

Table S2. Statistical parameters characterizing unimodal computer-simulated pH distributions.

|   | Gaussian $\delta$ distributions |                  | Gaussian pH distributions |                  |
|---|---------------------------------|------------------|---------------------------|------------------|
|   | pH <sub>e1</sub>                | pH <sub>e2</sub> | pH <sub>e1</sub>          | pH <sub>e2</sub> |
| weighted average (mean), $\overline{\text{pH}}_e$ | 7.21                            | 6.45             | 7.19                      | 6.49             |
| weighted median, $\widetilde{\text{pH}}_e$        | 7.20                            | 6.48             | 7.19                      | 6.49             |
| mode, pH <sub>e,n</sub>                           | 7.20                            | 6.53             | 7.19                      | 6.49             |
| skewness, G1                                      | 0.69                            | -0.96            | 0.00                      | 0.00             |
| kurtosis, G2                                      | 1.79                            | 2.04             | -0.08                     | -0.08            |
| entropy, H  | 4.04                            | 4.01             | 4.04                      | 4.04             |

Data are based on simulated Gaussian NMR resonances (left pH<sub>e1</sub> and pH<sub>e2</sub> columns; Fig. S2 E, bottom), and on simulated Gaussian pH distributions (right pH<sub>e1</sub> and pH<sub>e2</sub> columns; Fig. S2 F, bottom). Curves were constructed such that pH modes coincided with nominal pH values close to 7.2 and 6.5. As expected, for each Gaussian pH distribution  $\overline{\text{pH}}_e$ ,  $\widetilde{\text{pH}}_e$  and pH<sub>e,n</sub> values were identical, and G1 was zero. In these distributions, kurtosis slightly deviated from the ideal value of G2 = 0 due to truncation of the distribution tails. By contrast, for pH distributions calculated from simulated Gaussian spectral lines, there is a negative skew for the pH<sub>e2</sub> mode, and a positive skew for the pH<sub>e1</sub> mode (see also Fig. S2 E, bottom). Diverging  $\overline{\text{pH}}_e$ ,  $\widetilde{\text{pH}}_e$  and pH<sub>e2</sub> values are another consequence of skewed pH distributions:  $\overline{\text{pH}}_e < \widetilde{\text{pH}}_e < \text{pH}_{e2}$  (since pH<sub>e2</sub> < pK<sub>a2</sub>), and  $\overline{\text{pH}}_e > \widetilde{\text{pH}}_e > \text{pH}_{e1}$  (since pH<sub>e1</sub> > pK<sub>a2</sub>). In these simulated unimodal distributions, H was not affected significantly by ppm-to-pH or pH-to-ppm conversions. However, asymmetric pH curves calculated from Gaussian spectral lines were clearly leptokurtic, with G2  $\approx$  2.