

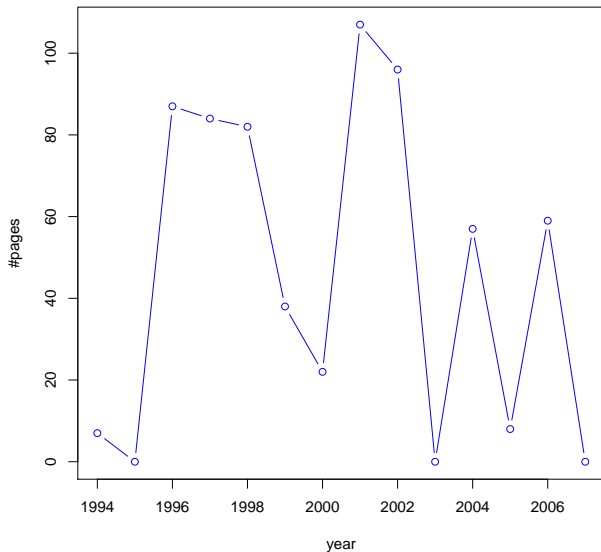
Exploring Neutral Networks for RNA Sequences

Sarah J. Berkemer

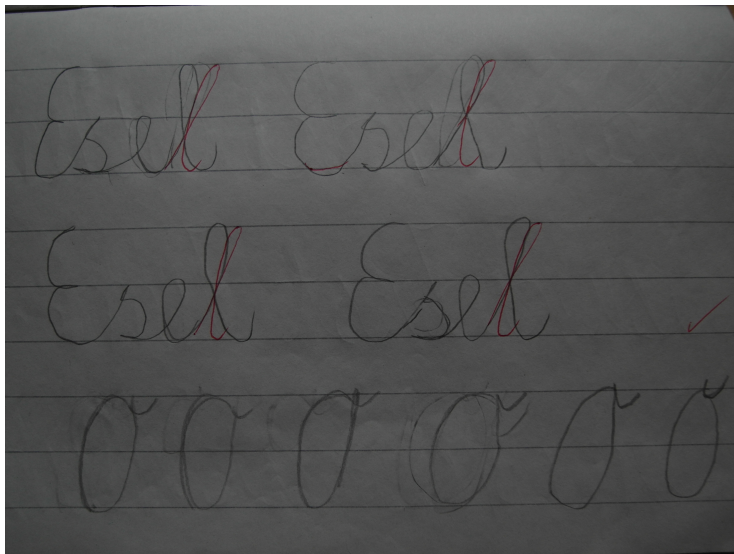
Bioinformatics Leipzig

Winterseminar 2019

Existing Work



Time Frame: 1990ies



Fitness Landscapes

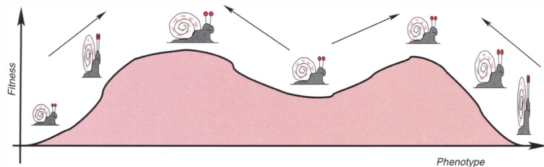


Figure: Snail fitness by [Reidys & Stadler, 2002].

Fitness Landscapes

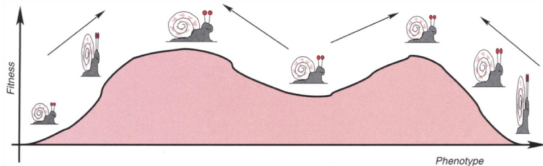


Figure: Snail fitness by [Reidys & Stadler, 2002].

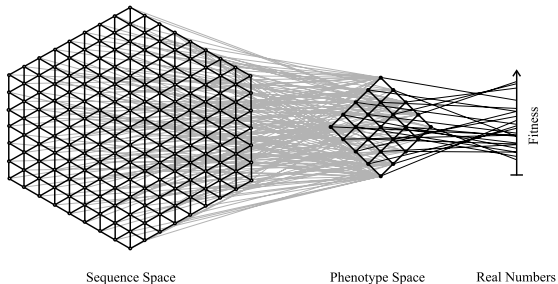


Figure: Genotype space to phenotype space to fitness by [Schuster, 2002].

Neutral Networks

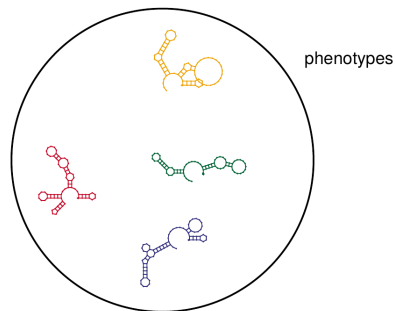


Figure: Phenotypes [Fontana, 2002]

Neutral Networks

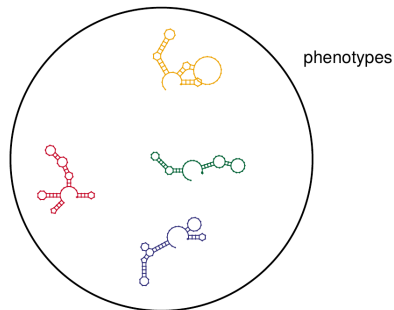


Figure: Phenotypes [Fontana, 2002]

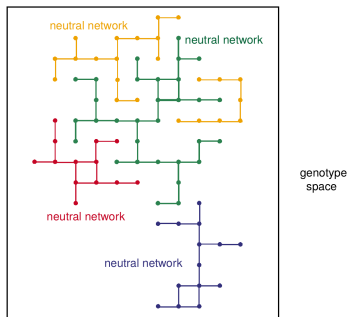


Figure: Neutral networks [Fontana, 2002]

Neutral Networks

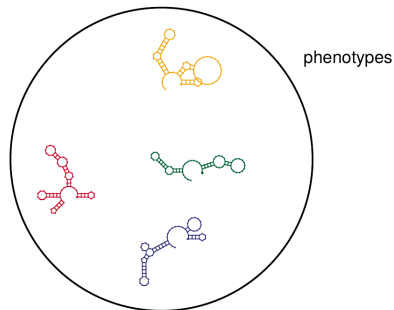


Figure: Phenotypes [Fontana, 2002]

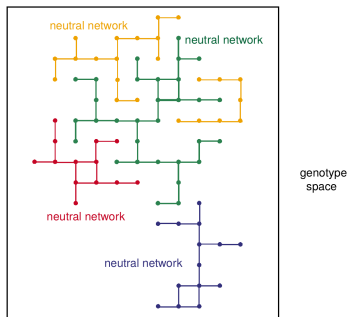
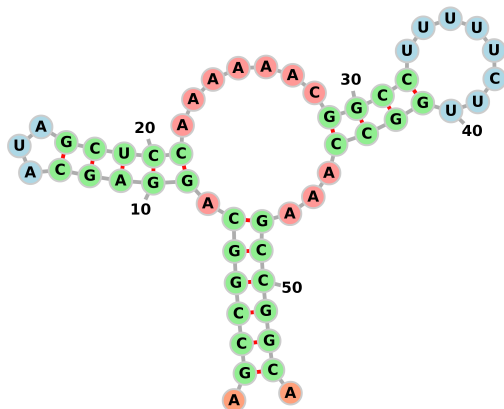


Figure: Neutral networks [Fontana, 2002]

Questions

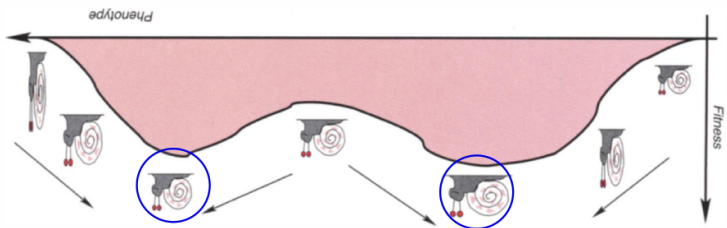
- 1 When are two sequences adjacent?
- 2 What is the criterion for neutrality or fitness?

Target Structure

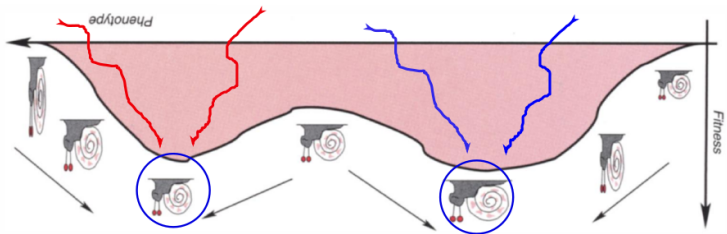


Hammerhead ribozyme type III, length 54nt
. $((((((((((((((...)))))).....((((.....))))))...))))))$.

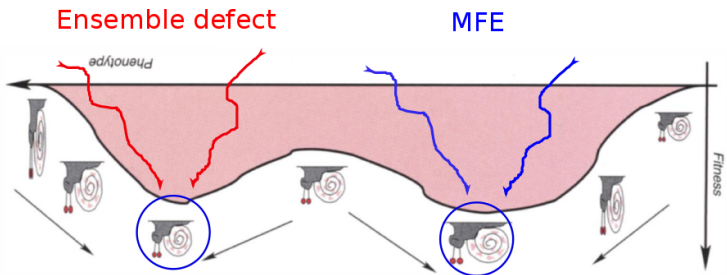
Creation of Neutral Networks aka Sampling



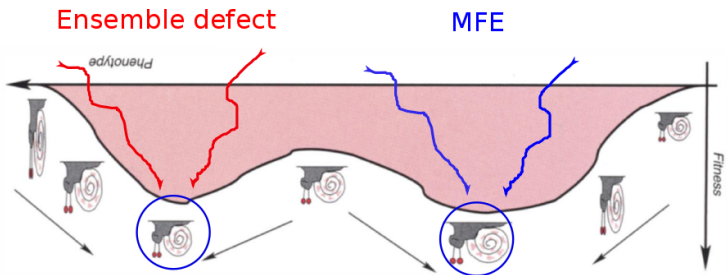
Creation of Neutral Networks aka Sampling



Creation of Neutral Networks aka Sampling



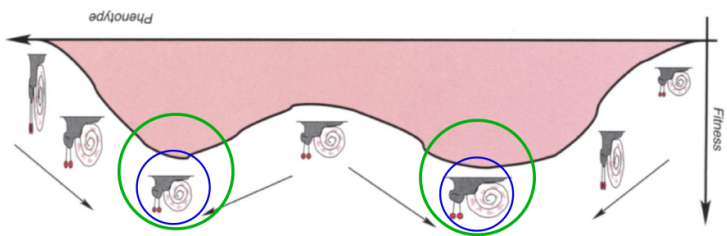
Creation of Neutral Networks aka Sampling



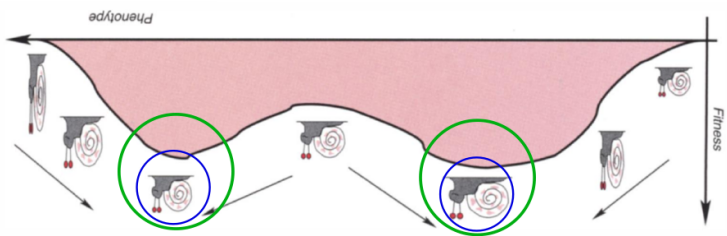
Method

This is done using *RNABluePrint* [Hammer et al., 2017].

Exploring the Neighborhood

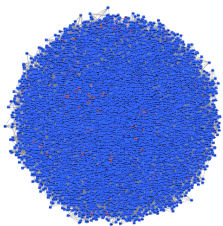


Exploring the Neighborhood

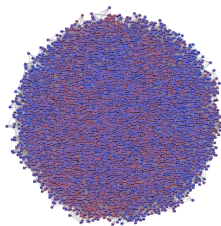


For each of the initial sequences (mfe or ed), we explore the local neighborhood using *RNABluePrint* [Hammer et al., 2017].

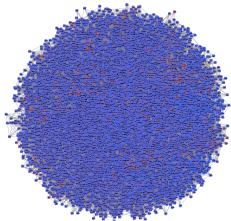
Graph Representation (blue=small)



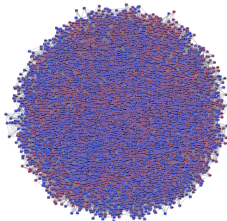
ensemble optimized,
ensemble defect colored



ensemble optimized,
MFE colored

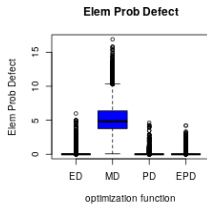
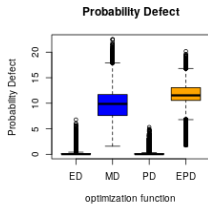
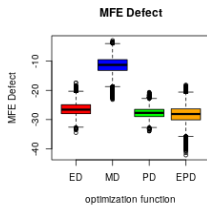
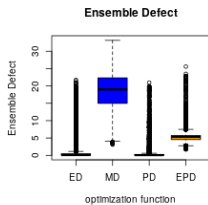


MFE optimized,
ensemble defect colored

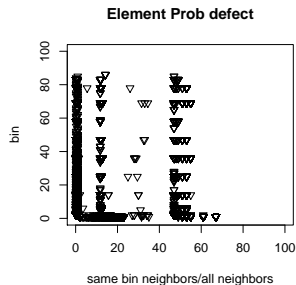
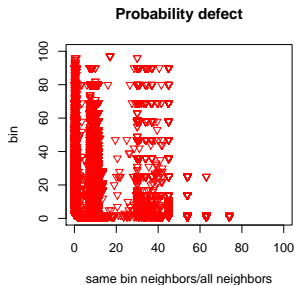
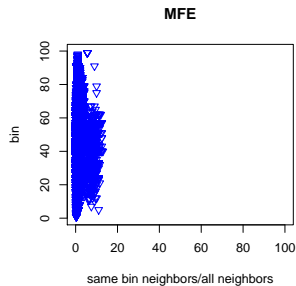
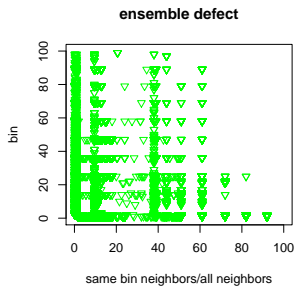


MFE optimized,
MFE colored

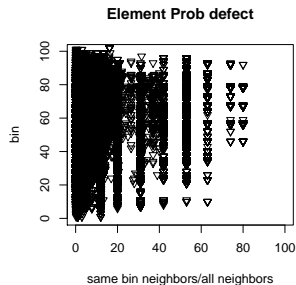
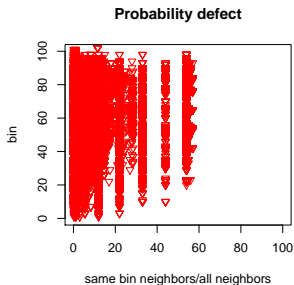
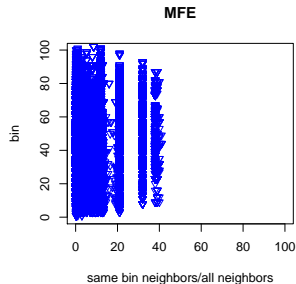
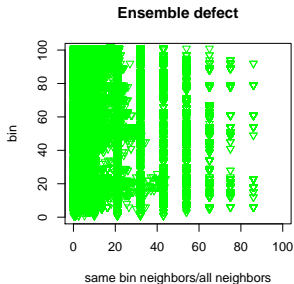
Defect Values



Neighborhood - Ensemble Optimized



Neighborhood - MFE Optimized



Thank you for your attention!

Questions?

References



Fontana, W. (2002).

Modelling 'evo-devo' with rna.
BioEssays, 24(12), 1164–1177.



Hammer, S., Tschitschek, B., Flamm, C., Hofacker, I. L., & Findeiß, S. (2017).

Rnablueprint: flexible multiple target nucleic acid sequence design.
Bioinformatics, 33(18), 2850–2858.



Reidys, C. M. & Stadler, P. F. (2002).

Combinatorial landscapes.
SIAM review, 44(1), 3–54.



Schuster, P. (2002).

A testable genotype-phenotype map: Modeling evolution of RNA molecules.
In *Biological Evolution and Statistical Physics* (pp. 55–81). Springer.