

ESM Table 1: Protocol for freeze substitution of HPF samples

Step	T start (°C)	T end (°C)	Time (hr)	Reagent	Concentration
1	-90	-90	5	cocktail	1% osmium tetroxide, 0.1% uranyl acetate in pure acetone
2	-90	0	18	cocktail	1% osmium tetroxide, 0.1% uranyl acetate in pure acetone
3	0	0	0.2	Acetone	100%
4	0	0	0.2	Acetone	100%
5	0	0	0.2	Acetone	100%
6	RT	RT	2	Epon:Acetone	1:3
7	RT	RT	2	Epon:Acetone	1:1
8	RT	RT	2	Epon:Acetone	3:1
9	RT	RT	2	Epon	100%
10	60	60	24-48	Epon	100%