# Curriculum Vitae of Paulien Hogeweg

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## Research interests

The aim of my research is to understand biotic systems as dynamic information processing systems at many interconnected levels. In the seventies we identified the study of informatic processes in biotic systems as an open and promising research area for which we coined the term *Bioinformatics*[1]. Bioinformatics in this broad sense provides us with a unified framework for a research area for which a variety of names have now become fashionable, which includes, apart from bioinformatics ss (i.e. data-analysis of e.g. genomic data), the dynamic modeling approaches referred to as "systems biology", "computational life sciences", "computational biology", and which partially overlaps with "complex systems research" and "Artificial Life".

Realizing that the main challenge in modeling biotic systems is choosing interesting simplifying assumptions which do not 'beg the question' relative to the complexity of the biotic systems studied, we pioneered the use of novel computational modeling frameworks to study fundamental biological questions. Currently the focus is on evolutionary and developmental processes at multiple space and time scales, including the interplay between regulatory and evolutionary adaptation, information accumulation in prebiotic evolution morphogenesis at the inter-phase between regulatory and mechanic processes ecosystem embedded learning processes.

Below, I summarize my main contributions to computational methods and to bioinformatic theory in chronological order. The numbers refer to publications in the list of selected publications listed below.
A full list of publications is available at my website (http://bioinformatics.bio.uu.nl/ph/publications).

### Computational methods

- Introduction of individual based modeling strategies to study animal behavior. This modeling strategy has led to insight in the explanatory power of "opportunity based" rather than "optimality based" description for behavior. Moreover it provides a substrate for studying evolution and learning. Our methodology of individual based modeling helped define the research under the heading "artificial life' - and is now generally known as agent based modeling.**(cf. 38-40,42,45-47;34,36,30,14)**
- When in the beginning of the 80th the first sequence data became publicly available, we developed some data-analyzing methods which have proven their lasting usefulness. We introduced an algorithm for tree based multiple sequence alignment; This approach is now standard practice. for global multiple sequence alignment. Iterative methods were introduced at that time as well and are gaining more and more support. We also pioneered studies in RNA secondary structures and proposed the so-called mountain range representation of RNA secondary structure which is now incorporated in standard folding packages. **(cf. 43-44,41,35,50)**
- Introduction of individual based cellular automata as useful tools to study spatial ecological processes. The spatial patterns emerging due to local interactions between individuals were shown not only to be crucial for coexistence of species but also provide a rich substrate for

[1] the Oxford dictionary defines the word in this broad sense because we were the first to use it

evolution. The combination of CA and evolutionary algorithms has been shown to be important in studying biological evolution, and has provided new methods for evolutionary optimization.(cf. 37,32-33,29,25,20,6)

- As a framework for multilevel modeling of developmental processes in which we can combine informatic regulatory processes with mechanical interactions we extended the 2-scale CA model of Glazier and Graner to incorporate chemotaxis, cell growth and cell death, cell polarity, and internal molecular dynamics. In this way a powerful modeling framework is created for studying morphogenesis.(cf. 27,21-23,17-19,9)
- Evolution based modeling methodology to (1) deal with the parameter uncertainty inherent in large scale biological models(cf. 10,3) (2) uncover "generic non-generic phenomena" and therewith to tackle complex to complex mapping in biotic systems.24)

**Bioinformatic theory**

- *self-organization in socioinformatic processes*
  Damped positive feedback on dominance (also called winner-looser effect) together with opportunity(rather than optimality) based behavior as an explanation of social interactions in animal groups and its automatic adaptation to environmental changes. We demonstrated this in models of bumblebee colonies as well as abstract entities. This insight has later been used for explaining other e.g. primate social structures, and is now being applied to study social learning and the development of animal cultures. (cf. 45-46,30,14,9)
- *eco-evolutionary processes in space*
  We were the first to demonstrate the profound influence of local interaction in space on ecological and evolutionary phenomena. When we first published these results they were hailed by Robert May in Nature as "growth area" - and this has indeed been the case. We have shown:
  - Ecological interactions (predation,parasitism,competition and mutualism) give rise to spatial pattern formation. Spatial pattern formation (SPF)enslaves the dynamics of the replicators.
  - SPF leads to stable coexistence in many cases where extinction is wrongly predicted with classical models (cf. 32-33, 16)
  - SPF leads to multilevel selection and therewith to counter intuitive selection pressures, e.g. positive selection for decay
  - In particular, due to SPF, ecological and evolutionary timescales interlock - refuting the long held requirement of immediate benefits.(cf. 25-26, 15)
  - Multiple level selection and interlocking timescales appear to be requisites for the evolution of 'complex' versatile organisms which adapt to the environment through physiological rather than evolutionary changes 6,20)
- *nonlinear genotype-phenotype mapping*
  This is an other important inroad to understand the evolution of the complexity of biotic systems.
  - RNA folding. We took the RNA sequence to secondary structure mapping as paradigm as this is the only model for genotype-phenotype mapping which is explicitly computable. Our (and related) research has uncovered to importance of neutral path in adaptive evolution, the feasibility of multiple coding and the evolution toward robustness.(cf. 31,28,29,5,13)
  - Regulatory networks and the interplay between regulatory and evolutionary adaptation. (cf. 7,10)
- *Morphogenesis at the interface between dynamic and informatic processes*
  Although it is a truism to say that organisms are physical dynamical systems which have evolved, they are rarely studied as such. The modeling methodology we developed as extension for Glazier Graner (CPM) model gives us a versatile way to do so. Using it we have demonstrated:
  - the dynamic unfolding of the life-cycle of *Dictyostelium discoideum* through interaction of cell

signaling, chemotaxis and differential adhesion with a role of cell differentiation only during culmination.(cf. 27,23,19,17)

- the generic nature of a number of morphogenetic mechanisms like mistimes, convergence extension, engulfing, by the interaction of of cell adhesion and cell differentiation.(cf. 21-22)
- mosaic evolution and mutational priming of morphological features. (cf. 18)

Current research continues on eco-evolutionary dynamics and morphogenesis and newly focuses on "adaptive genomics" in which we combine pattern analysis of genomic data and dynamic (multi-level modeling) bioinformatic approaches to study the interface between gene regulation and evolution in uni- and multicellular organisms. Our experience with both static and dynamic bioinformatics is rather unique and gives exciting opportunities to convert the flood of genomic data into theory. Recent (2006-2007) results and current work include the demonstration of evolution of evolvability (mutational priming), both at the level of genome organization due to transposon dynamics and at the level of regulatory networks(cf. 7,in press), the identification of some regulatory network features as a side-effect of the mutational processes(cf. 12) and the intriguing observation that at the onset of the major prokaryotic lineages large changes the ratio between the number of transcription factors and genome size occurred and then remained essential fixed within that lineage.(cf. 8) We have demonstrated complexification in the RNA world due to interactions between RNA secondary structure formation and spatial pattern formation (cf 4,(in press)), and we have shown that an evolutionary perspective is very help full to validate large scale system biology models.(cf. 10,3,in press) Moreover, we have developed, and experimentally verified, a detailed model of root development spanning various orders of magnitude in space and timescales: am auxin capacitor governes root growth from seconds to weeks.(cf. 1)

## Selected Publications (updated Feb 2008)


1. **Grieneisen V.A., Xu J., Maree A.F., Hogeweg P. & Scheres B. (2007)**, Auxin transport is sufficient to generate a maximum and gradient guiding root growth. Nature, 449: 1008-1013.
2. **Van Hoek M.J. & Hogeweg P. (2007b)**, The role of mutational dynamics in genome shrinkage. Mol. Biol. Evol., 24: 2485-2494
3. **Van Hoek M. & Hogeweg P. (2007a)**, The effect of stochasticity on the lac operon: an evolutionary perspective. PLoS. Comput. Biol., 3: e111.
4. **Takeuchi N. & Hogeweg P. (2007b)**, The Role of Complex Formation and Deleterious Mutations for the Stability of RNA-Like Replicator Systems. J. Mol. Evol., 65: 668-686.
5. **Takeuchi N. & Hogeweg P. (2007a)**, Error-threshold exists in fitness landscapes with lethal mutants. BMC. Evol. Biol., 7: 15
6. **Hogeweg P. (2007)**, From population dynamics to ecoinformatics: Ecosystems as multilevel information processing systems. Ecological Informatics, 2: 103-111.
7. **Crombach A. & Hogeweg P. (2007)**, Chromosome rearrangements and the evolution of genome structuring and adaptability. Mol. Biol. Evol., 24: 1130-1139.
8. **Cordero O.X. & Hogeweg P. (2007)**, Large changes in regulome size herald the main prokaryotic lineages. Trends Genet., 23: 488-493
9. **Marée AFM, Grieneisen VA, Hogeweg P (2007)** The Cellular Potts Model and Biophysical Properties of Cells, Tissues and Morphogenesis in: Single-Cell-Based Models in Biology and Medicine (eds Anderson ARA, Chaplin MAJ and Rejniak KA) Birkhauser Verlag Basel/Switserland 2007 Maree AFM, Grieneisen VA, Hogeweg P The Cellular Potts Model and Biophysical Properties of Cells, Tissues and Morphogenesis in: Single-Cell-Based Models in Biology and Medicine (eds Anderson ARA, Chaplin MAJ and Rejniak KA) Birkhauser Verlag Basel/Switserland
10. **Van Hoek M.J. & Hogeweg P. (2006)**, In silico evolved lac operons exhibit bistability for artificial inducers, but not for lactose. Biophys. J., 91: 2833-2843
11. **Van Der Post D.J. & Hogeweg P. (2006)**, Resource distributions and diet development by trial-and-error learning. Behav. Ecol. Sociobiol., 61: 65-80
12. **Cordero O.X. & Hogeweg P. (2006)**, Feed-forward loop circuits as a side effect of genome evolution. Mol. Biol. Evol., 23: 1931-1936
13. **Takeuchi N., Poorthuis P.H. & Hogeweg P. (2005)**, Phenotypic error threshold; additivity and epistasis in RNA evolution. BMC. Evol. Biol., 5: 9
14. **Van der Post D.J. & Hogeweg P. (2004)**, Learning what to eat: Studying inter-relations between learning, grouping and evironmental conditions in an artificial world. LNCS, 3305: 492-501.
15. **Hogeweg P. & Takeuchi N. (2003)**, Multilevel selection in models of prebiotic evolution: compartments and spatial self-organization. Orig Life Evol Biosph., 33: 375-403.
16. **Groenenboom M.A.C. & Hogeweg P. (2002)**, Space and the persistence of male-killing endosymbionts in insect populations. Proc. R. Soc. Lond. B. Biol. Sci., 269: 2509-2518.
17. **Mare A.F.M. & Hogeweg P. (2002)**, Modelling Dictyostelium discoideum morphogenesis: the culmination. Bull. Math. Biol., 64: 327-353
18. **Hogeweg P. (2002a)**, Computing an organism: on the interface between informatic and dynamic processes. Biosystems, 64: 97-109
19. **Marée A.F.M. & Hogeweg P. (2001)**, How amoeboids self-organize into a fruiting body: Multicellular coordination in Dictyostelium discoideum. Proc. Natl. Acad. Sci. USA, 98: 3879-3883
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22. **Hogeweg P. (2000a)**,
Evolving mechanisms of morphogenesis: on the interplay between differential adhesion and cell differentiation. J. theor. Biol., 203: 317-333.
23. **Marée AF, Panfilov AV, Hogeweg P (1999a)**,
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24. **Hogeweg, P. (1998)**,
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26. **Savill, N. J. , Rohani, P. and Hogeweg, P. (1997c)**,
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27. **Savill, N. J. and Hogeweg, P (1997a)**,
Modeling morphogenesis: from single cells to crawling slugs J. theor. Biol 184:229-235
28. **Huynen, M.A. and Hogeweg, P. (1994)**,
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29. **Hogeweg, P. (1994)**,
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30. **te Boekhorst IJA and Hogeweg, P. (1994)**,
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31. **Huynen, M.A., D.A.M. Konings and P. Hogeweg (1993)**,
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32. **Boerlijst, M.A. and Hogeweg, P. (1991)**,
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45. **Hogeweg, P. and B. Hesper (1983)**,
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47. **Hogeweg, P. and B. Hesper (1981a)**,
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51. **Hogeweg, P. and B. Hesper (1974)**,
A model study on biomorphological description. Pattern recognition 6, 165-179.

## Personalia

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| Doctoraal Biologie (Msc) | 1969 | University of Amsterdam.<br>major: Vegetation Science (Fieldwork in India) |
| Promotie (PhD) | 1976 | Utrecht University.<br>Thesis Topics in Biological Pattern Analysis<br>Promotores: Prof Dr.C. Raven and Prof. Dr. F. van der Blij |
| Group Leader | 1977 - 1991 | Bioinformatics Group, Faculty Biology, Utrecht University. |
| Full Professor | 1991 - present | Theoretical Biology and Bioinformatics, Utrecht University<br>(and leader of the group with the same name) |
| Member editorial board | | Journal Theoretical Biology<br>Bulletin Mathematical Biology<br>Biosystems<br>Artificial Life Journal<br>Ecological Informatics |
| Program committee member | | numerous<br>(mainly) biology and artificial life |