



December 1, 2003

To whom it may concern,

It is my pleasure to write this letter in strong support of Dr. Stephan Thiberge's application for a tenure-track assistant professor position. Stephan has been working in my lab for almost a year as a postdoctoral fellow, and during that time he has demonstrated many abilities that will serve him very well in developing a strong academic research program that should have an impact in the field of his choice. Stephan has shown to me that he can quickly acquire expertise in a new field, gain insight into the important issues, and then be able to carry out important research with sound experimental results.

Stephan has worked with me on several projects within the field of synthetic biology. In the context of systems biology, synthetic gene networks are emerging as an important tool in engineering new cell behaviors, as well as understanding the dynamics of naturally occurring genetic circuits. Progress in this area will likely have a significant impact in many fields, including biomedicine, biomaterial fabrication, environmental sensing, and functional genomics. Stephan was involved in a pulse generator project where we built a synthetic bacterial system that included sender and receiver cells. The sender cells were programmed to send a biochemical signal to nearby receiver cells, and the receivers responded with transient expression of a green fluorescent protein. Similar transient gene expression responses can be found in several naturally occurring systems, but analyzing this network motif in isolation from most other host factors can provide improved insight into its dynamic properties. This network also serves as another important building block for the synthetic biology toolkit. As part of this project, we engineered and then analyzed the spatiotemporal properties of several genetic variants of this system. Stephan played an integral role in this project where he performed both wetlab experiments with bacterial cells harboring the circuits and developed software for single-cell analysis of the time-series microscope fluorescence images.

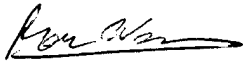
Stephan has also been actively involved in two other projects. He is developing a system for highly sensitive and accurate measurements of gene expression in single cells. The system barcodes cDNA from reverse transcription of cellular RNA using oligonucleotides that are tagged with differently colored Quantum Dots. Stephan is both developing software algorithms and a microscope hardware setup to accomplish the project's goals. Finally, Stephan is also involved in a project to investigate noise and modularity in genetic circuits. In this project, we are constructing a library of synthetic gene networks, where some of the constructs are subcircuits of larger circuits in our library. By measuring the steady-state and dynamic behavior of the circuits, we hope to

identify whether gene expression noise is attenuated or intensified in genetic regulatory cascades. We also hope to determine how well the behavior of compound circuits can be predicted from the behavior of their components.

Overall, Stephan not only has succeeded in experimental and theoretical work, but has also gained insight into the important issues in this field. His statement of purpose shows maturity and vision that will enable him to develop a significant research program. I therefore strongly recommend Stephan for a tenure-track position in your department.

If you have any additional questions, please do not hesitate to contact me.

Sincerely,

A handwritten signature in black ink, appearing to read "Ron Weiss", with a long horizontal flourish extending to the right.

Ron Weiss

Assistant Professor

Departments of Electrical Engineering and Molecular Biology

Princeton University