

Supporting Information

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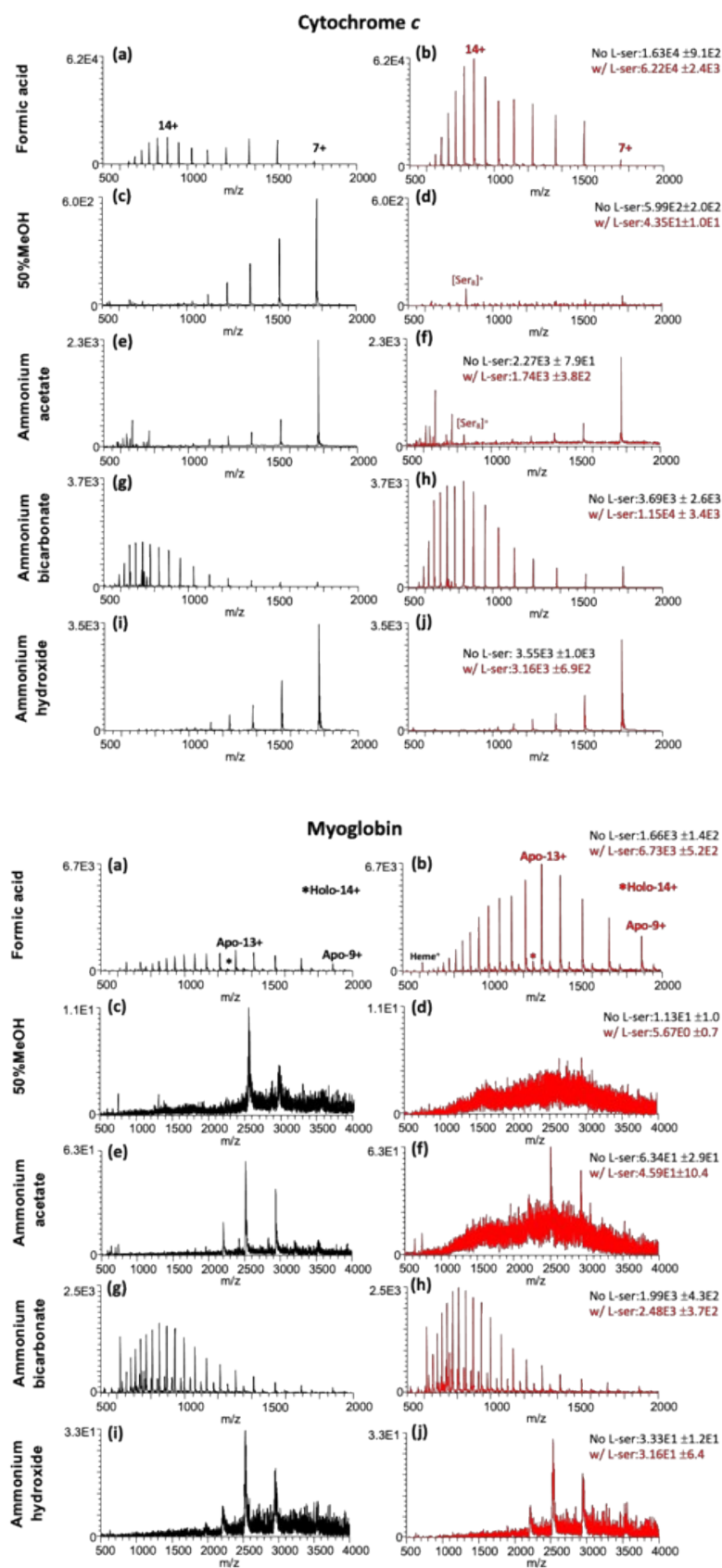


Figure S1. Representative DESI-MS spectra of natively deposited cytochrome *c* and myoglobin analyzed with five different desorption solvent systems with 100 μ M L-serine (shown in red) and without it (shown in black) arranged by increasing desorption solvent pH. (a), (b) 0.1% formic acid in 50% MeOH. (c), (d) 50% MeOH. (e), (f) 200 mM ammonium acetate in 50% MeOH. (g), (h) 200 mM ammonium bicarbonate in 50% MeOH. (i), (j) 1% ammonium hydroxide in 50% MeOH. The intensities reported are the average intensity of the highest observed charge state (HICS) of the protein in each solvent system with L-serine (in red) and without it (in black). Statistically significant improvement in signal intensity were observed for cytochrome *c* (b) and (h) and myoglobin (b) (p-value<0.001).

Table S1- Improvement in signal intensity for each protein with addition of L-serine to the five different solvent systems.

	pH	Average fold change Cyt c HICS Intensity	Average fold change Cyt c Integrated Intensity	Average fold change apo-Myo HICS Intensity	Average fold change Apo-myo Integrated Intensity	Average fold change holo-Myo HICS Intensity	Average fold change Holo-myo Integrated Intensity
Formic acid	2.99	3.8±0.1	3.1±0.4	4.3± 0.3	3.7± 0.2	3.5± 0.3	3.31±0.3
50% MeOH	5.75	0.1± 0.02	0.4±0.02	N/A	N/A	0.5± 0.05	N/A
Ammonium acetate	7.32	0.8± 0.2	0.7±0.1	N/A	N/A	0.7±0.2	N/A
Ammonium bicarbonate	7.97	3.1± 0.2	3.1±0.3	1.4± 0.2	1.2± 0.2	1.3± 0.2	1.3± 0.2
Ammonium hydroxide	10.02	0.9± 0.2	0.8±0.2	N/A	N/A	0.9± 0.2	N/A

Table S2. Approximate net charge on protein and serine in different solvent systems.

Cytochrome c						
Solvent	Intensity Fold Change	≈pH	Protein Net Charge (pI 10.3)	Serine Population	pH-pK_{a1} (2.21)	pH-pK_{a2} (9.15)
Formic acid	3.1	3	+	60-70% zwitterion 30-40% positive	0.79	
50% MeOH	0.8	6	+	100% zwitterion	3.79	
Ammonium acetate	0.8	7	+	99% zwitterion 1% negative		-2.15
Ammonium bicarbonate	3.1	8	+	92-94% zwitterion 6-8% negative		-1.15
Ammonium hydroxide	0.9	10	-	10-20% zwitterion 80-90% negative		0.85

Myoglobin						
Solvent	Intensity Fold Change	≈pH	Protein Net Charge (pI 7.4)	Serine Population	pH-pK_{a1} (2.21)	pH-pK_{a2} (9.15)
Formic acid	3.7	3	+	60-70% zwitterion 30-40% positive	0.79	
50% MeOH	0.5	6	+	100% zwitterion	3.79	
Ammonium acetate	0.7	7	-	99% zwitterion 1% negative		-2.15
Ammonium bicarbonate	1.2	8	-	92-94% zwitterion 6-8% negative		-1.15
Ammonium hydroxide	0.9	10	-	10-20% zwitterion 80-90% negative		0.85

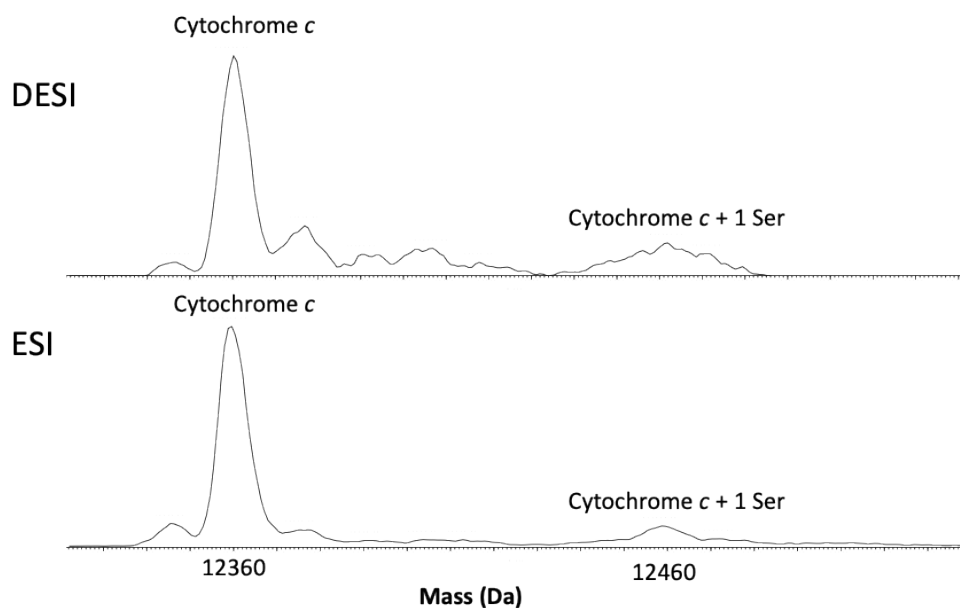


Figure S2. Representative deconvoluted spectra of cytochrome *c* shows presence of L-serine adducts on cytochrome *c* peaks that were detected at low temperature (70°C) in DESI and ESI with 0.1% formic acid in 50% MeOH with 100 μ M L-serine as desorption solution and working solution respectively.