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**Electrostatic and Hydrophobic Nature of the  
Cytochrome c-Membrane Interaction**

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Cytochrome c (cyt c) binds to acidic membranes at low ionic strength. Replacement of Lys-72 or Lys-87 by Glu reduced the binding affinity of cyt c toward large unilamellar vesicles (LUV) in liquid crystalline phase. The differences were smaller for LUV in gel phase. A fraction of bound cyt c was non-electrostatically associated. A larger fraction of cyt c became associated hydrophobically when sonicated vesicles were employed instead of LUV. Electron paramagnetic resonance spectra of spin-labeled cyt c showed that there were at least two different conformers of bound cyt c in rapid equilibrium. Optical absorption demonstrated that the structure of bound cyt c is largely intact although a fraction suffers disruption of the Fe-Met bond. Reduced cyt c (ferrocyt c) has lower affinity than ferricyt c. This redox state dependence was demonstrated for the first time and it may have interesting implications for the mitochondrial electron transfer and oxidative stress.