

# ESR Presentation

**Christoph Feinauer**

**03/02/2013**

## 1 Background

- University Education

## 2 Past Research

- Electroporation Pipettes
- Zinc Finger Protein Modeling

## 3 Current and Future Work

- Protein Residue Contact Inference by Evolutionary Information
- Future Directions
- Secondments

## 1 Background

### ■ University Education

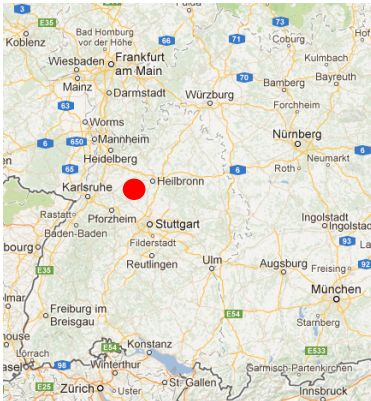
## 2 Past Research

- Electroporation Pipettes
- Zinc Finger Protein Modeling

## 3 Current and Future Work

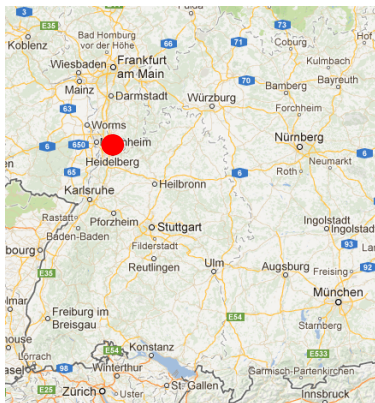
- Protein Residue Contact Inference by Evolutionary Information
- Future Directions
- Secondments

■ Country of origin:  
Germany



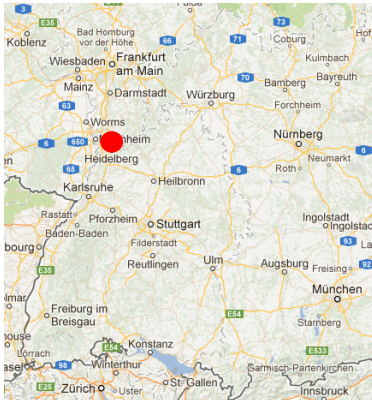
© Google Maps





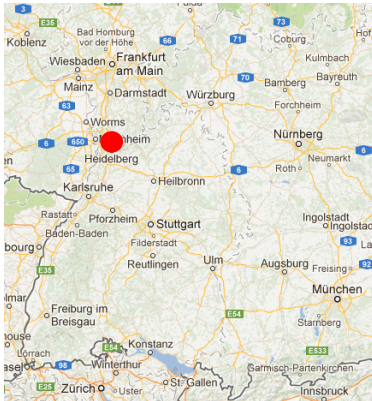
© Google Maps

- **Country of origin:  
Germany**
- **First part of diploma:  
Technical University of  
Munich**
- **Second part of diploma:  
University of Heidelberg**



© Google Maps

- **Country of origin:  
Germany**
- **First part of diploma:  
Technical University of  
Munich**
- **Second part of diploma:  
University of Heidelberg**
- **Main Focus: Biophysics**



© Google Maps

- **Country of origin: Germany**
- **First part of diploma: Technical University of Munich**
- **Second part of diploma: University of Heidelberg**
- **Main Focus: Biophysics**
- **Now: Riccardo Zecchina's group, Optimization and Inference, Turin**



## 1 Background

- University Education

## 2 Past Research

- **Electroporation Pipettes**
- Zinc Finger Protein Modeling

## 3 Current and Future Work

- Protein Residue Contact Inference by Evolutionary Information
- Future Directions
- Secondments

# Electroporation Pipettes

- **Andreas T. Schaefer**  
**Group, Behavioural**  
**Neurophysiology**
- **Max Planck Institute for**  
**Medical Research,**  
**Heidelberg**

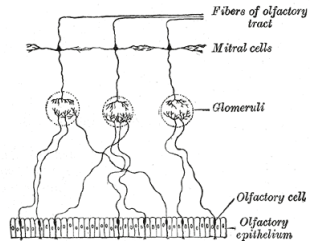
# Electroporation Pipettes

- **Andreas T. Schaefer**  
**Group, Behavioural**  
**Neurophysiology**
- **Max Planck Institute for**  
**Medical Research,**  
**Heidelberg**
- **Main contributor:**  
**Daniel Schwarz**

# Electroporation Pipettes

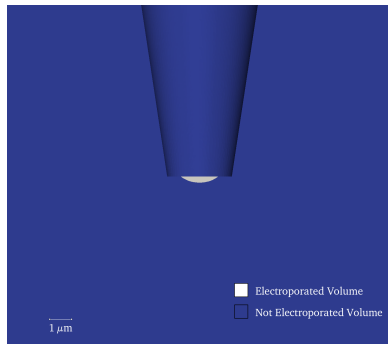
- **Andreas T. Schaefer**  
Group, Behavioural  
Neurophysiology
- **Max Planck Institute for  
Medical Research,  
Heidelberg**
- **Main contributor:  
Daniel Schwarz**

## ■ Olfactory Bulb

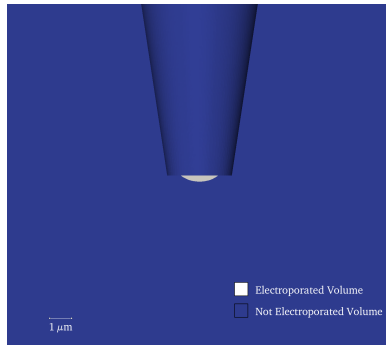


<http://en.wikipedia.org/wiki/File:Gray772.png>

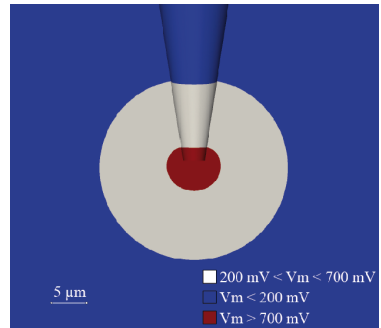
## ■ Membrane poration by transmembrane potential



## ■ Membrane poration by transmembrane potential

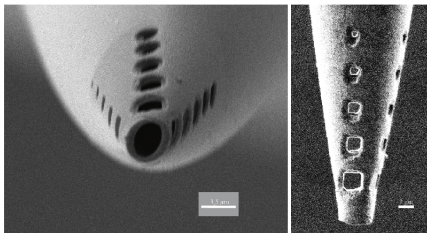


## ■ Useless for network tracing



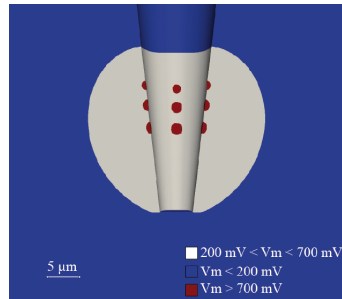
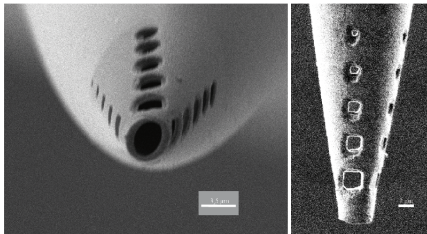
## ■ New pipette design

## ■ New pipette design

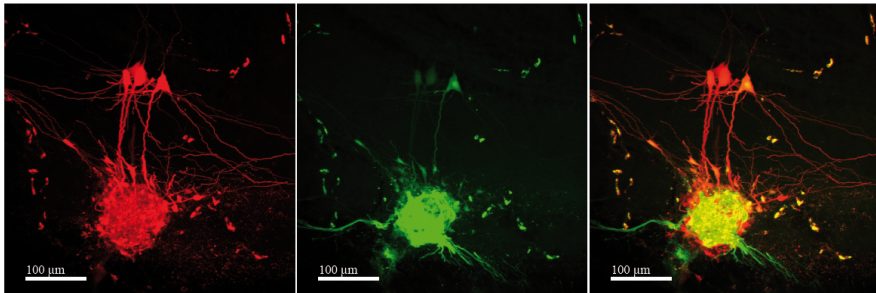




## ■ New pipette design



## ■ Reliable labeling of about 80 percent in the glomerulus



## 1 Background

- University Education

## 2 Past Research

- Electroporation Pipettes
- **Zinc Finger Protein Modeling**

## 3 Current and Future Work

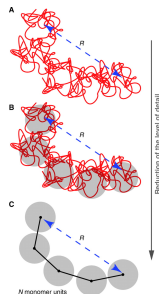
- Protein Residue Contact Inference by Evolutionary Information
- Future Directions
- Secondments

# Zinc Finger Proteins

- **D.W. Heermann Group,  
Statistical Physics and  
Theoretical Biophysics,  
ITP Heidelberg**

# Zinc Finger Proteins

- D.W. Heermann Group,  
Statistical Physics and  
Theoretical Biophysics,  
ITP Heidelberg



**Chromatin folding: from biology to polymer models and back** Mariliis Tark-Dame, Roel van Driel, Dieter W. Heermann, 2011 J Cell Sci 124, 839-845

# 1D Lattice Model for Zinc Finger Protein Binding

- **CTCF: 11-Zinc Finger Protein, Involved in DNA looping**

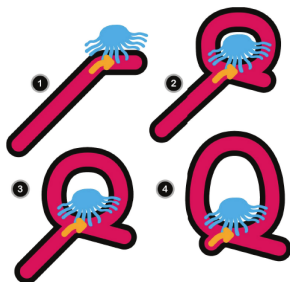


Figure: MacPherson, M. J., Sadowski, P. D. The CTCF insulator protein forms an unusual DNA structure. *BMC molecular biology* 11, 101 (2010).

# 1D Lattice Model for Zinc Finger Protein Binding

- **CTCF: 11-Zinc Finger Protein, Involved in DNA looping**

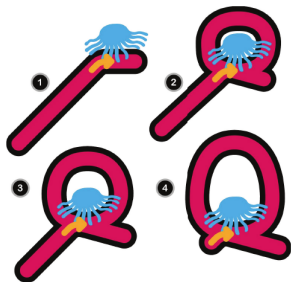
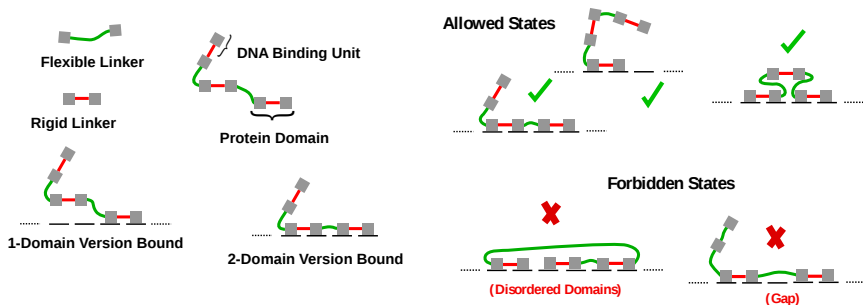


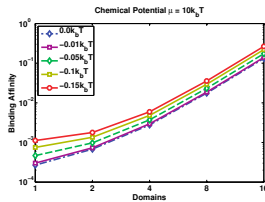
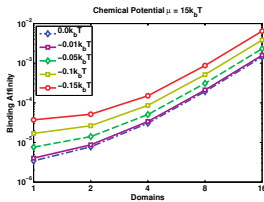
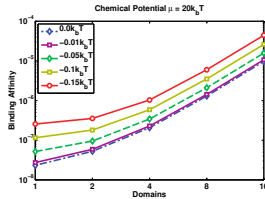
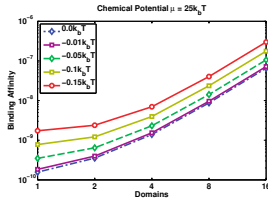
Figure: MacPherson, M. J., Sadowski, P. D. The CTCF insulator protein forms an unusual DNA structure. *BMC molecular biology* 11, 101 (2010).

- **Thesis: The Effect of Flexible Linkers on the Binding Affinity and the Binding Distribution of Zinc Finger Proteins**

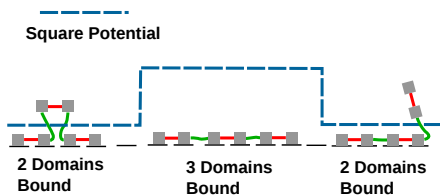




## ■ Increased non-specific binding affinity through domains



## ■ Influence of an increased non-specific binding energy on binding characteristics



- **Christoph J. Feinauer, Andreas Hofmann, Sebastian Goldt, Lei Liu, Gabriell Mate, Dieter W. Heerman. Zinc Finger Proteins and the 3D Organisation of Chromosomes, Advances in Protein Chemistry and Structural Biology, accepted 2012**

- 1 Background
  - University Education
- 2 Past Research
  - Electroporation Pipettes
  - Zinc Finger Protein Modeling
- 3 **Current and Future Work**
  - **Protein Residue Contact Inference by Evolutionary Information**
  - Future Directions
  - Secondments

# Protein Residue Contact Inference by Evolutionary Information

- A mutation in a protein residue leads to a changed evolutionary pressure in protein residues with which it is in contact

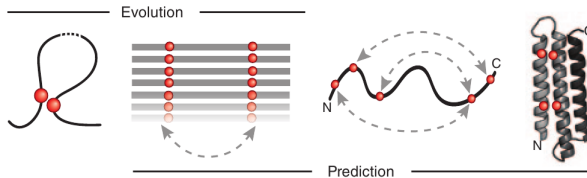


Figure: Marks et al. Protein structure prediction from sequence variation. *Nature biotechnology* 30, (2012).

# Protein Residue Contact Inference by Evolutionary Information

- A mutation in a protein residue leads to a changed evolutionary pressure in protein residues with which it is in contact

- Sequence data → predicted residue contacts

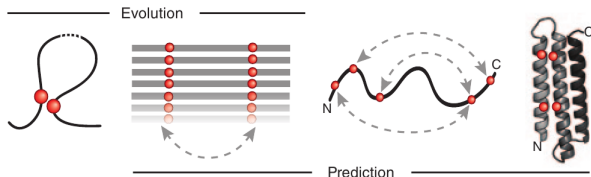


Figure: Marks et al. Protein structure prediction from sequence variation. *Nature biotechnology* 30, (2012).

- **Several approaches exist:**

## ■ Several approaches exist:

- 1 **Mutual Information** *Dunn et al. Mutual information without the influence of phylogeny or entropy dramatically improves residue contact prediction. Bioinformatics (2008)*



## ■ Several approaches exist:

- 1 Mutual Information** *Dunn et al. Mutual information without the influence of phylogeny or entropy dramatically improves residue contact prediction. Bioinformatics (2008)*
- 2 Direct Coupling Analysis** *Morcos, F. et al. Direct-coupling analysis of residue coevolution captures native contacts across many protein families. Proceedings of the National Academy of Sciences of the United States of America 108 (2011)*

## ■ Several approaches exist:

- 1 Mutual Information** *Dunn et al. Mutual information without the influence of phylogeny or entropy dramatically improves residue contact prediction. Bioinformatics (2008)*
- 2 Direct Coupling Analysis** *Morcos, F. et al. Direct-coupling analysis of residue coevolution captures native contacts across many protein families. Proceedings of the National Academy of Sciences of the United States of America 108 (2011)*
- 3 Correlated Changes in inferred Phylogenetic Trees** *Miyazawa, S. Prediction of Contact Residue Pairs Based on Co-Substitution between Sites in Protein Structures. PLoS ONE 8 (2013)*

## ■ Several approaches exist:

- 1 Mutual Information** *Dunn et al. Mutual information without the influence of phylogeny or entropy dramatically improves residue contact prediction. Bioinformatics (2008)*
- 2 Direct Coupling Analysis** *Morcos, F. et al. Direct-coupling analysis of residue coevolution captures native contacts across many protein families. Proceedings of the National Academy of Sciences of the United States of America 108 (2011)*
- 3 Correlated Changes in inferred Phylogenetic Trees** *Miyazawa, S. Prediction of Contact Residue Pairs Based on Co-Substitution between Sites in Protein Structures. PLoS ONE 8 (2013)*
- 4 Bayesian Inference** *Burger L, van Nimwegen E (2010) Disentangling direct from indirect co- evolution of residues in protein alignments. PLoS Comp Biol 6: e1000633.i*

## ■ Several approaches exist:

- 1 Mutual Information** *Dunn et al. Mutual information without the influence of phylogeny or entropy dramatically improves residue contact prediction. Bioinformatics (2008)*
- 2 Direct Coupling Analysis** *Morcos, F. et al. Direct-coupling analysis of residue coevolution captures native contacts across many protein families. Proceedings of the National Academy of Sciences of the United States of America 108 (2011)*
- 3 Correlated Changes in inferred Phylogenetic Trees** *Miyazawa, S. Prediction of Contact Residue Pairs Based on Co-Substitution between Sites in Protein Structures. PLoS ONE 8 (2013)*
- 4 Bayesian Inference** *Burger L, van Nimwegen E (2010) Disentangling direct from indirect co- evolution of residues in protein alignments. PLoS Comp Biol 6: e1000633.i*

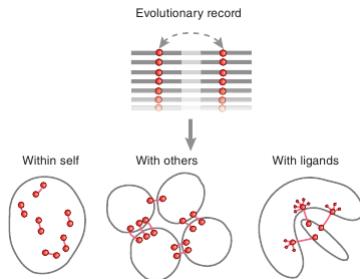
## ■ ⇒ Write a Review

# Future Directions

- **Combinations of Methods should be possible**

# Future Directions

- Combinations of Methods should be possible
- Protein-Protein Networks



# Secondments

- La Sapienza
- KTH, Stockholm

# The End

**Thank you for your attention!**