Molecular simulations in electrochemistry

*Electron and proton transfer reactions mediated by flavins in different molecular environments*

Kılıç, M.

Citation for published version (APA):
# Contents

1 Introduction .................................................. 1
   1-1 Electron transfer in chemistry ............................. 2
   1-2 Proton transfer in chemistry ................................ 3
   1-3 Flavins in chemistry ........................................ 4
   1-4 Molecular simulation ....................................... 5
   1-5 Model and methods ......................................... 5
   1-6 This thesis ................................................ 6

2 Techniques .................................................... 9
   2-1 Marcus theory ............................................... 10
   2-2 Calculation of $pK_a$ using molecular simulation ............ 13
   2-3 Statistical thermodynamics .................................. 15
   2-4 Molecular dynamics ....................................... 16
   2-5 DFT–based molecular dynamics .............................. 17
      2-5.1 Density Functional Theory ............................... 19
      2-5.2 Born–Oppenheimer molecular dynamics .................. 21
   2-6 Hybrid quantum mechanics / molecular mechanics ........... 22

3 First and second one-electron reduction of lumiflavin in water – a first principles molecular dynamics study 23
   3-1 Introduction ............................................... 24
   3-2 Methods .................................................. 25
      3-2.1 Computational setup ...................................... 29
   3-3 Results .................................................. 30
      3-3.1 Lumiflavin in the gas phase .............................. 30
      3-3.2 Lumiflavin in water, the solvent structure ............... 33
      3-3.3 Lumiflavin in water, redox properties .................... 39
      3-3.4 Non–linearity, inner sphere fluctuations, temperature and finite size effects 41
   3-4 Conclusions ............................................... 44
   3-5 Supporting information .................................... 46
4 A microscopic picture of the solvent reorganization during electron transfer to flavin in water

4-1 Introduction ........................................... 52
4-2 Methods .............................................. 53
  4-2.1 Calculation of redox potential .......... 53
  4-2.2 Computational setup .................... 55
4-3 Results ............................................. 56
  4-3.1 Reduction of lumiflavin in vacuum .... 56
  4-3.2 Reduction of lumiflavin in water solvent 58
  4-3.3 Inner sphere and solvent reorganization, solvation shell structure rearrangement .... 62
  4-3.4 Solvent reorganization, electronic effects 63
  4-3.5 Solvent reorganization, electrostatic potential and fluctuations ................. 67
4-4 Conclusions ....................................... 69
4-5 Appendix ......................................... 74

5 Acidity constants of lumiflavin from first principles molecular dynamics simulations

5-1 Introduction ........................................ 76
5-2 Methods ............................................ 79
  5-2.1 Calculation of $pK_a$ from constrained dynamics 79
  5-2.2 Computational details ..................... 81
5-3 Results and discussion ............................ 82
5-4 Conclusions ....................................... 87
5-5 Supplementary information ..................... 89
  5-5.1 Radial distribution functions ............ 89
  5-5.2 Free energy profiles using the addition $H_3O^+$ restraint ................. 91

6 The reorganization free energies for electron transfer in proteins: Redox properties of flavin in BLUF and LOV Domains

6-1 Introduction ....................................... 94
6-2 Methods .......................................... 97
  6-2.1 Computational setup ....................... 98
6-3 Results .......................................... 99
  6-3.1 Reduction of flavin in different environments .... 99
  6-3.2 Characterization of protein and solvent coupling with flavin redox properties ... 103
6-4 Conclusions .................................... 118

Summary ............................................. 121

Samenvatting ......................................... 123