

**Evolutionary Computation for  
Optimization and Model Discovery in Biological Systems**

**by**

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For Sean – may life be good to you.

“42”

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# **Abstract**

Evolutionary Computation encompasses a large group of stochastic problem solving methods loosely inspired on biological evolutionary processes such as selection, mutation and recombination. These methods are commonly referred to as Evolutionary Algorithms and all have in common the use of populations of candidate solutions which reproduce, compete, and are subjected to selective pressures and random variation – the four basic elements of evolution. Some of the best known Evolutionary Algorithms include Genetic Algorithms, Genetic Programming and Evolution Strategies. Evolutionary Algorithms are suited to optimization of complex non linear problems, making them appropriate to optimization of biological problems which are usually complex and non linear. In this thesis Evolutionary Algorithms were developed and used to optimize biological problems. For the first problem, Differential Evolution was used to optimize nutrition model parameters in beef cattle, predict weight gains and formulate rations; results indicate a good fit of predicted values to observed measurements. A second problem addressed was the multiple sequence alignment of amino acid and nucleotide residues. A Genetic Algorithm was developed and results indicate that the method can improve on Clustal-W alignments. Genetic Algorithms were also used to optimize the experimental design of spotted microarrays. Optimization is treated as a multicriteria problem and the heuristic uses a weighted multi objective function to balance conflictive design considerations. Results evidence that, for a given set of constraints, near optimal designs can be found that are more efficient than common designs. Differential Evolution is also used to parameterize biochemical systems modelled as S-systems differential equations, which adhere to a fixed functional form, yet fit well to diverse complex systems. Results show that time series data can efficiently parameterize the evaluated models. The last problem evaluated was full model discovery and parameterization from time series data. A hybrid Differential Evolution and Gene Expression Programming algorithm was developed and compared against other heuristic methods. Alongside the development of methods, a major component of this project was the production of computational tools that implement the methods; five tools – one for each research topic – were developed and are freely available. Evolutionary Computation is a powerful approach to optimization of complex biological problems; this is clearly evidenced through the different problems that were addressed in this thesis.

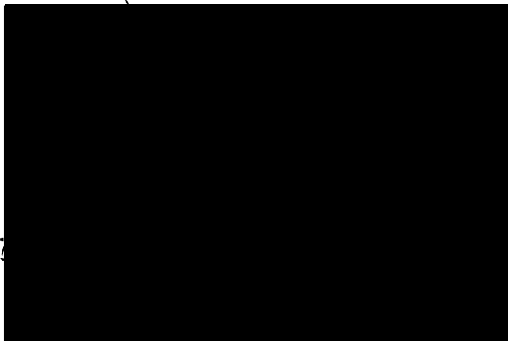
**Keywords:** *evolutionary computation; evolutionary algorithms; gene expression programming; differential evolution; genetic algorithms; cattle nutrition models; bioinformatics; computational biology; multiple sequence alignment; microarray experimental design; s-systems; delay differential equations; biochemical systems; genetic networks.*

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## **Declaration**

I certify that the substance of this thesis has not already been submitted for any degree and is not currently being submitted for any other degree or qualification.

I certify that any help received in preparing this thesis, and all sources used, have been acknowledged in this thesis.



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# **Abbreviations**

BLOSUM – Blocks Amino Acid Substitution Matrix  
Cy3 – Cyanine-3  
Cy5 – Cyanine-5  
DE – Differential Evolution  
DP – Dynamic Programming  
EA – Evolutionary Algorithms  
EC – Evolutionary Computation  
EP – Evolutionary Programming  
ERDP – Effective Rumen Degradable Protein  
ES – Evolution Strategies, Effective Size  
EST – Expressed Sequence Tag  
ET – Expression Tree  
FME – Fermentable Metabolizable Energy  
GAs – Genetic Algorithms  
GEP – Gene Expression Programming  
GP – Genetic Programming  
GUI – Graphical User Interface  
HC – Stochastic Hill Climbing  
HDE-GEP – Hybrid Differential Evolution and Gene Expression Programming  
KEGG – Encyclopedia of Genes and Genomics  
LCS – Learning Classifier Systems  
LP – Linear Programming  
MEP – Multi Expression Programming  
MOP – Multiple-Objective Programming  
MSA – Multiple Sequence Alignment  
NCBI – National Center for Biotechnology Information  
NFL – No-free-lunch Theorem  
NIH – National Institutes of Health  
NP – No Polynomial  
ORF – Open Reading Frame  
OF – Objective Function  
PAM – Percent of Accepted Mutation  
RS – Random Search  
SA – Simulated Annealing  
SAGE – Serial Analysis of Gene Expression  
SBML – Systems Biology Markup Language  
SDE – System of Differential Equations  
XML – Extensible Markup Language