured concentration (y-axis) vs. predicted concentration (x-axis) for attributes from OPLS2 model in the calibration data set (red) and test data set (blue).

Figure S2: (A) Contribution plot from the predicted component of the hierarchical model for DOE3 vs. DOE4 at 36h, 184h and 326h; (B) Contribution plot from the orthogonal component of the hierarchical model for DOE3 vs. DOE4 at 36h, 184h and 326h. Yellow colored variables are outside their 3 std dev. range.

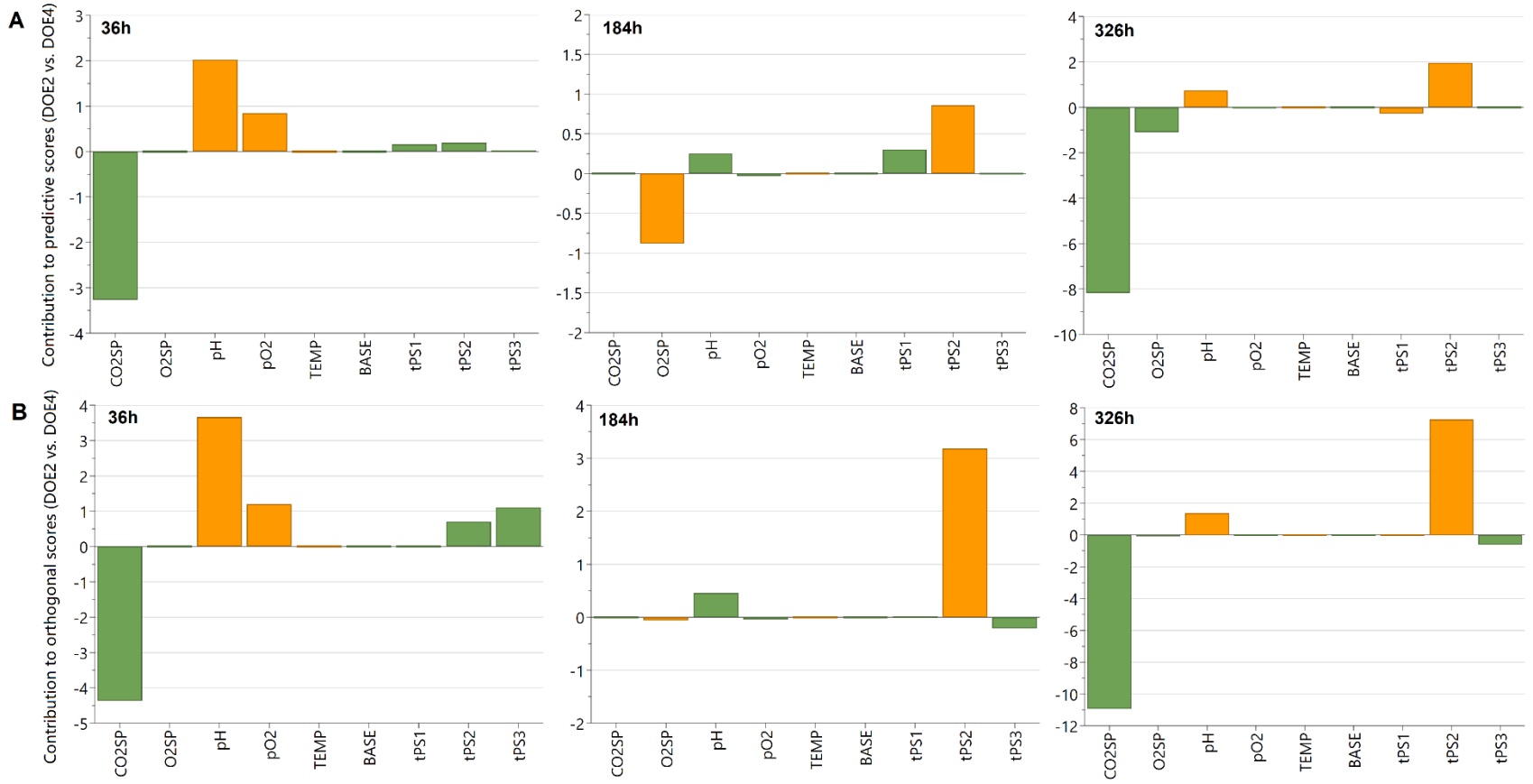


Figure S3: (A) Contribution plot from the predicted component of the hierarchical model for DOE2 vs. DOE4 at 36h, 184h and 326h; (B) Contribution plot from the orthogonal component of the hierarchical model for DOE2 vs. DOE4 at 36h, 184h and 326h. Yellow colored variables are outside their 3 std dev. range.