Supplemental Material

Development of Raman Calibration Model Without Culture Data for In–Line Analysis of Metabolites in Cell Culture Media

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Figure S1. Raman spectra of aqueous glucose solutions: (a) raw spectra, (b) difference spectra obtained by subtracting the Raman spectrum of water.



Figure S2. Raman spectra of aqueous lactate solutions: (a) raw spectra, (b) difference spectra obtained by subtracting the Raman spectrum of water.



Figure S3. Raman spectra of aqueous glutamine solutions: (a) raw spectra, (b) difference spectra obtained by subtracting the Raman spectrum of water.



Figure S4. Raman spectra of aqueous glutamate solutions: (a) raw spectra, (b) difference spectra obtained by subtracting the Raman spectrum of water.



Figure S5. Raman spectra of aqueous ammonia solutions: (a) raw spectra, (b) difference spectra obtained by subtracting the Raman spectrum of water.



Figure S6. Raman spectra of antibody PBS solutions: (a) raw spectra, (b) difference spectra obtained by subtracting the Raman spectrum of PBS.



Figure S7. Raman spectra of viable cell PBS solutions: (a) raw spectra, (b) difference spectra obtained by subtracting the Raman spectrum of PBS.



Figure S8. Raman spectra of the medium: (a) raw spectra, (b) difference spectra obtained by subtracting the Raman spectrum of water.



Figure S9. Raman spectra of the feed agent: (a) raw spectra, (b) difference spectra obtained by subtracting the Raman spectrum of water.

Table S1. The result of wavenumber regions (cm^{-1})	with the minimum RMSECV (shown in
Table II, center) for each pretreatment condition.	

No.	Pretreatment set			Glucose	Lactate	Antibody
1	_	_	_	1014–1113	1013–1112	1648–1747
2	Baseline removal	-	-	926–1125	986–1085	1663–1762
3	First deriv.	_	-	430–529	242–341	1669–1868
4	Second deriv.	_	-	430–629	888–1087	1674–1773
5	SNV	_	-	2745–2944	895–994	1633–1732
6	Baseline removal	SNV	_	936–1135	959–1058	1639–1738
7	First deriv.	SNV	-	1007–1206	2956–3155	1664–1863
8	Second deriv.	SNV	-	937–1136	2961-3160	1643–1742
9	Normalization by sapphire	-	_	1075–1174	1012–1111	1646–1845
10	Normalization by sapphire	Baseline removal	_	442–541	2940–3039	1663–1762
11	Normalization by sapphire	First deriv.	_	429–528	429–528	1162–1261

12	Normalization by sapphire	Second deriv.	-	430–629	2951–3150	1492–1691
13	Normalization by sapphire	SNV	_	2745–2944	895–994	1633–1732
14	Normalization by sapphire	Baseline removal	SNV	936–1135	959–1058	1639–1738
15	Normalization by sapphire	First deriv.	SNV	1007–1206	2956–3155	1664–1863
16	Normalization by sapphire	Second deriv.	SNV	937–1136	2961–3160	1643–1742
17	Normalization by water	_	_	1079–1178	2866–2965	1647–1846
18	Normalization by water	Baseline removal	-	1064–1163	788–987	1638–1737
19	Normalization by water	First deriv.	_	428–527	854–953	1645–1744
20	Normalization by water	Second deriv.	_	1131–1330	807–1006	1557–1756
21	Normalization by water	SNV	_	2745–2944	895–994	1633–1732
22	Normalization by water	Baseline removal	SNV	936–1135	959–1058	1639–1738
23	Normalization by water	First deriv.	SNV	1007–1206	2956–3155	1664–1863
24	Normalization by water	Second deriv.	SNV	937–1136	2961–3160	1643–1742