

Subject: proposal for international connections
From: Dimitrios Vavylonis <vavylonis@Lehigh.EDU>
Date: 3/5/2013 10:45 AM
To: Cindy Hart <cmh505@lehigh.edu>

Dear Cindy,

please find attached a proposal for a faculty grant for international connections. I am also sending it to you via campus mail.

Best Regards,

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—Attachments:—

vavylonis_int_connections.pdf

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Application for a 2013-2014 Faculty Grant for International Connections

Combining modeling and experiment to study mating partner selection by fission yeast

Dimitrios Vavylonis, Department of Physics, Lehigh University

1. SUMMARY AND PROFESSIONAL GOALS

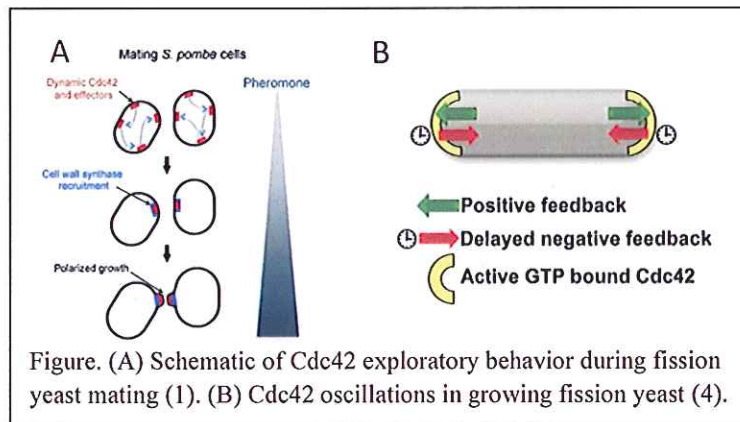
This is an application for a Faculty Grant for International Connections. The grant will support a two-week visit to the laboratory of Associate Professor Sophie Martin in the Department of Fundamental Microbiology at the University of Lausanne, Switzerland (http://www.unil.ch/dmf/page81926_en.html).

Sophie Martin is a cell biologist leading a group of 5 postdoctoral scientists, 4 graduate students and a technician. She has received prestigious awards by ASCB and EMBO for her innovative and high-quality studies on the role of actin and microtubule cytoskeleton in cell polarization, division and mating. I have been working to model these processes with mathematical and computational methods. Our interests in mechanistic studies of cellular organization overlap greatly. For example, with my postdoc H. Wang we wrote a paper modeling actin cables in fission yeast (2) that was directly motivated by one of her 2006 studies (3). More recently she wrote a comment in Science Signaling (5) highlighting our work on protein Cdc42 oscillations that was published last year (4). Despite our common interests, we did not have a chance to work closely on a joint project.

Recent studies by our groups provide an opportunity to initiate a collaboration. Fission yeast cells are not motile so they have to grow extensions towards one another for mating. This process is regulated by signaling proteins such as Cdc42 that direct the cellular cytoskeleton to

assemble at sites of Cdc42 accumulation and thus locally direct cell growth. Postdoctoral scientist Felipe Bendezu and Sophie Martin recently discovered that mating fission yeast cells pick their partners through an exploratory process involving a fluctuating Cdc42 signal (1), see panel A in Figure. This process has many similarities to the Cdc42 fluctuations and oscillations that my group has modeled in (4), see panel B in Figure. They found that the fluctuating patch of Cdc42 is stabilized with increased pheromone concentration. Pheromones are secreted by the neighboring cells at sites of Cdc42 accumulation. Thus the process of Cdc42 fluctuations, pheromone secretion, diffusion and cell growth is a highly interesting and complex process involving a variety of physical and biochemical mechanisms.

The main aim of the visit is to work with F. Bendezu and S. Martin and develop detailed mechanistic models describing how fission yeast cells pick their partner out of many possible neighboring ones. The above mechanisms are very new and fundamental so if the project is successful, *it will have a high impact in the field*. On my part this would involve working with them to design experiments, set up mathematical and computational models for Cdc42 behavior, secretion and digestion of pheromones, and cell growth.



2. EXPECTED OUTCOMES

Short-term: I expect that by the end of my visit we would have solid preliminary data and detailed plans for future experiments and models. I have performed similar visits in the past. I found that the most crucial ideas (in one case eventual external funding) originated in such short and focused visits supported by small seed grants. During my visit I will offer to give presentations about work at Lehigh.

Long-Term: I expect our work will result in one or more publications. This might lead to a long-term collaboration with the Martin group. In this case, we would apply for external funding.

3. NATURE OF INTERACTION

The work during my visit will involve postdoctoral scientist Felipe Bendezu, Prof. Sophie Martin and myself. The three of us met recently at the poster session of the Annual Meeting of the Society for Cell Biology in December, 2012. We had a discussion and the idea of a scientific collaboration was initiated.

4. PRE-PLANNING PREPARATION

I am planning on having a physics REU student work with a graduate student in my group (Haosu Tang or Tyler Drake) on this project over the summer. Shortly before, during, and after the visit, F. Bendezu will work to perform experiments to compare to models developed by members of my group and myself. We will work to find a two-week slot of time that the three of us can devote to the project. July, August or Fall of 2013 are likely dates.

5. EXPECTED FOLLOW UP

Upon my return to Lehigh I would involve a graduate student and/or postdoc in this project to work towards one or more publications. I would be more than happy to give presentations and inform the Lehigh community (especially the Bioengineering, Biology, and Chemistry faculty) about my experience and opportunities for interaction with the University of Lausanne.

6. PROPOSED BUDGET

Taxi and round-trip airfare to Lausanne:	\$2,000
Local hotel accommodation (Max State Dept rate \$242):	\$2,500
Per Diem (Max State Dept rate: \$404):	\$1,500
Total:	\$6,000

References

1. Bendezu, F. O., and S. G. Martin. 2013. Cdc42 explores the cell periphery for mate selection in fission yeast. *Curr Biol* 23:42-47.
2. Wang, H., and D. Vavylonis. 2008. Model of For3p-mediated actin cable assembly in fission yeast. *PLoS ONE* 3:e4078.
3. Martin, S. G., and F. Chang. 2006. Dynamics of the formin for3p in actin cable assembly. *Curr. Biol.* 16:1161-1170.
4. Das, M., T. Drake, D. J. Wiley, P. Buchwald, D. Vavylonis, and F. Verde. 2012. Oscillatory dynamics of Cdc42 GTPase in the control of polarized growth. *Science* 337:239-243.
5. Bendezu, F. O., and S. G. Martin. 2012. Cdc42 oscillations in yeasts. *Sci Signal* 5:pe53.



UNIL | Université de Lausanne
Département de microbiologie fondamentale
bâtiment Biophore bureau 2310
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Lausanne, March 4th 2013

Invitation to a two-week collaborative visit

Dear Dimitris,

I am happy to send you this invitation to a two-week collaborative visit to my lab. As discussed first at the 2012 ASCB meeting and further through email, the aim will be to initiate a collaboration joining cell biological and modelling approaches to investigate the mechanisms by which fission yeast cells select and orient growth towards partner cells during the mating process. My postdoc Felipe Bendezu and myself are very excited that you are interested in pursuing this idea with us.

This project builds on our respective recent advances in describing the dynamics of the master polarity regulator Cdc42 in fission yeast. We showed that Cdc42 explores the periphery of the cells during the mating process in search of a partner cell (Bendezu and Martin, *Current Biology* 2013). Your work described mathematically analogous oscillatory dynamic behaviour of Cdc42 during mitotic growth (Das et al, *Science* 2012). The aim of the visit will be to discuss between you, Felipe and myself the experimental and modelling set-ups for the project.

During your visit, I will be happy to host you for seminars to present your current work and discuss with other scientists both in our department and beyond at the University of Lausanne and at the EPFL.

I look forward to initiate this collaboration with you. We will undoubtedly benefit a lot from direct on-site interactions.

Best wishes,

Sophie

Faculté de biologie et de médecine
Département de microbiologie fondamentale



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