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Professor Rob de Ruyter, Chair
Faculty Search Committee
Biocomplexity Institute
Indiana University
Swain Hall West 117
Bloomington, IN, 47405-7105

Dear Professor de Ruyter,

Please consider my application for the **tenure-track faculty** position advertised on the Physics Today and the Biocomplexity Institute web site.

Enclosed, please find my CV, publication list, description of my research experience and its integration to my future research plans and the summary of my teaching experience and interest. The list of my reference sources with the names and contact information is also included.

Should you find my application interesting, please contact me to arrange an interview at your convenience. Thank you for your consideration.

Sincerely,

László Kálmán

References:

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RESEARCH EXPERIENCE AND FUTURE PLANS

Research interest: structure-function relationship in proteins of photosynthetic organisms. Correlation between electron and proton transfer reactions.

Object of research: membrane proteins and membrane preparations of photosynthetic bacteria.

Methods applied: biophysical and biochemical techniques, such as optical and EPR spectroscopy, potentiometry combined with site-directed mutagenesis.

Summary of background

The life on Earth strongly depends upon photosynthesis. All of our food directly or indirectly trough herbivores, the oxygen content of the atmosphere and the fuel we burn are all linked to current or ancient photosynthetic activity. Photosynthetic organisms capture light energy in order to drive energy consuming synthesis of molecules needed for the growth and maintenance of the organism. The central part of this process is the link between the electron and proton transfer reactions.
The structural motif of the photosyntheteic pigment-protein complexes that generate a charge-separated state across the membrane by the absorption of light is remarkably conserved between the reaction center of purple photosynthetic bacteria (the first integral membrane protein to yield a high resolution X-ray structure) and photosystem II of plants, cyanobacteria and algae. The two systems are evolutionary related despite of their differences in their function, namely photosystem II is able to oxidize water to molecular oxygen involving a tyrosine residue and a manganese complex. One of the most important events in the development of the Earth was the emergence of organisms capable of water oxidation and thus had an unlimited source of electrons by using water as a reductant. The tremendous increase in molecular oxygen provided an opportunity for the development of organisms using aerobic respiration.

Research experience

*Numbers in brackets refer to articles in the publication list

Postdoctoral research

Critical for the ability of photosystem II to oxidize water is that it is the strongest natural oxidant. The bacterial RC was converted to a very strong oxidant by using multiple site- directed mutations. The genetic alteration made the bacterial reaction centers capable of tyrosine and manganese oxidation, reactions that occur only in photosystem II but not in native bacterial reaction centers [8, 10, 12]. Both the oxidation of the tyrosyne residues and the binding of metals to the reaction centers involve the transfer of protons. By inserting tyrosine residues and their proton acceptors to different positions, the properties of the oxidized tyrosyl radicals and the fate of the phenolic proton has been significantly altered [9, 11]. In the modified bacterial reaction centers some of the generated tyrosyl radicals resembled the properties of those found in photosystem II. These modified bacterial systems can serve not only as a structural but also some extent as a functional model to the photosystem II. Correlation has been found between the electrostatic proton release and the electrochromic absorption changes upon tyrosine oxidation

[13]. Continuing the improvement of the bacterial model system to mimic photosystem II, several functional mononuclear manganese(II)-binding sites was designed and characterized [16]. The binding of these manganese(II)-ions is electrostatically compensated by proton release to the aqueous solution [manuscript in preparation]. The conversion of water to molecular oxygen, however, requires the ability to accumulate four electron equivalents. To develop such a functionally active metal cluster is a challenge and part of future long-term research effort.

Graduate research

Electrostatic interactions play a key role in the coupling of electron and proton transfer in membrane protein complexes during the conversion of the energy stored in sunlight or reduced substrates into biochemical energy via transmembrane electrochemical proton gradient. Besides the transmembrane proton transfer, the light-induced charges are stabilized within the photosynthetic reaction centers by electrostatic proton uptake/release. Changes in local electrostatics induced either by replacing the critical cofactors [2] or by genetic alterations of nearby residues [5] or by the combination of these two methods [7] resulted in altered protonational pattern and stability of the light induced charge separated states. Upon continuous illumination the pigment-protein complex undergoes structural changes near the critical cofactors. In the light-adapted conformation the observed high proton release is connected to a conformational switch, which is controlled by the ionization states of the protonatable side chains [6]. To measure the accessibility of the protonatable residues to the aqueous phase we developed a novel technique by measuring the buffering capacity of the entire water-detergent-protein system [3, 4].

Research plan

Incorporation of reaction centers into liposomes

Project rationale:
Photosynthetic bacteria are studied most widely in the reaction center level. During the isolation of the reaction centers, however, the native membrane is removed and replaced by different detergent micelles. Many responses of the complex to light excitation (e.g. the rate of charge recombination and proton uptake etc) are altered in detergent solubilized reaction centers compared to those determined in the natural membrane environment. These observations raise the question as to how the environment of the protein perturbs the properties and functions of the major redox groups. Part of my research plan is to reconstitute the detergent-solubilized photosynthetic reaction centers into different lipid vesicles, which are better approximations of the natural membrane milieu.

Specific aims:
- To determine how the lipid vesicles modify the conformational flexibility of the reaction center protein upon illumination?
- To characterize the electrostatic proton uptake/release (kinetics and stoichiometry) in the presence of different lipid vesicles?
- To elaborate strategies for altering systematically the electrochemical properties (e.g. redox midpoint potential) of the cofactors by selecting different lipids?

- To determine how the accessibility of the protonatable residues change upon lipid reconstitution, knowing that the detergent belt around the protein is about 5 Å narrower than the hydrophobic zone of the protein?
- To obtain information how the binding of metals and the protonation of the secondary quinone are altered?

Metal binding to reaction centers

Preliminary work
In bacterial reaction centers binding of certain metals can facilitate electron and impair proton transfer reactions. In one of our previous study we have found several loosely bound manganese(II)-ions to be associated with the reaction center in excess manganese concentrations [12]. The functional roles of only two metals are known so far. Preliminary observation showed that in the presence of manganese(II) the long lived charge separated state (indication of an altered conformation) was not detectable [unpublished result]. This suggests that the metal binding effects the conformational response of the protein to light excitation.

Aims:

-To determine how specific the effect is to manganese(II)-ion.
-To assess functional and perhaps novel metal binding roles.
-To develop multinuclear metal clusters, serving as secondary electron donor

Major research facilities

Protein purification, sample preparation
Sterile box, preparative and ultracentrifuges, French pressure cell or sonicator

Sample characterization
UV-VIS-NIR spectrophotometer, single beam kinetic spectrophotometer (local design), X (Q, W) –band EPR spectrometer (optional)

TEACHING EXPERIENCE AND PHILOSOPHY

Teaching experience

Courses taught:

(*solely responsible)

- *Biophysics for undergraduates (juniors) lecturing, grading; 4 semesters,
- Biophysics lab instructor (junior, senior and graduate level); total of 9 years,
- Medical physics lab instructor (freshmen); total of 9 years,
- *Biological proton pumps: (for graduate students); lecturing, grading; 2 semesters.

Development of teaching materials:

- Co-author of two laboratory textbooks (medical and biophysics) at SZOTE and JATE Universities (after integration in year 2000 both part of University of Szeged),

Teaching diversities:

- As a member of the medical physics teaching group (for 9 years) in the frame of the program conducted in English, taught medical students from many countries (Canada, Egypt, Germany, Greece, Iran, Kuwait, Norway, Sweden, U.S.A.) with diverse socioeconomic, cultural and ethnic backgrounds.

Integration of teaching and research:

- Supervised a thesis for MS in physics (biophysics): Tibor Jánosi (2001 spring).
- Integrated research topics (see publication list articles #2, 5,7) into graduate course " Biological proton pumps".

Awards associated with teaching:

- Award for "Development of Teaching Biophysics", Hungarian Biophysical Society (1995).

Teaching philosophy

Course development and design:

For non-majors (most probably large classes).

- Building a teaching team with TAs.
- Providing interactive teaching materials.
- Home works and frequent testing.

For majors (smaller classes)

- Provide learner centered environment by class participation and collaborative learning (group work).
- Teach techniques that will empower students to be self sufficient learners.

For graduate studies

- Provide provoking subjects originating from ongoing research.

- Create an intellectual environment that promotes collaboration and mentoring.

I believe students can learn the most through problem solving. This is a great opportunity to organize, recall and synthetize knowledge and helps the students to develop creative thinking.

Teaching interest

I would be happy to teach/develop a biophysics/biophysical chemistry course.
I would feel comfortable teaching general and physical chemistry.