Jul 26th , 2011

Kristin Rae Swanson, Ph.D.
Department of Pathology
University of Washington
Seattle, WA 98104

Dear Dr. SwanSon:

I am writing to apply for the postdoctoral fellow position in your research lab. I am currently a postdoctoral fellow in the Department of Biomedical Engineering at Johns Hopkins University, Baltimore, MD. Prior to this position, I received a Ph.D. degree in 2008 from the Department of Chemical and Biological Engineering at State University of New York at Buffalo, NY.

In this letter I wish to convey my strong interest in one of your research projects "Patient-specific clinical-scale mathematical modeling of brain tumor growth and response to therapy ". By combing mathematical models of tumor growth/therapy response with clinical imaging data, such project has great potential clinical importance since the usage of quantitative mathematical models may provide predictive power for patient therapy. I believe my research experience and my education background in the areas of systems biology and mathematical modeling, make me a good fit for this position. One of my key strengths relevant to the position is that I have substantial experience in mathematical modeling of biological systems and processes which range from signal transduction pathways, to glycosylation pathways, to angiogenesis process under physiological conditions. In addition, I have published 10 papers in peer-reviewed journals, and several manuscripts in submission/in preparation.

During my postdoctoral training in Johns Hopkins University, I have worked on several projects in the area of angiogenesis modeling, including multiscale modeling of angiogenesis in skeletal muscle at exercise conditions, effects of fiber type and size on oxygen distribution and VEGF (vascular endothelial growth factor) gradients in exercising skeletal muscle, and a mathematical model of VEGFR2 trafficking. In one project, I developed a multiscale model that describes a multistep process of angiogenesis from the molecular level to tissue level. A module-based integration strategy was used to link currently available models using different modeling methodologies including algebraic equations, ordinary and partial differential equations and agent-based models with complex logical rules. This integrated model was then used to simulate exercise-induced angiogenesis in skeletal muscle and predict capillary growth patterns at different exercise conditions (Pac Symp Biocomput, 2009; Theor Biol Med Model, 2011). In addition, I utilized the multiscale model to understand the effects of fiber type and size on the heterogeneity of oxygen distribution, VEGF distribution and angiogenesis response (In Preparation). In another project, I formulated an integrative model of VEGF receptor trafficking to understand how receptors are regulated at the plasma membrane and in the endosomes by receptor modifications (Submitted to PLoS Comp Biol).

While at Buffalo, I completed several projects about mathematical modeling of biochemical reaction networks. In one paper that I published in the journal Bioinformatics (2005), I have demonstrated the use of multivariate statistical tools in the analysis of complex biological reaction networks. Taking a classical signal transduction cascade (EGF/TNF mediated signaling) as an example, I demonstrated that sensitivity analysis can be coupled with multivariate analysis methods to define critical rate limiting and allow definition of key systems perturbation wet-lab experiments. In addition, I have developed a new software toolbox to perform network analysis of complex biological processes at the molecular level (Bioinformatics

2008). In one project I collaborated with my colleagues on the computational and experimental analysis of cellular glycosylation pathways. Using a reverse-engineering approach to analyze the experimental data, we predict the *in vivo* glycosylation reaction pathway and its enzyme kinetic constants (Bioinformatics 2008, Glycobiology 2011).

Overall, I have a sustained record of excellence in the area of computational systems biology. I also have strong analytical, technical and problem-solving skills. I am confident of my ability to work independently and to design creative solutions to research problems not only because of my experience but also because the work carried out in my projects is largely my own with my advisors only providing input at conceptual levels. Further, I strongly believe that I am a talented, and committed individual who can succeed in the academic environment.

Enclosed is a copy of my curriculum vitae, which more fully details my qualifications for this position. I would appreciate the opportunity to be considered for a personal interview. If you have any questions about my application or would like to talk with me, I can be reached at (716) 601-4310 or you can email me at gangliu@jhmi.edu.

I look forward to hearing from you and thank you for your time and consideration.

Best Regards,

Gang Liu
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OBJECTIVE

- To obtain a challenging Computational Biologist Position that utilizes my technical expertise in the field of systems biology and bioinformatics

SUMMARY

- Eight years experience in the development and implementation of computational and mathematical models to address diverse biological questions
- Proficient in an array of modeling techniques such as ordinary/partial differential equation simulation, stochastic simulation, agent-based modeling, statistical analysis etc
- Experienced in non-linear dynamic analysis, optimization and control theory
- Strong knowledge and background in engineering, systems biology, and pharmacology
- Fluent in a range of languages including MATLAB, SimBiology, FORTRAN, C, JAVA and Perl.
- Two years experience in Graphical User Interface design and software package development

PROFESSIONAL EXPERIENCE

Postdoctoral Fellow, Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD 03/08-Present

Projects: Exercise-induced Skeletal Muscle Angiogenesis: A Multiscale *In Silico* Study; A VEGF-induced receptor 2 trafficking model; and Effects of fiber type/size on oxygen distribution, VEGF gradients in exercising skeletal muscle, Advisor: Dr. Aleksander S Popel

- Extensive literature review of skeletal muscle angiogenesis
- Developed a multiscale skeletal muscle angiogenesis model that includes blood flow, oxygen convection-diffusion process, vascular endothelial growth factor (VEGF) reaction-diffusion process as well as endothelial cell (EC) migration, EC proliferation, and vascular growth
- Reconstructed an agent-based model from *in vitro* to *in vivo* in order to fit physiological conditions
- Designed a "plug and play" modular integration methodology to model angiogenesis at multiple spatial and time scales
- Used the multiscale model to predict capillary growth under physiological conditions
- Utilized the multiscale model to study the effects of heterogeneous muscle fiber type/size on oxygen distribution, VEGF distribution, and angiogenesis response
- Developed a mathematical model of crosstalk activation between VEGR2 and integrin, and used bifurcation analysis to analyze the model structure and parameter space
- Developed a computational model of VEGFR2 receptor trafficking by fitting the experimental data with the constraints from kinetic analysis of the resting state
- Established and led a multiscale modeling team including one master's student and three undergraduates

Research Assistant and Teaching Assistant, State University of New York, Buffalo, NY 08/01–03/08

Thesis: System-Level Modeling and Analysis of Biochemical Reaction Networks in Signal Transduction and Glycosylation", Advisor: Dr. Sriram Neelamegham

- Developed a systematic approach to construct a glycosylation reaction network via evolutionary inference in the case of P-selectin glycoprotein ligand-1 glycosylation in human promyelocytic leukemia (HL-60) cells
- Utilized a genetic algorithm to optimize the reaction network and estimate the rate constants
- Applied OpenGL Fortran language to visualize the glycosylation reaction pathway
- Utilized object-oriented programming concepts in Fortran 90 codes to construct the glycosylation pathway and generate its subsets
- Constructed a computational model for tumor necrosis factor (TNF)-induced signaling to understand the dynamic control of nuclear factor-κB oscillatory behavior
- Developed a software package including cellular reaction network simulation and sensitivity analysis coupled with principal component analysis and singular value decomposition to aid formulation, testing and reduction of theoretical biochemical reaction networks

- Applied direct differential method coupled with principal component analysis in order to analyze signal transduction network in the case of epidermal growth factor-induced signaling
- Introduced a novel algorithm to reduce model complexity using sensitivity analysis combined with flux analysis
- Served as a teaching assistant for two undergraduate courses (Unit Operation and Chemical Engineering Principles) and one graduate course (Biochemical Engineering)

Research Assistant, Xiamen University, Xiamen, China 09/98–07/01

Thesis: "Simultaneous Biosorption of heavy metals ions using Biomass" Advisor: Dr. Qingbiao Li

- Biosorption capacity of Cd^{2+}/Pb^{2+} in biomass of *Phanerochaete chrysosporium*
- Mathematical model of biosorption process and adsorption mechanism

EDUCATION

Ph.D., 2008 **Department of Chemical and Biological Engineering**
State University of New York at Buffalo, Buffalo, NY

M.S., 2001 **Department of Chemical Engineering**
Xiamen University, Xiamen, China

B.E., 1998 **Chemical Engineering (Minor in Computer Science)**
Xiamen University, Xiamen, China

HONORS

- NYS/GSEU Professional Development Award, 2002
- Wu Simin's Scholarship–awarded to a chemical engineer with outstanding promise for professional success, 1999
- First-class Academic Scholarship 1994-1998– awarded to students in the Top 5% of the class

COMPUTER SKILLS

- Certification: Sun Certified Java Programmer (SCJP)
- Language: MATLAB, JAVA, C/C++, FORTRAN, PERL,SimBiology
- Database: MYSQL; Statistical Software: MATLAB; Others: OpenGL, XML

COURSES

- Kinetics, Thermodynamics, Transport Phenomena, Advanced Analysis
- Molecular Cell Biology, Biochemistry, Statistical Genomics
- Tissue Engineering, Metabolic Engineering, Biochemical Engineering

PROFESSIONAL SOCIETY MEMBERSHIP

- Biochemical Medical Engineering Society (BMES)
- American Institute of Chemical Engineering (AICHE)
- International Society of Systems Biologists (ISSB)

INTERNSHIP AND ENGINEERING TRAINING

- Engineering training in ethylene synthesis in Sinopec Shanghai Petrochemical Company Ltd., Shanghai, China. (1998)
- Engineering training in industrial manufacture of PVC at Fujian Petrochemical Company Ltd., Fujian, China (1997)

PUBLICATIONS

1. **G.Liu**, F Mac Gabhann ,A.Popel, Source of heterogeneity in angiogenesis response to endurance exercise in skeletal muscle: quantification of fiber type/size effects, ***In Preparation***
2. **G.Liu**, F Mac Gabhann ,A.Popel, Receptor modification regulates VEGF receptor endocytosis and trafficking: insights from a computational model, ***submitted***

3. **G. Liu,** A.Qutub, P. Vempati, F Mac Gabhann, A. Popel, Module-based multiscale simulation of angiogenesis in skeletal muscle, ***Theoretical Biology and Medical Computing***, *2011,8***:**6
4. S. Neelamegham**, G.Liu,** Systems glycobiology: biochemical reaction networks regulating glycan structure and function, ***Glycobiology***, *2011,* in press
5. A. Qutub, **G. Liu**, P. Vempati, A. Popel, Integration of angiogenesis modules at multiple scales: from molecules to tissue, ***Pacific Symposium in Biocomputing 2009***, 316-27
6. **G.Liu**, D.Marathe, S.Neelamegham, System-level modeling of cellular glycosylation reaction networks: O-linked glycan formation on natural selectin ligands, ***Bioinformatics***, 2008, 24(23):2740-7
7. **G.Liu**, S.Neelamegham, Analysis of cell signal transduction pathways using the Insilico Biochemical Reaction Network Analysis (IBReNA) package, ***Bioinformatics***, 2008, 24(8):1109-11
8. **G.Liu**, M.T. Swihart, and S. Neelamegham, Sensitivity, principal component and flux analysis applied to signal transduction: the case of epidermal growth factor mediated signaling. ***Bioinformatic***s, 2005, 21(7):1194-202.
9. Q. Li, S. Song, **G. Liu** et al, Simultaneous biosorption of cadmium (II) and lead (II) ions by pretreated biomass of Phanerochaete chrysosporium, ***Separation and Purification Technology***, 2004, 34:135-142
10. **G. Liu**, Q. Li, Advances in the research on Biosorption fundamentals and process, ***Technology of Water Treatment***, 2002, 28:17-21
11. Q. Li, **G. Liu**, S.Song, et al. Study on the cadmium (II) adsorption mechanism by the pretreated biomass of *Phanerochate Chrysosprium*, ***Chemical Industry and Engineering Progress***, 2002,1:182-5
12. W. Li, J. Wu, Q. Li, X. Deng, **G. Liu**, Desorption of Pb2+ from *Phanerochaete chrysosporium*, ***Journal of Natural Science in Xiamen University***, 2000, 39(4):481-4

PRESENTATIONS and POSTERS

1. **G.Liu,** F Mac Gabhann ,A.Popel, Receptor modification regulates VEGF receptor endocytosis and trafficking: insights from a computational model, **BMES 2011, (*Accepted as oral presentation)***
2. **G. Liu**, A.Qutub, P. Vempati, F Mac Gabhann, A. Popel, Module-based multiscale simulation of angiogenesis in skeletal muscle, **BMES 2011, (*Accepted as oral presentation)***
3. A. Qutub**, G.Liu**, P. Vempati, A. Popel, Integration of angiogenesis modules at multiple scales: from molecules to tissue, Experimental Biology 2009, New Orleans, LA
4. **G.Liu**, D.Marathe, S.Neelamegham, System-level Modeling of cellular glycosylation reaction networks, ***BMES*** 2008, Saint Louis, MO
5. **G.Liu**, D.Marathe, S.Neelamegham, Inferring O-linked glycosylation pathways in human leukocytes, ***BMES*** 2007, Los Angeles, CA
6. **G.Liu**, D.Marathe, S.Neelamegham, System-level modeling of O-linked glycosylation pathways in human leukocytes, ***AICHE*** 2007, Salt Lake City, UT
7. **G.Liu**, S.Neelamegham, From ligand binding to transcription activation: *in silico* simulation of tumor necrosis factor-induced nuclear factor kappa B activation using IBReNA software package, ***AICHE*** 2006, San Francisco, CA
8. **G.Liu**, S.Neelamegham, Analysis of cell signal transduction pathways using the In silico Biochemical Reaction Network Analysis (IBReNA) package, ***ICSB*** 2005, Boston, MA
9. **G. Liu**, M.T. Swihart, and S. Neelamegham, Sensitivity, principal component analysis and model reduction applied to signal transduction: the case of epidermal growth factor mediated signaling, ***AICHE*** 2004, Austin, TX
10. **G. Liu**, M.T. Swihart, and S. Neelamegham, Sensitivity and flux analysis applied to signal transduction: the case of epidermal growth factor mediated signaling, ***BMES*** 2004, Philadelphia, PA
11. **G. Liu**, Q.Li, Extraction of beta-carotenoid from *halobacterium*, ***The National Conference of Chemical technology*** (China), 2000, Xiamen, China

LEADERSHIP, COMMUNITY SERVICE AND EXTRACURRICULAR ACTIVITIES

- Departmental Senator, Graduate Student Association, SUNY at Buffalo
- Treasurer, Soccer Club, SUNY at Buffalo

References

Available Upon Request