Curriculum Vitae

Mark L Paddock, Ph.D.

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Summary:

Research experience in design and development of site-directed mutagenesis system including expression in photosynthetic bacteria, membrane protein purification, biochemical cofactor substitution and development of optical methods used to characterize novel genetically engineered systems. Obtained Ph.D. in physics (biophysics) and have 20 additional years of academic research experience. Successfully completed numerous photosynthetic and mitochondrial projects. Supervised students and postdocs and initiated international collaborations.

Accomplishments:

- Designed and constructed site-directed mutagenesis system to identify the pathway of proton transfer in photosynthetic bacteria. Isolated and characterized membrane bound photosynthetic proteins. Traced and identified the pathway for proton transfer, a finding that has been achieved in relatively few systems. This provided the foundation for the majority of my 73 publications and 20 domestic and international invited talks. It provided the necessary cornerstone for hiring and supervising 4 technical staff.
- Performed biochemical cofactor substitution and developed optical kinetic assay to determine sequential order of electron and proton transfer to catalytic site of photosynthetic reaction centers. Allowed us to deconvolute the proton-coupled reduction (and hence oxidation) of quinone in the photosynthetic reaction center, an accomplishment that has been done in very few other systems.
- Improved quantum efficiency of reaction centers lacking the primary electron acceptor (natural electron transfer pathway) through a combination of mutations (along the B-branch) from 0.5% to 30%.
- Identified the previously unknown nature of the cofactor in the membrane anchored diabetic drug target mitoNEET. This initiated several new collaborations with internationally renowned professors. It also provided the framework for several graduate student projects.
- Crystallized and determined the unique structure of the only identified outer mitochondrial membrane iron sulfur (CDGSH) proteins. The structure was unique amongst the greater than 70,000 deposited structures and provided the necessary prerequisite information for the construction of mutations designed to vary the redox potential over an unprecedented range of 700 mV.

Education:

Ph.D. Physics (Biophysics), University of California, San Diego, La Jolla, California, 1991
Thesis Work: Characterization of Mutant Photosynthetic Reaction Centers from *Rhodobacter sphaeroides*: Investigation of Herbicide-Resistance and the Proton Transfer Pathway.
Advisors: Prof. Melvin Okamura, Prof. George Feher

M.S. Physics, University of California, San Diego, La Jolla, California, 1984

B.S. Physics, Harvey Mudd College, Claremont, California, 1983

Professional Experience at University of California, San Diego:

2005-Present Project Scientist

Implemented several **photosynthetic** research projects using site-directed mutagenesis, membrane protein purification, biochemical quinone substitution, EPR and ENDOR spectroscopy, X-ray crystallography in collaboration with Professors Melvin Okamura and George Feher. Implemented spectroscopic studies, prepared biochemical samples and made optical measurements. Supervised molecular biology technician and aided in supervising graduate research.

More recently initiated studies on a new class of mitochondrial proteins important for diabetes therapies. Studies resulted in over 20 international oral presentations with 17 talks/posters over the last 3 years.

2002-Present	Lecturer Prepared lectures for Physics 1C, Physics 2BL and Physics 2CL courses, supervised teaching assistants, coordinated with lab technician for experimental setups.
1999-2005	Associate Project Scientist Involved in projects using site-directed mutagenesis, biochemical quinone substitution, EPR spectroscopy, X-ray crystallography.
1993-1999	Assistant Project Scientist
1991-1993	Postdoctoral Research Physicist
1984-1991	Research Assistant
1983-1984	Teaching Assistant

Selected Publications (from 73 peer-reviewed publications, complete list here)

1. **Paddock, M.L.**, Ädelroth, P., Beatty, J.T., Feher, G. and Okamura, M.Y. (2002) Determination of Proton Transfer Rates by Chemical Rescue: Application to Bacterial Reaction Centers. *Biochemistry*, **41**(50), 14716 – 14725.
2. **Paddock, M.L.**, Feher, G. and Okamura, M.Y. (2003) Proton Transfer Pathways and Mechanism in Bacterial Reaction Centers. *Febs Lett.* **555**, 45-50.
3. **Paddock, M.L.**, Chang, C., Xu, Q., Abresch, E.C., Axelrod, H.L., Feher, G. and Okamura, M.Y. (2005) Quinone (Q_B) reduction by B-branch electron transfer in mutant bacterial reaction centers from Rhodobacter sphaeroides: quantum efficiency and X-ray structure. *Biochemistry* **44**, 6920-6928.
4. **Paddock, M. L.**, Flores, M., Isaacson, R., Chang, C., Abresch, E. C., Selvaduray, P. and Okamura, M. Y. (2006) Trapped conformational states of semiquinone $D^{+\cdot}Q_B^{\cdot}$ formed by B-Branch electron transfer at low temperature in *Rhodobacter sphaeroides* reaction centers. *Biochemistry* **45,** 14032-14042
5. Wiley, S.E., **Paddock, M.L.**, Abresch, E. C., Gross, L., van der Geer, P., Nechushtai, R., Murphy, A. N., Jennings, P.A. and Dixon, J.E. (2007) The outer mitochondrial membrane protein mitoneet contains a novel redox active 2Fe-2S cluster. *J. Biol. Chem* **282**, 23745-23749.
6. **Paddock, M.L.**, Wiley, S.E., Axelrod, H.L., Cohen, A. E., Roy, M., Abresch, E. C., Capraro, D., Murphy, A. N., Nechushtai, R., Dixon, J.E. and Jennings, P.A. (2007) MitoNEET is a uniquely folded 2Fe-2S outer mitochondrial membrane protein stabilized by pioglitazone, *Proc. Natl. Acad. Sci. USA* **104**, 14342-14347.
7. Conlan, A.R., Axelrod, H. L., Cohen, A. E., Abresch, E. C., Zuris, J., Yee, D., Nechushtai, R., Jennings, P. A. and **Paddock, M. L.** (2009) Crystal Structure of Miner1 shows that the Protein Causitive in Wolfram Syndrome 2 Contains Redox Active 2Fe-2S clusters. *J Mol Biol.* **392**, 143-153.
8. **Paddock, M.L.**, Flores, M., Isaacson, R., Shepherd, J.N. and Okamura, M.Y. (2010) EPR and ENDOR investigation of rhodosemiquinone in bacterial reaction centers formed by B-branch electron transfer. *Appl. Magn. Reson*. **37**, 39–48.
9. Dicus, M.M., Conlan, A., Nechushtai, R., Jennings, P.A., **Paddock, M. L.**, Britt, R.D. and Stoll, S. (2010) The Binding of Histidine in the (Cys)3(His)1-coordinated [2Fe-2S] Cluster of Human mitoNEET. *J. Am. Chem. Soc.* **32**, 2037-2049.
10. Zuris, J.A., Halim, D.A., Conlan, A.R., Abresch, E.C., Nechushtai, R., **Paddock, M.L.** and Jennings, P.A. (2010) Engineering the Redox Potential over a Wide Range within a New Class of FeS Proteins. *J. Am. Chem. Soc.* (Communication) **132**, 13120-13122.

Selected Invited Presentations (from 23 invited presentations)**:**

University of California, Riverside, California, Invited Speaker Biochemistry, June 2009
Gordon Conference on Iron-Sulfur Enzymes, New Hampshire, Invited Speaker, June 2008
Proton Transfer in Biology, Telluride, Colorado, Invited Speaker, July-August 2007
West Coast Photosynthesis Conference, Asilomar, California, Invited Speaker, January 2006
University of Illinois, Urbana, Illinois, Seminar Speaker, October 2004
International Meeting on Photosynthesis, Montreal, Canada, Invited Speaker, August 2004
Nobel Symposium on Membrane Proteins, Stockholm, Sweden, Invited Speaker, August 2003
University of California, Irvine, California, Invited Speaker Biophysics Department, November 2001

Collaborations (from greater than 13):

Professor Melvin Okamura, University of California, San Diego – Proton transfer and proton-coupled electron transfer studies on bacterial reaction centers (RCs).

Professor George Feher, University of California, San Diego – Proton transfer and proton-coupled electron transfer studies on bacterial reaction centers (RCs).

Professor Patricia Jennings, University of California, San Diego – Biochemical and biophysical characterization of the novel 2Fe-2S outer mitochondrial membrane protein mitoNEET.

Professor Rachel Nechushtai, The Hebrew University of Jerusalem, Israel – Characterization of native and mutant ferredoxin, purification and quantum efficiency of LH1:RC supercomplex; biochemical and biological investigations of mitoNEET orthologs in plants.

Professor J. David Britt, University of California, Davis – Pulsed EPR studies of the 2Fe-2S proteins.

Courses Taught:

Phys 2BL - Physics Laboratory: Experimental Methods of Physics

Measurements and errors, propagation of uncertainties, statistical analysis of random errors, normal distribution, least square fitting, probability distributions, physics of resonance, voltametry, measure density of the earth.

Phys 2CL - Physics Laboratory: Electricity and Magnetism, Waves and Optics

Measurements and errors, RLC circuits and circuit analysis, propagation of uncertainties, statistical analysis of random errors, normal distribution, least square fitting; probability distributions, physics of light reflection, refraction and interference, indices of refraction, lenses and the human eye.

Phys 1C – Waves, Optics and Modern Physics

Behavior of systems under combined thermal and electric forces, the interaction of light with matter as illustrated through optics and quantum mechanics. Topics include oscillations and waves, lenses, mirrors, cameras and telescopes, interference, diffraction and polarization, quantum mechanics, atoms, molecules, transistors, lasers and radioactivity and nuclear energy.

Recently Finished Research Support:

R01 GM41637 Okamura (PI) 2/1/07-6/31/11 NIH/GM
Electron and Proton Transfer in Reaction Centers
Role: Co-Investigator

References: Great References Available.