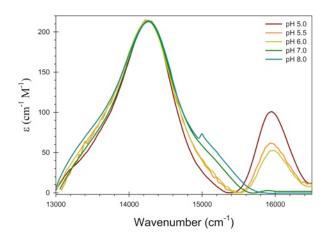
## The (Not Completely Irreversible) Population of a Misfolded State of Cytochrome c at Folding Conditions.

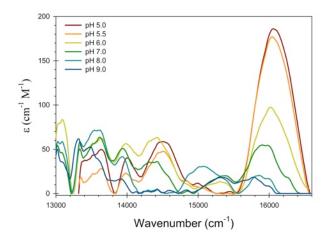
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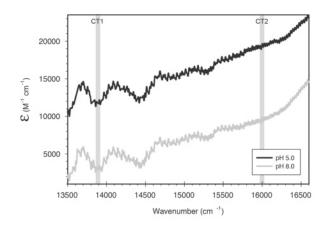
SUPPORTING INFORMATION



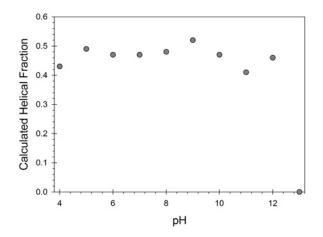
**Figure S1.** Baseline corrected absorption spectrum of horse heart ferricytochrome c measured between 13,000 and 17,000 cm<sup>-1</sup> at the indicated pH. Prior to the experiment the oxidized protein was exposed to alkaline conditions (pH 11.5) for two hours.



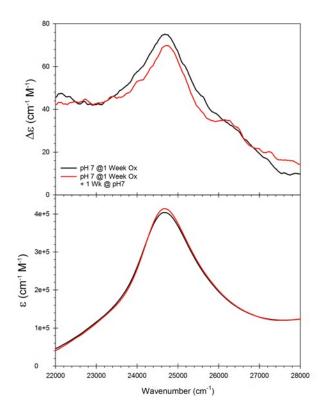
**Figure S2.** Baseline corrected absorption spectrum of horse heart ferricytochrome c measured between 13000 and 17000 cm<sup>-1</sup> at the indicated pH. Prior to the experiment the oxidized protein was exposed to alkaline conditions (pH 11.5) for one week.



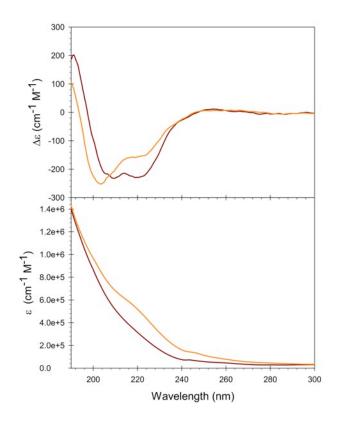
**Figure S3**. Charge transfer band region of the absorption spectrum of 0.05 mM ferricytochrome c (equine) measured between 13,500 and 16,600 cm<sup>-1</sup> at **PH** 5.0 and **PH** 8.0 in 0.1 mM potassium phosphate buffer. Prior to the measurement the oxidized protein was exposed to alkaline conditions (pH 11.5) for one week. The charge transfer bands CT1 and CT2 are explained in the text.



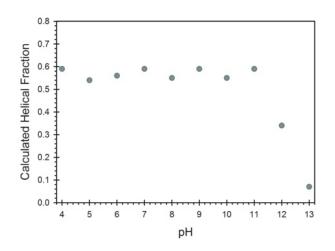
**Figure S4.** pH dependence of the  $\alpha$ -helical content of 0.05 mM ferricytochrome c after a one week incubation at pH 11.5. This information was obtained from UV-CD spectra of the sample as described in the main manuscript.



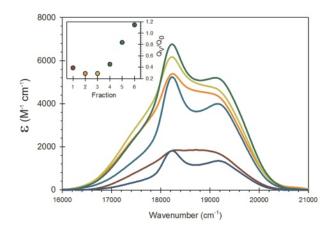
**Figure S5.** Visible CD (top) and absorption (bottom) spectra of the Soret band region of ferricytochrome c recorded at pH 7 after the protein was exposed to alkaline conditions (11.5) for one week and after it was allowed to sit at pH 7 for an additional week.



**Figure S6.** UV-CD (top) and absorption spectra (bottom) of ferricytochrome c at pH 11.5 recorded at room temperature (**■** red line) and after 10min at 373K (**■** orange line) under alkaline hydrolysis conditions.



**Figure S7.** Secondary structure comparison of 0.05 mM Cytochrome c after being oxidized for a week at pH 4 through 13, analysis made utilizing DichroWeb<sup>41, 42</sup> using the CDSSTR method<sup>43</sup> with SP175 reference set.<sup>44</sup>



**Figure S8.** Baseline corrected absorption spectra in the Q-band region of 0.5 mM cytochrome c after being oxidized for a week at pH 11.5. Inset show ratio of  $Q_v/Q_0$  for each aliquot sampled through the Sephadex column.