

Table S1. Statistical parameters characterizing pH<sub>e</sub> heterogeneities modeled by phantoms.

	I	J	K	L
weighted average (mean), $\overline{\text{pH}}_e$	7.13	7.19	7.30	7.42
weighted median, $\widetilde{\text{pH}}_e$	7.25	7.30	7.34	7.41
mode, pH <sub>e1</sub>	7.39	7.38	7.33	7.38
mode, pH <sub>e2</sub>	6.56	6.56	6.56	6.56
peak height ratios (pH <sub>e2</sub> / pH <sub>e1</sub> )	0.64	0.41	0.19	0.08
peak area ratios (pH <sub>e2</sub> / pH <sub>e1</sub> )				
- integrated	0.57	0.38	0.18	0.06
- deconvolved	0.53	0.37	0.18	0.07
skewness, G1	-0.22	-0.44	-0.61	-0.42
kurtosis, G2	-0.63	-0.22	0.79	1.52
entropy, H	5.07	5.00	4.82	4.53

Data are based on <sup>31</sup>P NMR spectra of 3-APP phantoms containing two test samples at different pH: 6.5 (pH<sub>e2</sub>) and 7.2 (pH<sub>e1</sub>). The divergence between pH<sub>e1</sub> (the principal mode),  $\overline{\text{pH}}_e$  and  $\widetilde{\text{pH}}_e$  was largest for the bimodal distribution with the most pronounced secondary mode (pH<sub>e2</sub>), and decreased with decreasing relative intensity of the pH<sub>e2</sub> mode from I to L (decreasing 3-APP concentration of the low-pH solution). As expected,  $\overline{\text{pH}}_e \ll \widetilde{\text{pH}}_e \ll \text{pH}_{e1}$  for the largest acidic (pH<sub>e2</sub>) contribution to the pH profile (I), whereas  $\overline{\text{pH}}_e$  and  $\widetilde{\text{pH}}_e$  converged toward pH<sub>e1</sub> with decreasing pH<sub>e2</sub> contribution (L). The pH distribution had a negative skew throughout because of its asymmetry (see also Fig. 4 I - L): the pH<sub>e2</sub> mode was consistently less pronounced than the pH<sub>e1</sub> mode. G1 became increasingly negative with increasing asymmetry from I to K. However, this trend was reversed when going from K to L because the intensity of the pH<sub>e2</sub> mode dropped to very low values so that the overall pH distribution was dominated by the symmetric pH<sub>e1</sub> mode. Consequently, for a secondary mode, pH<sub>e,n</sub>, below a particular threshold value, G1 of the overall distribution changes with increasing pH<sub>e,n</sub> intensity such as to indicate increasing asymmetry. However, as the pH<sub>e,n</sub> intensity rises above this threshold, G1 returns to values indicating decreasing asymmetry. Obviously, for pH<sub>e,n</sub> intensities increasing even further, this mode will eventually become the primary mode. Therefore, care has to be taken when interpreting parameters such as skewness in the context of multimodal distributions. Relative areas under the pH<sub>e1</sub> and pH<sub>e2</sub> modes were consistent between integrated and deconvolved values, with deconvolved ratios being slightly higher, probably due to contributions from the base of the pH<sub>e1</sub> mode to the pH<sub>e2</sub> mode.