

# Curriculum Vitae

## Technologist

Engineer by training. Proficient with various programming languages and software packages such as MATLAB, Mathematica, C/C++ and Python.

Able to quickly familiarize myself with new environments, software and equipment.

## Modeler

Experience modeling complex non-linear dynamical systems under uncertainty. Proficient with methods for parameter estimation, statistical inference and hypothesis testing.

## Researcher

Wide scientific background. Proficient in analyzing new problems, prioritizing issues and prototyping original solutions. Interested in challenging topics.

Capable of presenting my work in both scientific papers and oral presentations.

## Professional Experience

|             |   |  |
|-------------|---|--|
| 2013 - now  | <b>Eindhoven University of Technology</b><br>Researcher (NCSB Stimulus Project)<br>Keywords: Genome Scale   | Conducted research on thermodynamic flux balance analysis in genome scaled metabolic networks using data from Genome Wide Association Studies and metabolic profiling.   |
| 2009 – 2013 | <b>Eindhoven University of Technology</b><br>Researcher (PhD)<br>Keywords: Mathematical Modeling, Uncertainty Analysis, Profile Likelihood, Bayesian Estimation, Markov Chain Monte Carlo, Importance Sampling, Optimal Experiment Design | Conducted research on propagating uncertainty in biochemical computer models using Bayesian and likelihood based approaches. Developed methodologies for optimal experiment design for non-linear models hampered by large uncertainties due to limited available data. The key aim was to reduce uncertainty to improve prediction accuracy and allow model selection. Applied methodologies to signaling models and models of fatty acid handling. |
| 2009        | <b>Eindhoven University of Technology</b><br>Graduation Project (MSc)<br>Keywords: Magnetic Resonance Spectroscopy, Digital Signal Processing, Data Analysis, Quantification  | Compared state of the art Magnetic Resonance Spectroscopy quantification methods and set up a MATLAB toolbox for quantifying problematic data acquired during voluntary exercise in-vivo. The approach lead to improved concentration estimates in conditions hampered by baseline and poor field homogeneity.   |
| 2009        | <b>Medical College of Wisconsin</b><br>Researcher (MSc)<br>Keywords: Biochemical Modeling, Reaction Thermodynamics, Kinetics, Electrophysiology, Parsing  | Developed parser that automatically generates large scale models from thermodynamic databases and small kinetic sub models. This approach accounts for ionic strength, temperature, compartmentalization, electrophysiology and dynamic buffering of multiple ions and metabolites.  |
| 2008        | <b>Eindhoven University of Technology</b><br>Internship (MSc)<br>Keywords: Measurement, Digital Signal Processing, Data Analysis, Labview   | During my internship I developed tools for analyzing force production and oxygen consumption of murine skeletal muscle during electrical stimulation.  |

## Education

|             |   |  |
|-------------|---|--|
| 2009 – now  | <b>Eindhoven University of Technology</b><br>Researcher (PhD)           | PhD about biochemical modeling of signaling and reaction networks  |
| 2006 - 2009 | <b>Eindhoven University of Technology</b><br>MSc Biomedical Engineering | Masters degree in Biomedical Engineering<br>Biomedical Imaging and Modeling<br>Graduated with honors (cum laude) |
| 2004 - 2005 | <b>Eindhoven University of Technology</b><br>BSc Biomedical Engineering | Bachelor degree in Biomedical Engineering<br>Graduated with honors (cum laude)                                   |

## International Experience

|      |   |   |
|------|---|---|
| 2013 | Houffalize, Belgium   | Speaker at “32 <sup>nd</sup> Benelux Meeting on Systems and Control”                              |
| 2013 | Eindhoven University of Technology  | Hosted international workshop on Parameter Estimation and Uncertainty Analysis in Systems Biology |
| 2011 | Integrative Systems Biology Group<br>Linköping University, Sweden           | Invited speaker at “Conclusions Despite Uncertainties”  |
| 2011 | Center for Interdisciplinary Computing<br>University of Heidelberg, Germany | Invited speaker at 5 <sup>th</sup> Workshop on Monte Carlo Methods                                |
| 2005 | Biotechnology Bioengineering Center<br>Medical College of Wisconsin, USA    | Externship  |

## Competences

- Expert in **C, MATLAB, LaTeX**
- Proficient with **Python, C++, Delphi**
- Competent with **JAVA, PHP, Mathematica, SQL, SVN**
- Some experience with **GPGPU** (Both **CUDA** and **OpenCL**), **Opt++**, **GSL**, **Qt**
- Multidisciplinary skills focused on **modeling, signal processing, image analysis, dynamical systems** and **NMR**
- **Teaching** and **tutoring** experience
- Experience **presenting** my work in technical and non-technical settings
- Fluent in spoken and written **English** and **Dutch**. Novice in **German**

## Interests and Hobbies

Electronic music production (also coding my own audio algorithms), recreational distance running, game development, travel, cinema, adventure games

## Personal Details

| Birth details                                    | Address  | Nationality | Phone              | Email                  |
|--|--|-------------|--------------------|------------------------|
| February 17th 1985<br>Helden,<br>The Netherlands | Hooghuisstraat 5c,<br>5611 GS Eindhoven<br>The Netherlands | Dutch       | +31(0) 623 752 992 | joep.vanlier@gmail.com |

## Journal Publications

**Vanlier, J.**, Tiemann, C.A., Hilbers, P.A.J. & van Riel, N.A.W. (in press). Parameter uncertainty in biochemical models described by ordinary differential equations, *Mathematical Biosciences*

Van Riel, N.A.W., Tiemann, C.A., **Vanlier, J.**, Hilbers, P.A.J. (in press). Applications of analysis of dynamic adaptations in parameter trajectories, *Interface Focus*

**Vanlier, J.**, Tiemann, C.A., Hilbers, P.A.J. & van Riel, N.A.W. (2012). A Bayesian Approach to Targeted Experiment Design. *Bioinformatics*, 28(8):1136-1142

**Vanlier, J.**, Tiemann, C.A., Hilbers, P.A.J. & van Riel, N.A.W. (2012). An Integrated Strategy for Prediction Uncertainty Analysis. *Bioinformatics*. 28(8):1130-1135

Tiemann, C.A., **Vanlier, J.**, Hilbers, P.A.J. & van Riel, N.A.W. (2011). Parameter adaptations during phenotype transitions in progressive diseases. *BMC Systems Biology*, 5, 174-1/14

Schmitz, J.P.J., **Vanlier, J.**, van Riel, N.A.W. & Jeneson, J.A.L. (2011). Computational modeling of mitochondrial energy transduction. *Critical Reviews in Biomedical Engineering*, 39(5), 363-377

**Vanlier, J.**, Wu, F., Qi, F., Vinnakota K.C., Han, Y., Dash, R. K., Yang, F., Beard, D.A. (2009), BISEN: Biochemical Simulation Environment. *Bioinformatics*. 25(6), 836-837

## Conference Proceedings

**Vanlier, J.**, Tiemann, C.A., Hilbers, P.A.J. & van Riel, N.A.W. (2012). Designing optimal experiments to identify progressive adaptations in biological systems. *NCSB Symposium: From Models and Data to Real Life Applications*, November 1-2 2012, Soesterberg, The Netherlands (**Talk**)

**Vanlier J.**, Tiemann C.A., Hilbers, P.A.J. & van Riel, N.A.W. (2012). Targeted Experiment Design using the Posterior Predictive Distribution, *PEDS-II Workshop*, June 4-6 2012, Eindhoven, The Netherlands (**Talk**)

Foster, R.M., **Vanlier, J.** & Franz, V.H. (2012). A new measure of motor-estimated size early in the grasp. *35<sup>th</sup> annual European Conference on Visual Perception*, Alghero, Italy (Poster)

**Vanlier, J.**, Tiemann, C.A., Hilbers, P.A.J. & van Riel, N.A.W. (2011). A Bayesian approach to predictions despite uncertainties. *Workshop Conclusions Despite Uncertainties*, June 18-19 2011, Linköping Sweden (**Talk**)

**Vanlier, J.**, Tiemann, C.A., Hilbers, P.A.J. & van Riel, N.A.W. (2011). A Bayesian approach to hypothesis based experimental design. *12th International Conference on Systems Biology*, August 28 – September 1 2011, Mannheim, Germany (Poster)

**Vanlier, J.**, Tiemann, C.A., Jeneson, J.A.L., Hilbers, P.A.J. & van Riel, N.A.W. (2011). Strategies for parameter uncertainty analysis. *Proceedings of the 3<sup>rd</sup> Dutch BioMedical Engineering Conference*, January 20-21 2011, Egmond aan Zee, The Netherlands (Poster)

Tiemann, C.A., **Vanlier, J.**, Jeneson, J.A.L., Hilbers, P.A.J. & van Riel, N.A.W. (2011). Predicting parameter development in progressive diseases. *Proceedings of the 3<sup>rd</sup> Dutch BioMedical Engineering Conference*, January 20-21 2011, Egmond aan Zee, The Netherlands (Poster)

Yang, H., **Vanlier, J.**, Hilbers, P.A.J. & van Riel, N.A.W. (2011). Comparative study of global parameter sensitivity analyses of models based on Ordinary Differential Equations. *Proceedings of the 3<sup>rd</sup> Dutch BioMedical Engineering Conference*, January 20-21 2011, Egmond aan Zee, The Netherlands (Poster)

**Vanlier, J.**, Tiemann, C.A., Jeneson, J.A.L., Hilbers, P.A.J. & van Riel, N.A.W. (2011). Strategies for parameter uncertainty analysis. *5<sup>th</sup> Workshop on Monte Carlo Methods*, January 14<sup>th</sup> 2011, Heidelberg, Germany (**Talk**)

Tiemann, C.A., **Vanlier, J.**, Hilbers, P.A.J. & van Riel, N.A.W. (2011). Kinetic analysis of liver X receptor induced hepatic steatosis. *Proceedings of Lipid Biology and Lipotoxicity (E2)*, May 15-20 2011, Killarney, Ireland (Poster)

**Vanlier, J.**, Tiemann, C.A., Hilbers, P.A.J. & van Riel, N.A.W. (2011). Closing the loop: a Bayesian approach to targeted experimental design. *NCSB symposium: The Full Systems Biology Cycle*, October 31 – November 1 2011, Soesterberg, The Netherlands (**Talk**)

Tiemann, C.A., **Vanlier, J.**, Groen, A.K., Hilbers, P.A.J. & van Riel, N.A.W. (2011). Liver X receptor induced metabolic adaptations: testing of model predictions. *NCSB symposium: The Full Systems Biology Cycle*, October 31 – November 1 2011, Soesterberg, The Netherlands (Poster)

**Vanlier, J.**, Tiemann, C.A., Jeneson J.A.L., Hilbers, P.A.J. & van Riel, N.A.W. (2010). Strategies for parameter uncertainty analysis. *NCSB symposium*, October 21 – 22 2010, Soesterberg, The Netherlands (**Talk**)

Tiemann, C.A., **Vanlier, J.**, Jeneson J.A.L., Hilbers, P.A.J. & van Riel, N.A.W. (2010). Revealing liver X receptor induced molecular adaptations in hepatic lipid metabolism. *NCSB symposium*, October 21 – 22 2010, Soesterberg, The Netherlands (Poster)

**Vanlier, J.**, Tiemann, C.A., Jeneson J.A.L., Hilbers, P.A.J. & van Riel, N.A.W. (2010). Why parameterization of signaling pathways is inherently difficult. *Proceedings of the 11<sup>th</sup> International Conference on Systems Biology (ICSB 2010)*, October 11 – 14 2010, Edinburgh, UK (Poster)

Tiemann, **Vanlier, J.**, C.A., Jeneson J.A.L., Hilbers, P.A.J. & van Riel, N.A.W. (2010). A computational study of liver X receptor induced hepatic steatosis. *Proceedings of the 11<sup>th</sup> International Conference on Systems Biology (ICSB 2010)*, October 11 – 14 2010, Edinburgh, UK (Poster)

Tiemann, **Vanlier, J.**, C.A., Jeneson J.A.L., Hilbers, P.A.J. & van Riel, N.A.W. (2010). A computational model of hepatic lipid metabolism: identifying persistent behavior. *Proceedings of the Conference on Systems Biology of Mammalian Cells (SBMC 2010)*, June 3-5 2010, Freiburg, Germany (**Talk**)

**Vanlier, J.**, Wu, F., Qi, F., Vinnakota K.C., Han, Y., Dash, R. K., Jeneson, J.A.L., van Riel, N.A.W., Hilbers, P.A.J. & Beard, D.A. (2009). BISEN: Biochemical Simulation Environment. *Proceedings of the 3<sup>rd</sup> FEBS Advanced Lecture Course on Systems Biology: From Molecular Biology to Biological Function (FEBS-SysBio2009)*, March 7-13 2009, Alpbach, Austria (Poster)

**Vanlier, J.**, Wu, F., Qi, F., Vinnakota K.C., Han, Y., Dash, R. K., Jeneson, J.A.L., van Riel, N.A.W., Hilbers, P.A.J. & Beard, D.A. (2009). BISEN: Biochemical Simulation Environment. *Proceedings of the Cardiac Physiome: Multi-scale and Multi-physics Mathematical Modelling Applied to the Heart*, July 20-24 2009, Cambridge, UK (Poster/**Flash talk**)

**Vanlier, J.**, Miedema, J.H., Ligtenberg, W.P.A., Schmitz, J.P.J., van Riel, N.A.W., ten Eikelder, H.M.M., Bosnacki, D. & Hilbers, P.A.J. (2009). Ordinary differential equations on the GPU. *Proceedings of the 1<sup>st</sup> International Workshop on High Performance Computational Systems Biology (HiBi2009)*, October 14-16 2009, Trento, Italy (**Poster/Poster prize**)

## Scientific Achievements

During my internship, I developed tools for analyzing force production and oxygen consumption of murine skeletal muscle during electrical stimulation. Subsequently, using this experimental setup and my suite of tools, I investigated the role of temperature on force production in skeletal muscle. I assessed reproducibility and improved both the experimental setup and data analysis based on modeling considerations.

In my Master's thesis, I compared Magnetic Resonance Spectroscopy quantification methods and set up a MATLAB toolbox for quantifying problematic data acquired during voluntary exercise in-vivo. Rather than using a Lorentzian lineshape, field inhomogeneities were taken into account by including additional lineshape distortion parameters (the lineshape was considered a convolution of a Lorentzian or Gaussian with several delta functions normalized to unity). The parameters of this distortion were then constrained to be the same for all peaks in the spectrum, thereby avoiding over-parameterization. The new approach led to improved concentration estimates in conditions hampered by baseline and poor field homogeneity.

During my PhD I have worked on propagation of uncertainty in biochemical computer models comprised of ordinary differential equations (ODEs). After gaining some experience with both frequentist and Bayesian approaches to uncertainty analysis, I have come up with a strategy to tackle problems regarding uncertainty analysis (by compiling Profile Likelihood with geometry based Markov Chain Monte Carlo sampling). By applying this strategy, one obtains a sample of parameter sets proportional to the parameter uncertainty distribution which can be used for simulating predictive distributions. When I first started my thesis, most of the methodological development was focused on determining the parameter uncertainty distribution. The main contribution I have made to the field is to use these posterior predictive distributions for experiment selection by realising that both the model structure and data imply specific non-linear relations between these distributions. I have developed two novel approaches that exploit the relations between these predictive distributions. The first method is geared towards reducing the uncertainty of selected predictions of interest (Bioinformatics 2012), while the second method is aimed at designing experiments to allow for successful model selection (currently under review). The major advantage of using these predictive distributions over the commonly used linearizations and asymptotic approximations is that they work well when data is scarce. Furthermore, qualitative predictions can be used for design, which particularly improves the applicability of such methods to biochemical systems.

Subsequently I have applied these methods to a system of fatty acid handling in the liver in close collaboration with a colleague of mine (C.A. Tiemann). Here, we discovered that a time consuming, costly and invasive measurement of a specific liver flux could be replaced by a few simple measurements on fecal matter.

## Attended Workshops/Seminars

Advanced Lecture Course on Systems Biology: From Molecules to Function

The Cardiac Physiome: Multi-scale and Multi-physics Mathematical Modeling Applied to the Heart

Workshop High Performance Systems Biology (Best Poster Award)

Experimental Design in Systems Biology, data analysis and parameter identification

DISC: Mathematical Models of Systems

DISC: Flexible Multibody System Analysis for Control Purposes

Planning and Communication

2nd International Workshop on Computational Models for Cell Processes

Playing with Charisma

Biostatistics

5<sup>th</sup> Workshop on Monte Carlo Methods, Heidelberg

Workshop on Parameter Estimation for Dynamical Systems

Workshop Conclusions Despite Uncertainties

## References

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Relationship to me Lab leader / Employer

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Relationship to me Daily supervisor

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