

Sintetizando los Algoritmos Evolutivos: Algoritmos de Estimación de Distribuciones

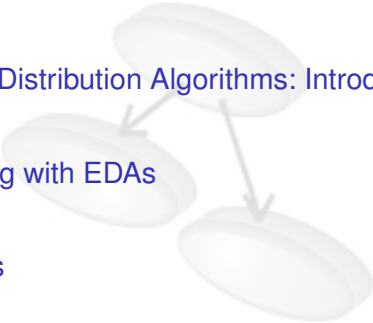
Jose A. Lozano

Intelligent Systems Group
The University of the Basque Country

EVIA 2014
(A Coruña, September 3rd, 2014)

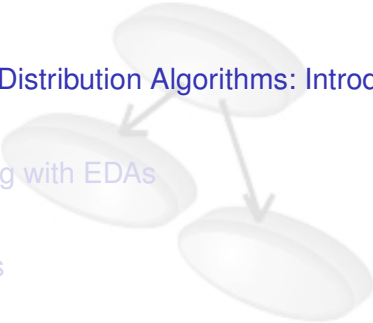


Outline of the presentation

- 1 Estimation of Distribution Algorithms: Introduction
 - 2 Protein Folding with EDAs
 - 3 Miscellaneous
 - 4 Conclusions
- 



Outline of the presentation

- 1 Estimation of Distribution Algorithms: Introduction
 - 2 Protein Folding with EDAs
 - 3 Miscellaneous
 - 4 Conclusions
- 



Evolutionary Computation

Genetic Algorithms (GAs)

- Based on mimicking natural evolution
- Keep a **population of solutions** at each step
- Use of reproduction operators: crossover and mutation
- Mathematically modeled as a Markov chain



Estimation of Distribution Algorithms (EDAs): The basics

Motivation: Drawbacks of Genetic Algorithms

- Too much heuristic algorithms
- Many parameters to set up
- Difficult to define good crossover and mutation operators
- Bad results in some trivial problems
- Lack of rigorous mathematical analysis

Basic Characteristics

- Delete the reproduction operators of GAs:
 - **Learn** a probability distribution from the selected individuals
 - **Sample** the probability distribution to obtain the new population



Estimation of Distribution Algorithms (EDAs): The basics

Motivation: Drawbacks of Genetic Algorithms

- Too much heuristic algorithms
- Many parameters to set up
- Difficult to define good crossover and mutation operators
- Bad results in some trivial problems
- Lack of rigorous mathematical analysis

Basic Characteristics

- Delete the reproduction operators of GAs:
 - **Learn** a probability distribution from the selected individuals
 - **Sample** the probability distribution to obtain the new population

Optimization of OneMax with EDAs

$$\max h(\mathbf{x}) = \sum_{i=1}^6 x_i$$

with $x_i = 0, 1$



Optimization of OneMax with EDAs

$$\max h(\mathbf{x}) = \sum_{i=1}^6 x_i$$

with $x_i = 0, 1$

	x_1	x_2	x_3	x_4	x_5	x_6	$h(\mathbf{x})$
1	1	0	1	0	1	0	3
2	0	1	0	0	1	0	2
3	0	0	0	1	0	0	1
4	1	1	1	0	0	1	4
5	0	0	0	0	0	1	1
6	1	1	0	0	1	1	4
7	0	1	1	1	1	1	5
8	0	0	0	1	0	0	1
9	1	1	0	1	0	0	3
10	1	0	1	0	0	0	2
11	1	0	0	1	1	1	4
12	1	1	0	0	0	1	3
13	1	0	1	0	0	0	2
14	0	0	0	0	1	1	2
15	0	1	1	1	1	1	5
16	0	0	0	1	0	0	1
17	1	1	1	1	1	0	5
18	0	1	0	1	1	0	3
19	1	0	1	1	1	1	5
20	1	0	1	1	0	0	3

Optimization of OneMax with EDAs

$$\max h(\mathbf{x}) = \sum_{i=1}^6 x_i$$

with $x_i = 0, 1$

	x_1	x_2	x_3	x_4	x_5	x_6	$h(\mathbf{x})$
1	1	0	1	0	1	0	3
2	0	1	0	0	1	0	2
3	0	0	0	1	0	0	1
4	1	1	1	0	0	1	4
5	0	0	0	0	0	1	1
6	1	1	0	0	1	1	4
7	0	1	1	1	1	1	5
8	0	0	0	1	0	0	1
9	1	1	0	1	0	0	3
10	1	0	1	0	0	0	2
11	1	0	0	1	1	1	4
12	1	1	0	0	0	1	3
13	1	0	1	0	0	0	2
14	0	0	0	0	1	1	2
15	0	1	1	1	1	1	5
16	0	0	0	1	0	0	1
17	1	1	1	1	1	0	5
18	0	1	0	1	1	0	3
19	1	0	1	1	1	1	5
20	1	0	1	1	0	0	3



Learning the probability distribution

	X_1	X_2	X_3	X_4	X_5	X_6
1	1	0	1	0	1	0
4	1	1	1	0	0	1
6	1	1	0	0	1	1
7	0	1	1	1	1	1
11	1	0	0	1	1	1
12	1	1	0	0	0	1
15	0	1	1	1	1	1
17	1	1	1	1	1	0
18	0	1	0	1	1	0
19	1	0	1	1	1	1

Learning the probability distribution

	X_1	X_2	X_3	X_4	X_5	X_6
1	1	0	1	0	1	0
4	1	1	1	0	0	1
6	1	1	0	0	1	1
7	0	1	1	1	1	1
11	1	0	0	1	1	1
12	1	1	0	0	0	1
15	0	1	1	1	1	1
17	1	1	1	1	1	0
18	0	1	0	1	1	0
19	1	0	1	1	1	1

$$p(\mathbf{x}) = p(x_1, \dots, x_6) = p(x_1) \cdot p(x_2) \cdot p(x_3) \cdot p(x_4) \cdot p(x_5) \cdot p(x_6)$$

Learning the probability distribution

	X_1	X_2	X_3	X_4	X_5	X_6
1	1	0	1	0	1	0
4	1	1	1	0	0	1
6	1	1	0	0	1	1
7	0	1	1	1	1	1
11	1	0	0	1	1	1
12	1	1	0	0	0	1
15	0	1	1	1	1	1
17	1	1	1	1	1	0
18	0	1	0	1	1	0
19	1	0	1	1	1	1

$$p(\mathbf{x}) = p(x_1, \dots, x_6) = p(x_1) \cdot p(x_2) \cdot p(x_3) \cdot p(x_4) \cdot p(x_5) \cdot p(x_6)$$

$$p(X_1 = 1) = \frac{7}{10}$$

Learning the probability distribution

	X_1	X_2	X_3	X_4	X_5	X_6
1	1	0	1	0	1	0
4	1	1	1	0	0	1
6	1	1	0	0	1	1
7	0	1	1	1	1	1
11	1	0	0	1	1	1
12	1	1	0	0	0	1
15	0	1	1	1	1	1
17	1	1	1	1	1	0
18	0	1	0	1	1	0
19	1	0	1	1	1	1

$$p(\mathbf{x}) = p(x_1, \dots, x_6) = p(x_1) \cdot p(x_2) \cdot p(x_3) \cdot p(x_4) \cdot p(x_5) \cdot p(x_6)$$

$$p(X_1 = 1) = \frac{7}{10} \quad p(X_2 = 1) = \frac{7}{10} \quad p(X_3 = 1) = \frac{6}{10} \quad p(X_4 = 1) = \frac{6}{10} \quad p(X_5 = 1) = \frac{8}{10} \quad p(X_6 = 1) = \frac{7}{10}$$



Learning the probability distribution

	X_1	X_2	X_3	X_4	X_5	X_6
1	1	0	1	0	1	0
4	1	1	1	0	0	1
6	1	1	0	0	1	1
7	0	1	1	1	1	1
11	1	0	0	1	1	1
12	1	1	0	0	0	1
15	0	1	1	1	1	1
17	1	1	1	1	1	0
18	0	1	0	1	1	0
19	1	0	1	1	1	1

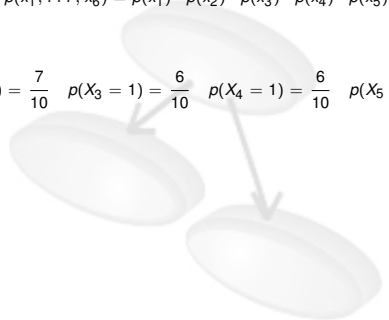
$$p(\mathbf{x}) = p(x_1, \dots, x_6) = p(x_1) \cdot p(x_2) \cdot p(x_3) \cdot p(x_4) \cdot p(x_5) \cdot p(x_6)$$

$$p(X_1 = 1) = \frac{7}{10} \quad p(X_2 = 1) = \frac{7}{10} \quad p(X_3 = 1) = \frac{6}{10} \quad p(X_4 = 1) = \frac{6}{10} \quad p(X_5 = 1) = \frac{8}{10} \quad p(X_6 = 1) = \frac{7}{10}$$

Learning the probability distribution

$$p(\mathbf{x}) = p(x_1, \dots, x_6) = p(x_1) \cdot p(x_2) \cdot p(x_3) \cdot p(x_4) \cdot p(x_5) \cdot p(x_6)$$

$$p(X_1 = 1) = \frac{7}{10} \quad p(X_2 = 1) = \frac{7}{10} \quad p(X_3 = 1) = \frac{6}{10} \quad p(X_4 = 1) = \frac{6}{10} \quad p(X_5 = 1) = \frac{8}{10} \quad p(X_6 = 1) = \frac{7}{10}$$



Learning the probability distribution

$$p(\mathbf{x}) = p(x_1, \dots, x_6) = p(x_1) \cdot p(x_2) \cdot p(x_3) \cdot p(x_4) \cdot p(x_5) \cdot p(x_6)$$

$$p(X_1 = 1) = \frac{7}{10} \quad p(X_2 = 1) = \frac{7}{10} \quad p(X_3 = 1) = \frac{6}{10} \quad p(X_4 = 1) = \frac{6}{10} \quad p(X_5 = 1) = \frac{8}{10} \quad p(X_6 = 1) = \frac{7}{10}$$

$$p(X_1 = 1, X_2 = 0, X_3 = 1, X_4 = 0, X_5 = 1, X_6 = 1) =$$



Learning the probability distribution

$$p(\mathbf{x}) = p(x_1, \dots, x_6) = p(x_1) \cdot p(x_2) \cdot p(x_3) \cdot p(x_4) \cdot p(x_5) \cdot p(x_6)$$

$$p(X_1 = 1) = \frac{7}{10} \quad p(X_2 = 1) = \frac{7}{10} \quad p(X_3 = 1) = \frac{6}{10} \quad p(X_4 = 1) = \frac{6}{10} \quad p(X_5 = 1) = \frac{8}{10} \quad p(X_6 = 1) = \frac{7}{10}$$

$$p(X_1 = 1, X_2 = 0, X_3 = 1, X_4 = 0, X_5 = 1, X_6 = 1) =$$

$$p(X_1 = 1) \cdot p(X_2 = 0) \cdot p(X_3 = 1) \cdot p(X_4 = 0) \cdot p(X_5 = 1) \cdot p(X_6 = 1) =$$



Learning the probability distribution

$$p(\mathbf{x}) = p(x_1, \dots, x_6) = p(x_1) \cdot p(x_2) \cdot p(x_3) \cdot p(x_4) \cdot p(x_5) \cdot p(x_6)$$

$$p(X_1 = 1) = \frac{7}{10} \quad p(X_2 = 1) = \frac{7}{10} \quad p(X_3 = 1) = \frac{6}{10} \quad p(X_4 = 1) = \frac{6}{10} \quad p(X_5 = 1) = \frac{8}{10} \quad p(X_6 = 1) = \frac{7}{10}$$

$$p(X_1 = 1, X_2 = 0, X_3 = 1, X_4 = 0, X_5 = 1, X_6 = 1) =$$

$$p(X_1 = 1) \cdot p(X_2 = 0) \cdot p(X_3 = 1) \cdot p(X_4 = 0) \cdot p(X_5 = 1) \cdot p(X_6 = 1) =$$

↓

$$\frac{7}{10}$$



Learning the probability distribution

$$p(\mathbf{x}) = p(x_1, \dots, x_6) = p(x_1) \cdot p(x_2) \cdot p(x_3) \cdot p(x_4) \cdot p(x_5) \cdot p(x_6)$$

$$p(X_1 = 1) = \frac{7}{10} \quad p(X_2 = 1) = \frac{7}{10} \quad p(X_3 = 1) = \frac{6}{10} \quad p(X_4 = 1) = \frac{6}{10} \quad p(X_5 = 1) = \frac{8}{10} \quad p(X_6 = 1) = \frac{7}{10}$$

$$p(X_1 = 1, X_2 = 0, X_3 = 1, X_4 = 0, X_5 = 1, X_6 = 1) =$$

$$p(X_1 = 1) \cdot p(X_2 = 0) \cdot p(X_3 = 1) \cdot p(X_4 = 0) \cdot p(X_5 = 1) \cdot p(X_6 = 1) =$$

$$\begin{array}{ccccccc} \downarrow & & \downarrow & & \downarrow & & \downarrow & & \downarrow & & \downarrow \\ \frac{7}{10} & \cdot & \frac{3}{10} & \cdot & \frac{6}{10} & \cdot & \frac{4}{10} & \cdot & \frac{8}{10} & \cdot & \frac{7}{10} \end{array}$$



Obtaining the new population

$$p(\mathbf{x}) = p(x_1, \dots, x_6) = p(x_1) \cdot p(x_2) \cdot p(x_3) \cdot p(x_4) \cdot p(x_5) \cdot p(x_6)$$

$$0.23 \quad p(X_1 = 1) = \frac{7}{10} \longrightarrow 1$$

$$0.45 \quad p(X_2 = 1) = \frac{7}{10} \longrightarrow 1$$

$$0.89 \quad p(X_3 = 1) = \frac{6}{10} \longrightarrow 0$$

$$0.12 \quad p(X_4 = 1) = \frac{6}{10} \longrightarrow 1$$

$$0.98 \quad p(X_5 = 1) = \frac{8}{10} \longrightarrow 0$$

$$0.54 \quad p(X_6 = 1) = \frac{7}{10} \longrightarrow 1$$



Obtaining the new population

$$p(\mathbf{x}) = p(x_1, \dots, x_6) = p(x_1) \cdot p(x_2) \cdot p(x_3) \cdot p(x_4) \cdot p(x_5) \cdot p(x_6)$$

$$0.23 \quad p(X_1 = 1) = \frac{7}{10} \longrightarrow 1$$

$$0.45 \quad p(X_2 = 1) = \frac{7}{10} \longrightarrow 1$$

$$0.89 \quad p(X_3 = 1) = \frac{6}{10} \longrightarrow 0$$

$$0.12 \quad p(X_4 = 1) = \frac{6}{10} \longrightarrow 1$$

$$0.98 \quad p(X_5 = 1) = \frac{8}{10} \longrightarrow 0$$

$$0.54 \quad p(X_6 = 1) = \frac{7}{10} \longrightarrow 1$$



Obtaining the new population

$$p(\mathbf{x}) = p(x_1, \dots, x_6) = p(x_1) \cdot p(x_2) \cdot p(x_3) \cdot p(x_4) \cdot p(x_5) \cdot p(x_6)$$

$$0.23 \quad p(X_1 = 1) = \frac{7}{10} \longrightarrow 1$$

$$0.45 \quad p(X_2 = 1) = \frac{7}{10} \longrightarrow 1$$

$$0.89 \quad p(X_3 = 1) = \frac{6}{10} \longrightarrow 0$$

$$0.12 \quad p(X_4 = 1) = \frac{6}{10} \longrightarrow 1$$

$$0.98 \quad p(X_5 = 1) = \frac{8}{10} \longrightarrow 0$$

$$0.54 \quad p(X_6 = 1) = \frac{7}{10} \longrightarrow 1$$

Obtaining the new population

$$p(\mathbf{x}) = p(x_1, \dots, x_6) = p(x_1) \cdot p(x_2) \cdot p(x_3) \cdot p(x_4) \cdot p(x_5) \cdot p(x_6)$$

$$0.23 \quad p(X_1 = 1) = \frac{7}{10} \longrightarrow 1$$

$$0.45 \quad p(X_2 = 1) = \frac{7}{10} \longrightarrow 1$$

$$0.89 \quad p(X_3 = 1) = \frac{6}{10} \longrightarrow 0$$

$$0.12 \quad p(X_4 = 1) = \frac{6}{10} \longrightarrow 1$$

$$0.98 \quad p(X_5 = 1) = \frac{8}{10} \longrightarrow 0$$

$$0.54 \quad p(X_6 = 1) = \frac{7}{10} \longrightarrow 1$$

Obtaining the new population

$$p(\mathbf{x}) = p(x_1, \dots, x_6) = p(x_1) \cdot p(x_2) \cdot p(x_3) \cdot p(x_4) \cdot p(x_5) \cdot p(x_6)$$

$$0.23 \quad p(X_1 = 1) = \frac{7}{10} \longrightarrow 1$$

$$0.45 \quad p(X_2 = 1) = \frac{7}{10} \longrightarrow 1$$

$$0.89 \quad p(X_3 = 1) = \frac{6}{10} \longrightarrow 0$$

$$0.12 \quad p(X_4 = 1) = \frac{6}{10} \longrightarrow 1$$

$$0.98 \quad p(X_5 = 1) = \frac{8}{10} \longrightarrow 0$$

$$0.54 \quad p(X_6 = 1) = \frac{7}{10} \longrightarrow 1$$



Obtaining the new population

	X_1	X_2	X_3	X_4	X_5	X_6	$h(\mathbf{x})$
1	1	1	0	1	0	1	5
2	1	0	1	0	1	1	4
3	1	1	1	1	1	0	5
4	0	1	0	1	1	1	4
5	1	1	1	1	0	1	5
6	1	0	0	1	1	1	4
7	0	1	0	1	1	0	3
8	1	1	1	0	1	0	4
9	1	1	1	0	0	1	4
10	1	0	0	1	1	1	4
11	1	1	0	0	1	1	4
12	1	0	1	1	1	0	4
13	0	1	1	0	1	1	4
14	0	1	1	1	1	0	4
15	1	1	1	1	1	1	6
16	0	1	1	0	1	1	4
17	1	1	1	1	1	0	5
18	0	1	0	0	1	0	2
19	0	0	1	1	0	1	3
20	1	1	0	1	1	1	5

Pseudocode for EDAs

Obtain an initial population of individuals D_0

Repeat until a stopping criterion is met

Select from D_i a subset of individuals D_i^S

Learn a probability distribution $p_i(\mathbf{x})$ from D_i^S

Sample $p_i(\mathbf{x})$ to obtain $D_{i+1/2}$

Create the new population D_{i+1} from D_i and $D_{i+1/2}$



What components should be set in EDAs?

- Population size
- Selection operator
- Probabilistic model
- Learning algorithm
- Sampling algorithm



What components should be set in EDAs?

- Population size
- Selection operator
- Probabilistic model
- Learning algorithm
- Sampling algorithm



What components should be set in EDAs?

- Population size
- Selection operator
- Probabilistic model
- Learning algorithm
- Sampling algorithm



What components should be set in EDAs?

- Population size
- Selection operator
- Probabilistic model
- Learning algorithm
- Sampling algorithm



What components should be set in EDAs?

- Population size
- Selection operator
- Probabilistic model
- Learning algorithm
- Sampling algorithm



What components should be set in EDAs?

- Population size
- Selection operator
- Probabilistic model
- Learning algorithm
- Sampling algorithm



Classification of EDAs

Two criteria to classify EDAs

- Keep the structure of the probabilistic model fixed
- Classification based on the complexity of the model structure



EDAs with fixed structure

- The structure of the probabilistic model keeps fixed during the search
- At each generation only parametric learning is carried out
- The fixed probabilistic model tries to mimic the structure of the function to optimize
- Most of the work has been done in the optimization of additive decomposable functions



EDAs that change the structure

Classification based on the model structure

- **Modify the structure ((in)dependences) of the probability model at each iteration:**
 - 1 Univariate model: all the variables are independent (UMDA, PBIL, CGA,...)(*)
 - 2 Bivariate model: consider second-order statistics (TREE, MIMIC)
 - 3 Unrestricted model: use of Bayesian networks (EBNA, LFDA, BOA)



EDAs that change the structure

Classification based on the model structure

- Modify the structure ((in)dependences) of the probability model at each iteration:
 - 1 Univariate model: all the variables are independent (UMDA, PBIL, CGA,...)(*)
 - 2 Bivariate model: consider second-order statistics (TREE, MIMIC)
 - 3 Unrestricted model: use of Bayesian networks (EBNA, LFDA, BOA)



EDAs that change the structure

Classification based on the model structure

- Modify the structure ((in)dependences) of the probability model at each iteration:
 - 1 Univariate model: all the variables are independent (UMDA, PBIL, CGA,...)(*)
 - 2 Bivariate model: consider second-order statistics (TREE, MIMIC)
 - 3 Unrestricted model: use of Bayesian networks (EBNA, LFDA, BOA)



EDAs that change the structure

Classification based on the model structure

- Modify the structure ((in)dependences) of the probability model at each iteration:
 - 1 Univariate model: all the variables are independent (UMDA, PBIL, CGA,...)(*)
 - 2 Bivariate model: consider second-order statistics (TREE, MIMIC)
 - 3 Unrestricted model: use of Bayesian networks (EBNA, LFDA, BOA)



EDAs that change the structure

Classification based on the model structure

- Modify the structure ((in)dependences) of the probability model at each iteration:
 - 1 Univariate model: all the variables are independent (UMDA, PBIL, CGA,...)(*)
 - 2 Bivariate model: consider second-order statistics (TREE, MIMIC)
 - 3 Unrestricted model: use of Bayesian networks (EBNA, LFDA, BOA)



No dependencies

Univariate Marginal Distribution Algorithm (UMDA)

- Probabilistic model: $p_I(\mathbf{x}) = \prod_{i=1}^n p_I(x_i)$
- Parameter learning: maximum likelihood (frequency counts)

Probabilistic Based Incremental Learning (PBIL)

- Probabilistic model: same as UMDA
- Parameter learning: maximum likelihood (frequency counts)
- Rule to modify the probabilistic model:

$$p_{I+1}(\mathbf{x}) = (1 - \alpha)p_I(\mathbf{x}) + \alpha \frac{1}{N} \sum_{k=1}^N x_{k:M}^I$$

Bivariate model

TREE

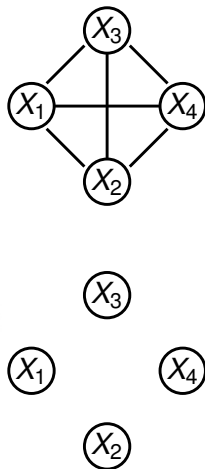
- Probabilistic model: $p(\mathbf{x}) = \prod_{i=1}^n p(x_i|x_{j(i)})$
- Structural learning: Chow and Liu algorithm
- Parametric learning: Maximum likelihood
- Sampling: Probabilistic logic sampling



Chow and Liu algorithm

i) For each X_i, X_j compute:

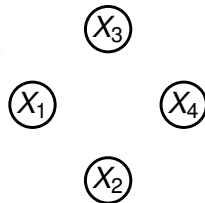
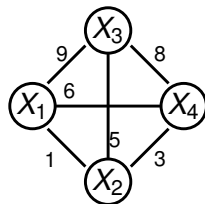
$$MI(X_i, X_j) = \sum_{x_i, x_j} p(x_i, x_j) \log \frac{p(x_i, x_j)}{p(x_i)p(x_j)}$$



Chow and Liu algorithm

i) For each X_i, X_j compute:

$$MI(X_i, X_j) = \sum_{x_i, x_j} p(x_i, x_j) \log \frac{p(x_i, x_j)}{p(x_i)p(x_j)}$$

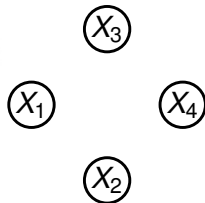
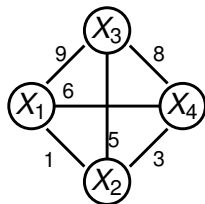


Chow and Liu algorithm

- i) For each X_i, X_j compute:

$$MI(X_i, X_j) = \sum_{x_i, x_j} p(x_i, x_j) \log \frac{p(x_i, x_j)}{p(x_i)p(x_j)}$$

- ii) Assign the two edges with the highest MI to the tree

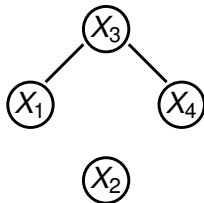
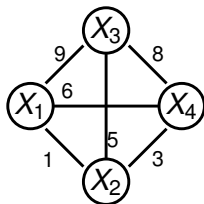


Chow and Liu algorithm

- i) For each X_i, X_j compute:

$$MI(X_i, X_j) = \sum_{x_i, x_j} p(x_i, x_j) \log \frac{p(x_i, x_j)}{p(x_i)p(x_j)}$$

- ii) Assign the two edges with the highest MI to the tree

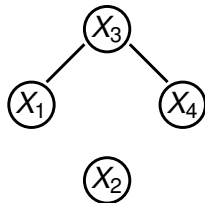
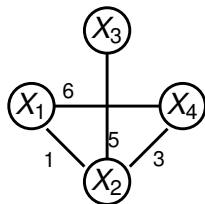


Chow and Liu algorithm

- i) For each X_i, X_j compute:

$$MI(X_i, X_j) = \sum_{x_i, x_j} p(x_i, x_j) \log \frac{p(x_i, x_j)}{p(x_i)p(x_j)}$$

- ii) Assign the two edges with the highest MI to the tree



Chow and Liu algorithm

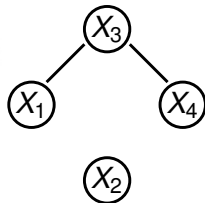
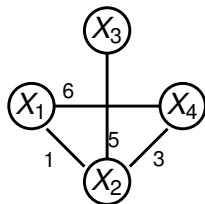
- i) For each X_i, X_j compute:

$$MI(X_i, X_j) = \sum_{x_i, x_j} p(x_i, x_j) \log \frac{p(x_i, x_j)}{p(x_i)p(x_j)}$$

- ii) Assign the two edges with the highest MI to the tree

- iii) Repeat until there are $n - 1$ edges in the tree:

Assign the edge with the highest MI value to the tree if it does not form a loop, otherwise delete it



Chow and Liu algorithm

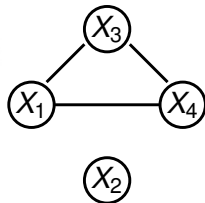
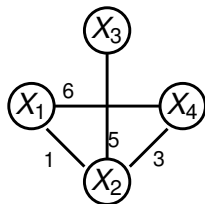
- i) For each X_i, X_j compute:

$$MI(X_i, X_j) = \sum_{x_i, x_j} p(x_i, x_j) \log \frac{p(x_i, x_j)}{p(x_i)p(x_j)}$$

- ii) Assign the two edges with the highest MI to the tree

- iii) Repeat until there are $n - 1$ edges in the tree:

Assign the edge with the highest MI value to the tree if it does not form a loop, otherwise delete it



Chow and Liu algorithm

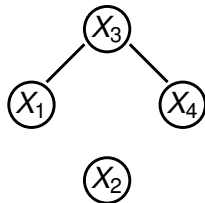
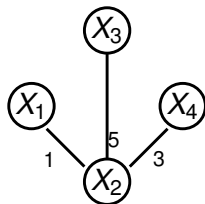
- i) For each X_i, X_j compute:

$$MI(X_i, X_j) = \sum_{x_i, x_j} p(x_i, x_j) \log \frac{p(x_i, x_j)}{p(x_i)p(x_j)}$$

- ii) Assign the two edges with the highest MI to the tree

- iii) Repeat until there are $n - 1$ edges in the tree:

Assign the edge with the highest MI value to the tree if it does not form a loop, otherwise delete it



Chow and Liu algorithm

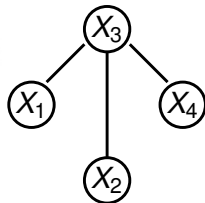
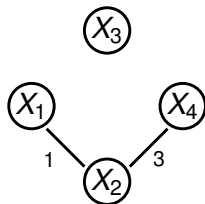
- i) For each X_i, X_j compute:

$$MI(X_i, X_j) = \sum_{x_i, x_j} p(x_i, x_j) \log \frac{p(x_i, x_j)}{p(x_i)p(x_j)}$$

- ii) Assign the two edges with the highest MI to the tree

- iii) Repeat until there are $n - 1$ edges in the tree:

Assign the edge with the highest MI value to the tree if it does not form a loop, otherwise delete it



Chow and Liu algorithm

- i) For each X_i, X_j compute:

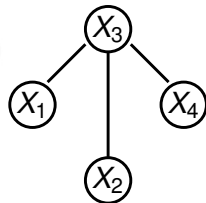
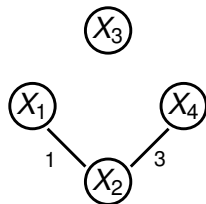
$$MI(X_i, X_j) = \sum_{x_i, x_j} p(x_i, x_j) \log \frac{p(x_i, x_j)}{p(x_i)p(x_j)}$$

- ii) Assign the two edges with the highest MI to the tree

- iii) Repeat until there are $n - 1$ edges in the tree:

Assign the edge with the highest MI value to the tree if it does not form a loop, otherwise delete it

- iv) Give orientation to the edges by choosing a node as the root

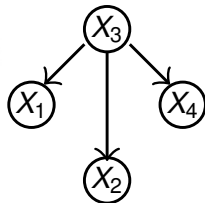
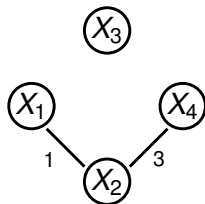


Chow and Liu algorithm

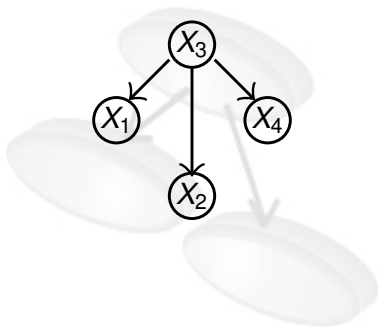
- i) For each X_i, X_j compute:

$$MI(X_i, X_j) = \sum_{x_i, x_j} p(x_i, x_j) \log \frac{p(x_i, x_j)}{p(x_i)p(x_j)}$$

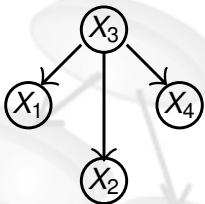
- ii) Assign the two edges with the highest MI to the tree
- iii) Repeat until there are $n - 1$ edges in the tree:
 Assign the edge with the highest MI value to the tree if it does not form a loop, otherwise delete it
- iv) Give orientation to the edges by choosing a node as the root



Chow and Liu algorithm



Chow and Liu algorithm



$$p(x_1, x_2, x_3, x_4) = p(x_1|x_3) \cdot p(x_2|x_3) \cdot p(x_3) \cdot p(x_4|x_3)$$

Parametric learning in TREE

$$p(x_1, x_2, x_3, x_4) = p(x_1|x_3) \cdot p(x_2|x_3) \cdot p(x_3) \cdot p(x_4|x_3)$$

X_1	X_2	X_3	X_4
1	0	0	1
1	1	0	0
0	1	1	0
0	0	0	1
0	1	1	1

$$p(X_1 = 1|X_3 = 0)$$

$$p(X_1 = 1|X_3 = 1)$$

Parametric learning in TREE

$$p(x_1, x_2, x_3, x_4) = p(x_1|x_3) \cdot p(x_2|x_3) \cdot p(x_3) \cdot p(x_4|x_3)$$

X_1	X_2	X_3	X_4
1	0	0	1
1	1	0	0
0	1	1	0
0	0	0	1
0	1	1	1

$$p(X_1 = 1|X_3 = 0)$$

$$p(X_1 = 1|X_3 = 1)$$

Parametric learning in TREE

$$p(x_1, x_2, x_3, x_4) = p(x_1|x_3) \cdot p(x_2|x_3) \cdot p(x_3) \cdot p(x_4|x_3)$$

X_1	X_2	X_3	X_4
1	0	0	1
1	1	0	0
0	1	1	0
0	0	0	1
0	1	1	1

$$p(X_1 = 1|X_3 = 0) = \frac{2}{3}$$

$$p(X_1 = 1|X_3 = 1)$$

Parametric learning in TREE

$$p(x_1, x_2, x_3, x_4) = p(x_1|x_3) \cdot p(x_2|x_3) \cdot p(x_3) \cdot p(x_4|x_3)$$

X_1	X_2	X_3	X_4
1	0	0	1
1	1	0	0
0	1	1	0
0	0	0	1
0	1	1	1

$$p(X_1 = 1|X_3 = 0) = \frac{2}{3}$$

$$p(X_1 = 1|X_3 = 1)$$

Parametric learning in TREE

$$p(x_1, x_2, x_3, x_4) = p(x_1|x_3) \cdot p(x_2|x_3) \cdot p(x_3) \cdot p(x_4|x_3)$$

X_1	X_2	X_3	X_4
1	0	0	1
1	1	0	0
0	1	1	0
0	0	0	1
0	1	1	1

$$p(X_1 = 1 | X_3 = 0) = \frac{2}{3}$$

$$p(X_1 = 1 | X_3 = 1) = \frac{0}{2}$$

Parametric learning in TREE

$$p(x_1, x_2, x_3, x_4) = p(x_1|x_3) \cdot p(x_2|x_3) \cdot p(x_3) \cdot p(x_4|x_3)$$

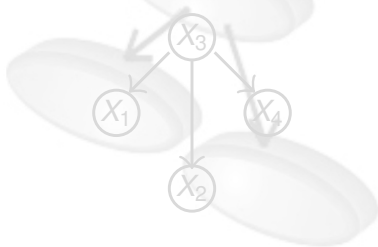
X_1	X_2	X_3	X_4
1	0	0	1
1	1	0	0
0	1	1	0
0	0	0	1
0	1	1	1

$$p(X_1 = 1|X_3 = 0) = \frac{2 + \epsilon}{3 + 2\epsilon}$$

$$p(X_1 = 1|X_3 = 1) = \frac{0 + \epsilon}{2 + 2\epsilon}$$

Sampling in TREE

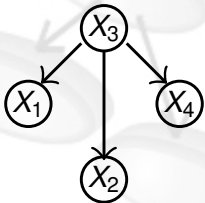
- Order the variables in such a way that parents variables come before children variables



- In our case: X_3, X_1, X_2, X_4
- Variables are sampled in this order

Sampling in TREE

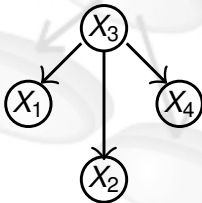
- Order the variables in such a way that parents variables come before children variables



- In our case: X_3, X_1, X_2, X_4
- Variables are sampled in this order

Sampling in TREE

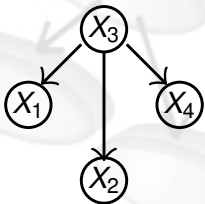
- Order the variables in such a way that parents variables come before children variables



- In our case: X_3, X_1, X_2, X_4
- Variables are sampled in this order

Sampling in TREE

- Order the variables in such a way that parents variables come before children variables



- In our case: X_3, X_1, X_2, X_4
- Variables are sampled in this order

Sampling in TREE

$$p(x_1, x_2, x_3, x_4) = p(x_1|x_3) \cdot p(x_2|x_3) \cdot p(x_3) \cdot p(x_4|x_3)$$

$$p(X_1 = 1|X_3 = 0) = 0,3 \quad p(X_2 = 1|X_3 = 0) = 0,1 \quad p(X_3 = 1) = 0,7 \quad p(X_4 = 1|X_3 = 0) = 0,5$$

$$p(X_1 = 1|X_3 = 1) = 0,2 \quad p(X_2 = 1|X_3 = 1) = 0,8 \quad p(X_4 = 1|X_3 = 1) = 0,6$$

Variable order: X_3, X_1, X_2, X_4

X_1	X_2	X_3	X_4
0,85	0,55	0,23	0,91



Sampling in TREE

$$p(x_1, x_2, x_3, x_4) = p(x_1|x_3) \cdot p(x_2|x_3) \cdot p(x_3) \cdot p(x_4|x_3)$$

$$p(X_1 = 1|X_3 = 0) = 0,3 \quad p(X_2 = 1|X_3 = 0) = 0,1 \quad p(X_3 = 1) = 0,7 \quad p(X_4 = 1|X_3 = 0) = 0,5$$

$$p(X_1 = 1|X_3 = 1) = 0,2 \quad p(X_2 = 1|X_3 = 1) = 0,8 \quad p(X_4 = 1|X_3 = 1) = 0,6$$

Variable order: X_3, X_1, X_2, X_4

X_1	X_2	X_3	X_4
0,85	0,55	0,23	0,91

↓ ↓ ↓ ↓

1



Sampling in TREE

$$p(x_1, x_2, x_3, x_4) = p(x_1|x_3) \cdot p(x_2|x_3) \cdot p(x_3) \cdot p(x_4|x_3)$$

$$p(X_1 = 1|X_3 = 0) = 0,3 \quad p(X_2 = 1|X_3 = 0) = 0,1 \quad p(X_3 = 1) = 0,7 \quad p(X_4 = 1|X_3 = 0) = 0,5$$

$$p(X_1 = 1|X_3 = 1) = 0,2 \quad p(X_2 = 1|X_3 = 1) = 0,8 \quad p(X_4 = 1|X_3 = 1) = 0,6$$

Variable order: X_3, X_1, X_2, X_4

X_1	X_2	X_3	X_4
0,85	0,55	0,23	0,91
↓	↓	↓	↓
0		1	

Sampling in TREE

$$p(x_1, x_2, x_3, x_4) = p(x_1|x_3) \cdot p(x_2|x_3) \cdot p(x_3) \cdot p(x_4|x_3)$$

$$p(X_1 = 1|X_3 = 0) = 0,3 \quad p(X_2 = 1|X_3 = 0) = 0,1 \quad p(X_3 = 1) = 0,7 \quad p(X_4 = 1|X_3 = 0) = 0,5$$

$$p(X_1 = 1|X_3 = 1) = 0,2 \quad p(X_2 = 1|X_3 = 1) = 0,8 \quad p(X_4 = 1|X_3 = 1) = 0,6$$

Variable order: X_3, X_1, X_2, X_4

X_1	X_2	X_3	X_4
0,85	0,55	0,23	0,91
↓	↓	↓	↓
0	1	1	0



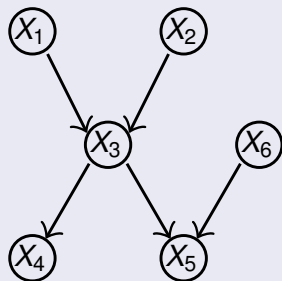
Unrestrictive models: Estimation of Bayesian Network Algorithm (EBNA)

Characteristics

- At each step a Bayesian network is learnt
- Parameters are learnt using maximum likelihood
- Probabilistic Logic Sampling is used to sample new solutions

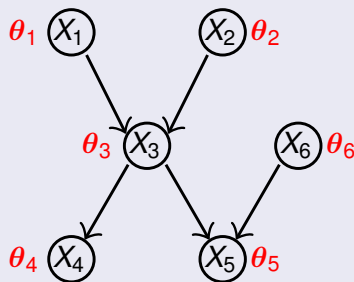


Bayesian networks



$$p(\mathbf{x}) = p(x_1) \cdot p(x_2) \cdot p(x_3|x_1, x_2) \cdot p(x_4|x_3) \cdot p(x_5|x_3, x_6) \cdot p(x_6)$$

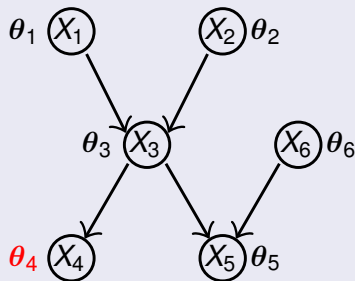
Bayesian networks



$$p(\mathbf{x}) = p(x_1) \cdot p(x_2) \cdot p(x_3|x_1, x_2) \cdot p(x_4|x_3) \cdot p(x_5|x_3, x_6) \cdot p(x_6)$$

Bayesian networks

$$\theta_4 = (\theta_{41}, \theta_{42})$$

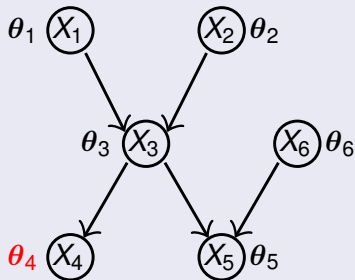


$$p(\mathbf{x}) = p(x_1) \cdot p(x_2) \cdot p(x_3|x_1, x_2) \cdot p(x_4|x_3) \cdot p(x_5|x_3, x_6) \cdot p(x_6)$$

Bayesian networks

$$\theta_4 = (\theta_{41}, \theta_{42})$$

$$\left\{ \begin{array}{l} \theta_{411} = p(X_4 = 0 \mid X_3 = 0) \\ \theta_{412} = p(X_4 = 1 \mid X_3 = 0) \end{array} \right.$$



$$p(\mathbf{x}) = p(x_1) \cdot p(x_2) \cdot p(x_3|x_1, x_2) \cdot p(x_4|x_3) \cdot p(x_5|x_3, x_6) \cdot p(x_6)$$

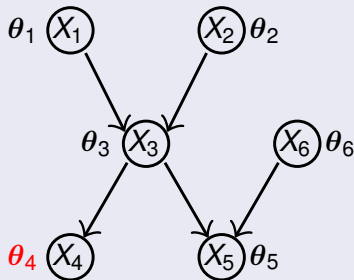
Bayesian networks

$$\theta_4 = (\theta_{41}, \theta_{42})$$

$$\left\{ \begin{array}{l} \theta_{411} = p(X_4 = 0 \mid X_3 = 0) \\ \theta_{412} = p(X_4 = 1 \mid X_3 = 0) \end{array} \right.$$

General case

$$\theta_{ijk} = p(X_i = x_i^k \mid \mathbf{Pa}_i = \mathbf{pa}_i^j)$$



$$p(\mathbf{x}) = p(x_1) \cdot p(x_2) \cdot p(x_3 | x_1, x_2) \cdot p(x_4 | x_3) \cdot p(x_5 | x_3, x_6) \cdot p(x_6)$$

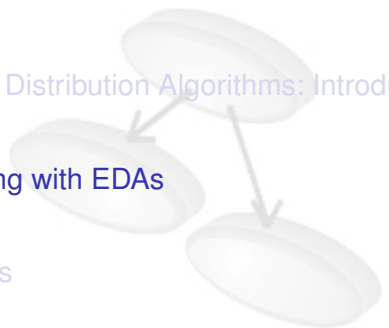
Which are the benefits of using explicit distributions?

- Search for solutions taking into account correlation between variables
- Incorporate information from the fitness function to the probability model:
 - Relations between the variables
 - Structural information
- It is possible to extract information about the objective function from the learnt model:
 - Relations between variables
 - Characteristics of the search space
 - A model of the process that is being optimized

Which are the benefits of using explicit distributions?

- Search for solutions taking into account correlation between variables
- Incorporate information from the fitness function to the probability model:
 - Relations between the variables
 - Structural information
- It is possible to extract information about the objective function from the learnt model:
 - Relations between variables
 - Characteristics of the search space
 - A model of the process that is being optimized

Outline of the presentation

- 1 Estimation of Distribution Algorithms: Introduction
 - 2 Protein Folding with EDAs**
 - 3 Miscellaneous
 - 4 Conclusions
- 



Proteins

Introduction

- **Proteins are essential components of living organisms**
- Formed by a sequence of (20 different types) amino acids or residues
- Under suitable conditions folded in 3-D to form a functional structure
- Each possible protein fold has associated free energy
- The native structure of a protein is the one for which the free energy achieves the global minimum



Proteins

Introduction

- Proteins are essential components of living organisms
- Formed by a sequence of (20 different types) amino acids or residues
- Under suitable conditions folded in 3-D to form a functional structure
- Each possible protein fold has associated free energy
- The native structure of a protein is the one for which the free energy achieves the global minimum



Proteins

Introduction

- Proteins are essential components of living organisms
- Formed by a sequence of (20 different types) amino acids or residues
- Under suitable conditions folded in 3-D to form a functional structure
- Each possible protein fold has associated free energy
- The native structure of a protein is the one for which the free energy achieves the global minimum



Proteins

Introduction

- Proteins are essential components of living organisms
- Formed by a sequence of (20 different types) amino acids or residues
- Under suitable conditions folded in 3-D to form a functional structure
- Each possible protein fold has associated free energy
- The native structure of a protein is the one for which the free energy achieves the global minimum



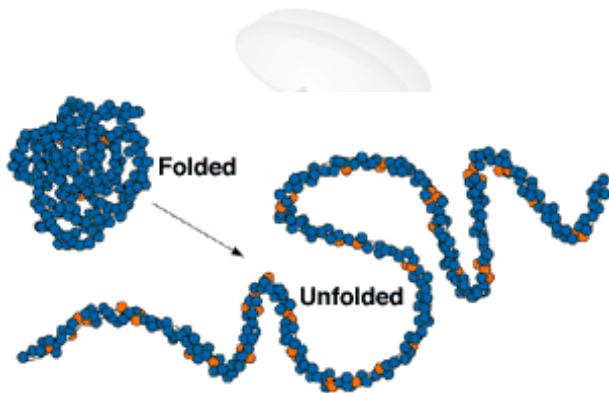
Proteins

Introduction

- Proteins are essential components of living organisms
- Formed by a sequence of (20 different types) amino acids or residues
- Under suitable conditions folded in 3-D to form a functional structure
- Each possible protein fold has associated free energy
- The native structure of a protein is the one for which the free energy achieves the global minimum



Proteins



Protein Folding

Protein Folding as an Optimization Problem

- Given a sequence of amino acids, which is the native structure of the protein?
- Problems:
 - To define an adequate energy function
 - An exponential number of folding possibilities
- Solutions: use of simplified protein models



Protein Folding

Protein Folding as an Optimization Problem

- Given a sequence of amino acids, which is the native structure of the protein?
- Problems:
 - To define an adequate energy function
 - An exponential number of folding possibilities
- Solutions: use of simplified protein models



Protein Folding

Protein Folding as an Optimization Problem

- Given a sequence of amino acids, which is the native structure of the protein?
- Problems:
 - To define an adequate energy function
 - An exponential number of folding possibilities
- Solutions: use of simplified protein models



Protein Folding

Protein Folding as an Optimization Problem

- Given a sequence of amino acids, which is the native structure of the protein?
- Problems:
 - To define an adequate energy function
 - An exponential number of folding possibilities
- Solutions: use of simplified protein models



Protein Folding

Protein Folding as an Optimization Problem

- Given a sequence of amino acids, which is the native structure of the protein?
- Problems:
 - To define an adequate energy function
 - An exponential number of folding possibilities
- Solutions: use of simplified protein models



Protein Folding

Protein Folding as an Optimization Problem

- Given a sequence of amino acids, which is the native structure of the protein?
- Problems:
 - To define an adequate energy function
 - An exponential number of folding possibilities
- Solutions: use of simplified protein models



The Hydrophobic-Polar (HP) Model

Introduction

- The HP model considers two types of residues: hydrophobic (H) residues and hydrophilic or polar (P) residues
- A protein is considered a sequence of these two types of residues, which are located in regular lattice models forming **self-avoided** paths
- Given two residues we consider two kinds of neighborhoods:
 - Connected neighbors: adjacent in the chain
 - Topological neighbors: adjacent in the lattice but not connected in the chain



The Hydrophobic-Polar (HP) Model

Introduction

- The HP model considers two types of residues: hydrophobic (H) residues and hydrophilic or polar (P) residues
- A protein is considered a sequence of these two types of residues, which are located in regular lattice models forming **self-avoided** paths
- Given two residues we consider two kinds of neighborhoods:
 - Connected neighbors: adjacent in the chain
 - Topological neighbors: adjacent in the lattice but not connected in the chain



The Hydrophobic-Polar (HP) Model

Introduction

- The HP model considers two types of residues: hydrophobic (H) residues and hydrophilic or polar (P) residues
- A protein is considered a sequence of these two types of residues, which are located in regular lattice models forming **self-avoided** paths
- Given two residues we consider two kinds of neighborhoods:
 - Connected neighbors: adjacent in the chain
 - Topological neighbors: adjacent in the lattice but not connected in the chain



The H-P model

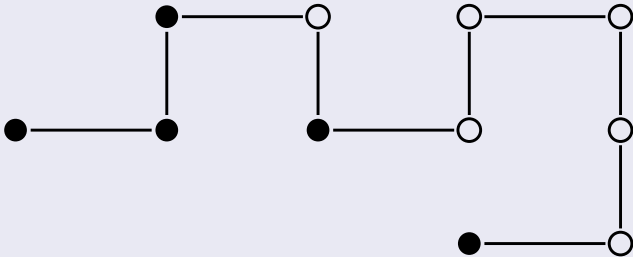
Energy function

- A energy function that measures the interaction between topological neighbor residues is defined as:
 - $\epsilon_{HH} = -1$
 - $\epsilon_{HP} = 0$
 - $\epsilon_{PP} = 0$



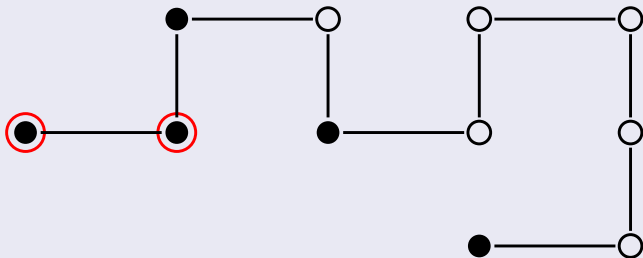
The H-P model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice



The H-P model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice

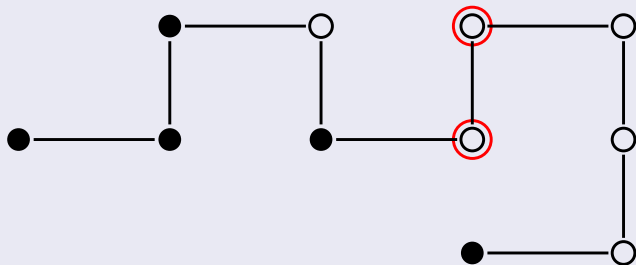


connected neighbors



The H-P model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice

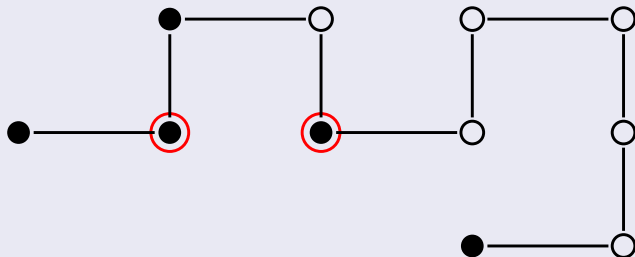


connected neighbors



The H-P model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice

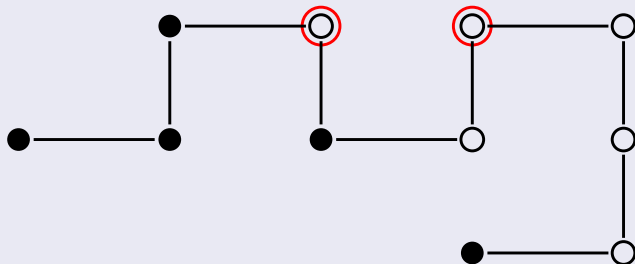


topological neighbors



The H-P model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice

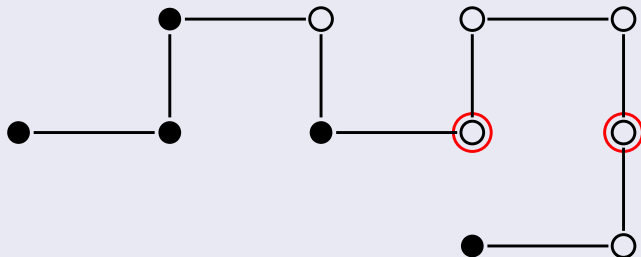


topological neighbors



The H-P model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice

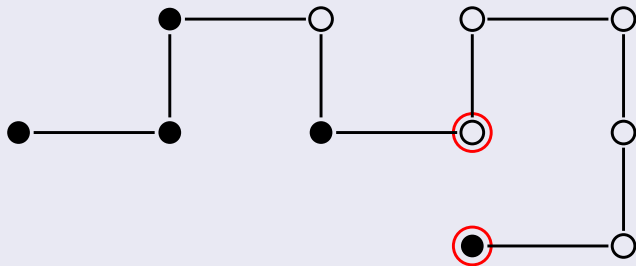


topological neighbors



The H-P model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice

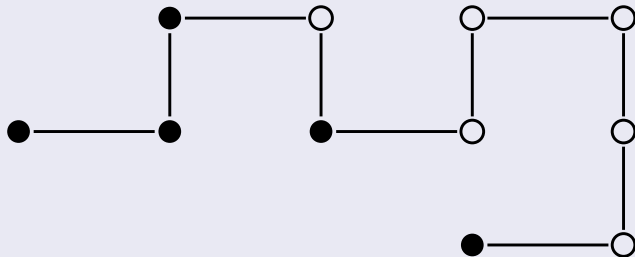


topological neighbors



The H-P model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice

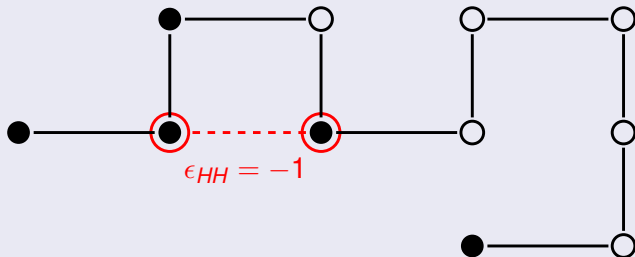


Energy=



The H-P model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice

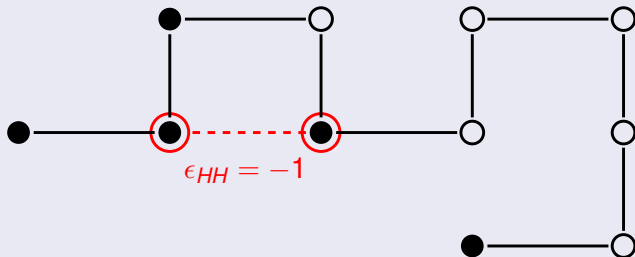


Energy=



The H-P model

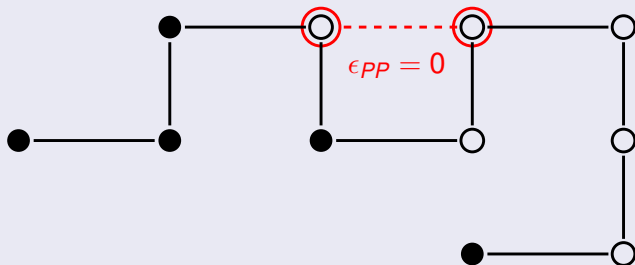
Example of folding of *HHHPHPPPPH* protein in a 2-D lattice



Energy = -1

The H-P model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice

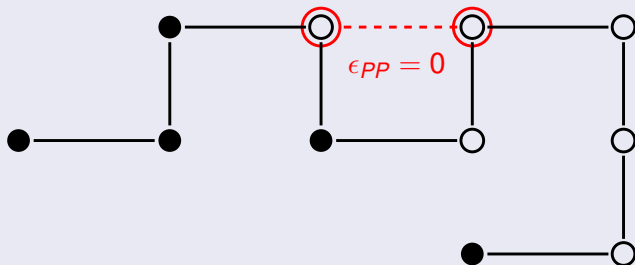


Energy = -1



The H-P model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice

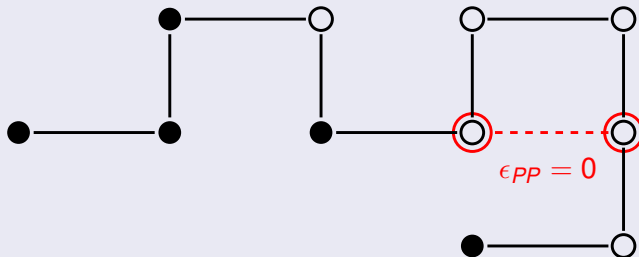


Energy = -1 + 0



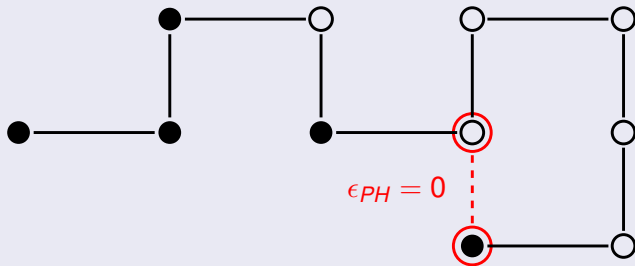
The H-P model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice



The H-P model

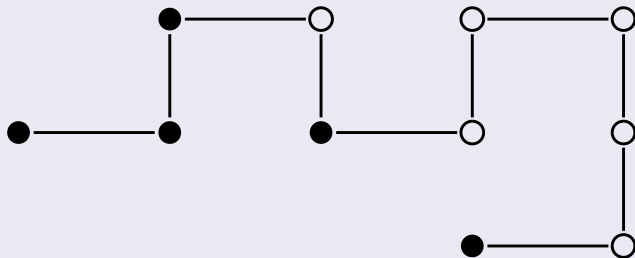
Example of folding of *HHHPHPPPPH* protein in a 2-D lattice



$$\text{Energy} = -1 + 0 + 0 + 0$$

The H-P model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice



$$\text{Energy} = -1 + 0 + 0 + 0 = -1$$

The functional model

Characteristics

- The functional model is a “shifted” H-P model
- This model has native states, some of which are not maximally compact
- They have cavities or potential binding sites
- The main difference with the H-P model is the definition of the energy



The functional model

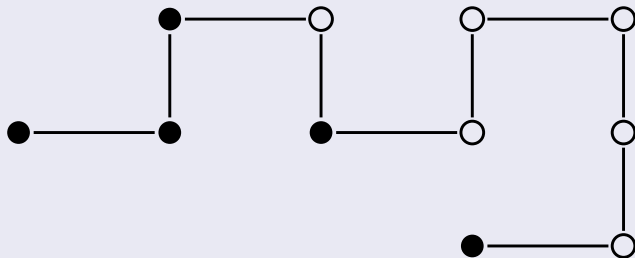
Energy function

- A energy function that measures the interaction between topological neighbor residues is defined as:
 - $\epsilon_{HH} = -2$
 - $\epsilon_{HP} = 1$
 - $\epsilon_{PP} = 1$



The functional model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice

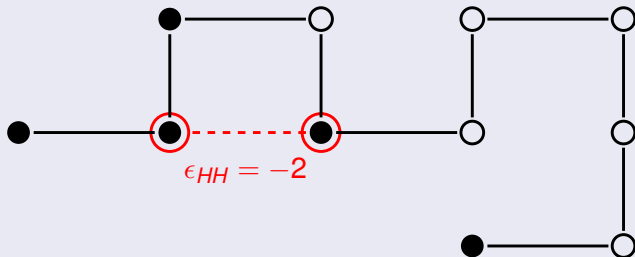


Energy=



The functional model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice

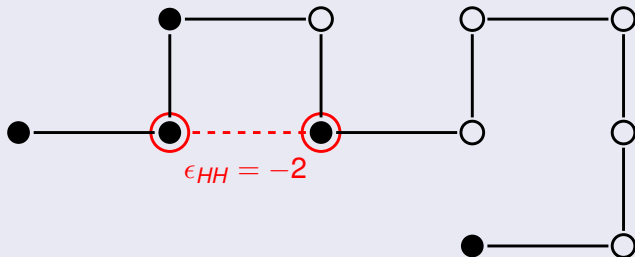


Energy=



The functional model

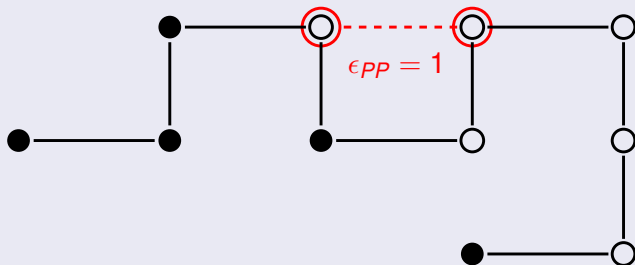
Example of folding of *HHHPHPPPPH* protein in a 2-D lattice



Energy = -2

The functional model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice

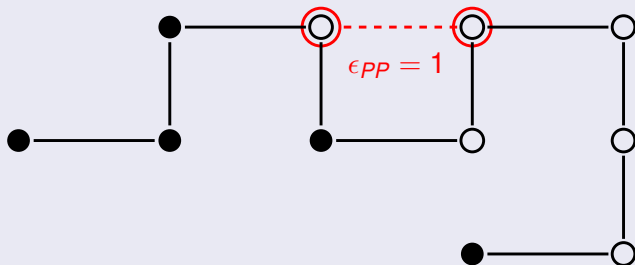


Energy = -2



The functional model

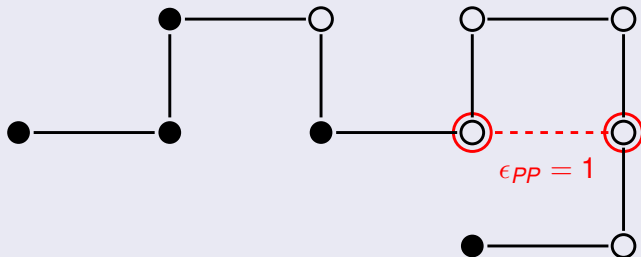
Example of folding of *HHHPHPPPPH* protein in a 2-D lattice



Energy = -2 + 1

The functional model

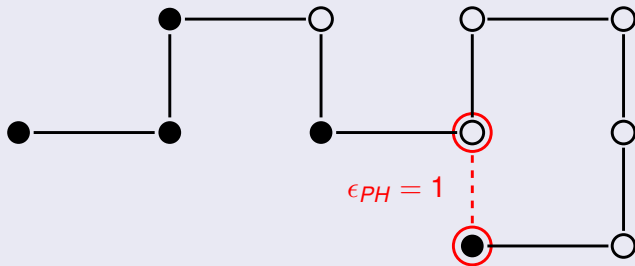
Example of folding of *HHHPHPPPPH* protein in a 2-D lattice



$$\text{Energy} = -2 + 1 + 1$$

The functional model

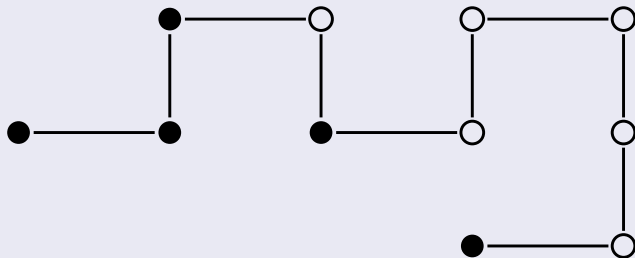
Example of folding of *HHHPHPPPPH* protein in a 2-D lattice



$$\text{Energy} = -2 + 1 + 1 + 1$$

The functional model

Example of folding of *HHHPHPPPPH* protein in a 2-D lattice



$$\text{Energy} = -2 + 1 + 1 + 1 = 1$$

EDAs applied to the H-P problem . Problem formalization

Solution representation

- Given a chain of length n a solution is an array of length n
- Absolute codification
 - Each position X_i in the array will represent the global move of residue i
- Relative codification:
 - Each position X_i in the array will represent the relative move of residue i in relation to the previous two residues
 - In this way for a 2-D lattice $X_i \in \{0, 1, 2\}$ and for a 3-D lattice $X_i \in \{0, \dots, 4\}$

EDAs applied to the H-P problem . Problem formalization

Solution representation

- Given a chain of length n a solution is an array of length n
- Absolute codification
 - Each position X_i in the array will represent the global move of residue i
- **Relative codification:**
 - Each position X_i in the array will represent the relative move of residue i in relation to the previous two residues
 - In this way for a 2-D lattice $X_i \in \{0, 1, 2\}$ and for a 3-D lattice $X_i \in \{0, \dots, 4\}$

Problem formalization

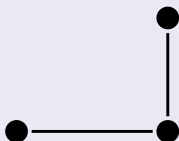
Solution representation



$(0, 0, -, -, -, -, -, -, -, -, -)$

Problem formalization

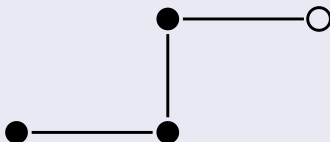
Solution representation



$(0, 0, 1, -, -, -, -, -, -, -)$

Problem formalization

Solution representation

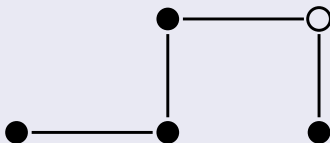


$(0, 0, 1, -1, -, -, -, -, -, -, -)$



Problem formalization

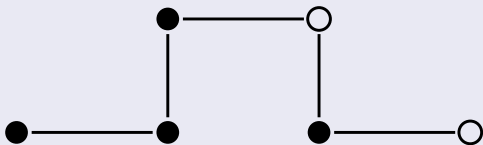
Solution representation



$(0, 0, 1, -1, -1, -, -, -, -, -, -)$

Problem formalization

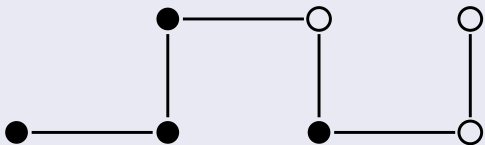
Solution representation



$(0, 0, 1, -1, -1, 1, -, -, -, -, -)$

Problem formalization

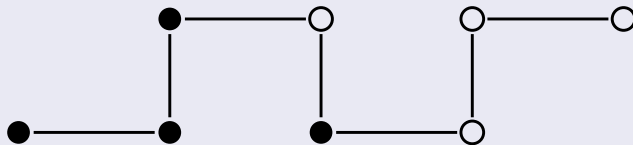
Solution representation



$(0, 0, 1, -1, -1, 1, 1, -, -, -, -)$

Problem formalization

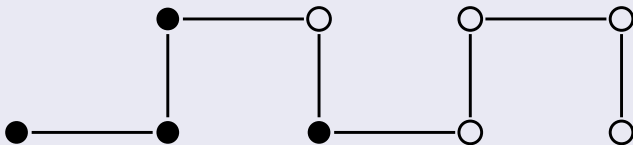
Solution representation



$(0, 0, 1, -1, -1, 1, 1, -1, -, -, -)$

Problem formalization

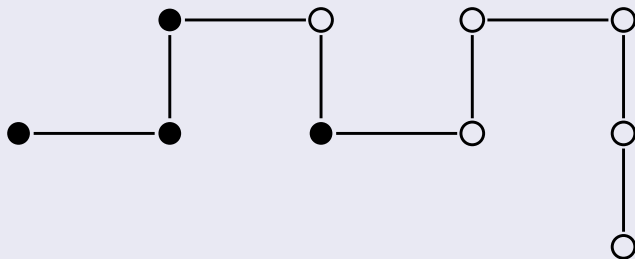
Solution representation



$(0, 0, 1, -1, -1, 1, 1, -1, -1, -, -)$

Problem formalization

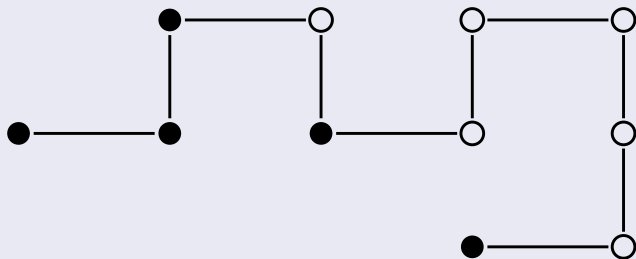
Solution representation



$(0, 0, 1, -1, -1, 1, 1, -1, -1, 0, -)$

Problem formalization

Solution representation



$(0, 0, 1, -1, -1, 1, 1, -1, -1, 0, -1)$

Problem formalization

Relative codification

- The proposed codification can give non self-avoided paths
- To have self-avoided paths a backtracking method is used



Estimation of Distribution Algorithms

Pseudocode for an EDA

Obtain an initial population of individuals D_0

Repeat until a stopping criterion is met

Select from D_i a subset of individuals D_i^S

Learn a probability distribution $p_i(\mathbf{x})$ from D_i^S

Sample $p_i(\mathbf{x})$ to obtain $D_{i+1/2}$

Create the new population D_{i+1} from D_i and $D_{i+1/2}$



Which probabilistic model to use?

Dependencies and regularities in the search space

- Our first idea is to use an independence model
$$p(\mathbf{x}) = \prod_{i=1}^n p(x_i)$$
- However, are there dependencies and regularities between the variables of the problem?
- How to look for dependencies and regularities between the variables of the problem?

Solution: **Boltzmann Distribution**



Boltzmann distribution

Definition

- Given a function $f(x)$ we define the Boltzmann distribution as:

$$p(x) = \frac{e^{\beta f(x)}}{\sum_y e^{\beta f(y)}}$$

where $\beta > 0$



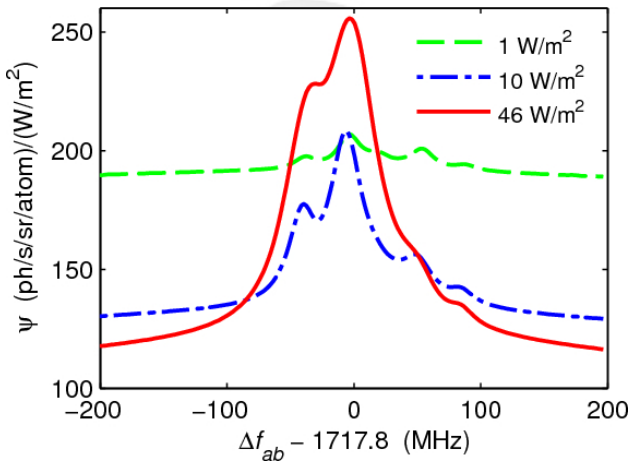
Properties of the Boltzmann distribution

Properties

- Establish a relation between the function to optimize and the probability distribution
- Assign probabilities such that if $f(x) > f(y)$ then $p(x) > p(y)$
- When $\beta \rightarrow \infty$, only optimal points have positive probabilities
- If we could efficiently sample the Boltzmann distribution the optimization problem would be solved



Boltzmann distribution



Relation between ADFs and the Boltzmann distribution

Additive decomposable functions

$$f(\mathbf{x}) = f_1(\mathbf{x}_{S_1}) + f_2(\mathbf{x}_{S_2}) + \dots + f_l(\mathbf{x}_{S_l})$$

Theorem

Given an ADF function $f(\mathbf{x}) = \sum_{i=1}^l f_i(\mathbf{x}_{S_i})$, if X_j y X_k are not in the argument of any $f_i(\mathbf{x}_{S_i})$ of $f(\mathbf{x})$ then X_j y X_k are conditionally independent given the rest of the variables for the Boltzmann distribution $p(\mathbf{x})$ associated to $f(\mathbf{x})$.



Which probabilistic model to use?

Dependencies and regularities in the search space

- Our first idea is to use an independence model
$$p(\mathbf{x}) = \prod_{i=1}^n p(x_i)$$
- However, are there dependencies and regularities between the variables of the problem?
- How to look for dependencies and regularities between the variables of the problem?

Solution: **Boltzmann Distribution**



Regularities in the search space

Experimental set-up

- Protein used: HHHPHPPPPPH
- We have calculated the whole search space

$H(\mathbf{x})$	-4	-3	-2	-1	0	1	2	3	4	5	invalid	total
HP_f	0	0	16	1428	9581	0	0	0	0	0	8658	19683

- Build the Boltzman distribution associated with the objective function of the protein:

$$p(\mathbf{x}) = \frac{e^{\frac{-H(\mathbf{x})}{t}}}{\sum_{\mathbf{x}'} e^{\frac{-H(\mathbf{x}')}{t}}}$$

- Calculated the marginal probability of (X_3, X_4, X_5) and the marginal of each variable separately



Marginal probabilities

Seq	$p_{HP}(X_3, X_4, X_5)$			Seq	$p_{HP}(X_3) \cdot p_{HP}(X_4) \cdot p_{HP}(X_5)$		
	0 --	1 --	2 --		0 --	1 --	2 --
-00	0,000	0,057	<u>0,069</u>	-00	0,036	0,042	0,036
-01	0,035	0,036	<u>0,038</u>	-01	0,036	<u>0,042</u>	0,036
-02	0,035	0,036	0,035	-02	0,036	<u>0,042</u>	0,036
-10	0,029	0,034	0,035	-10	0,033	0,038	0,033
-11	0,038	0,040	0,038	-11	0,033	0,039	0,033
-12	0,035	0,034	0,029	-12	0,033	0,038	0,033
-20	0,035	0,036	0,035	-20	0,036	0,042	0,036
-21	0,038	0,036	0,035	-21	0,036	<u>0,042</u>	0,036
-22	<u>0,069</u>	0,057	0,000	-22	0,036	<u>0,042</u>	0,036



Marginal probabilities

Seq	$p_{HP}(x_3, x_4, x_5)$			Seq	$p_{HP}(x_3) \cdot p_{HP}(x_4) \cdot p_{HP}(x_5)$		
	0 --	1 --	2 --		0 --	1 --	2 --
-00	0,000	0,057	<u>0,069</u>	-00	0,036	0,042	0,036
-01	0,035	0,036	0,038	-01	0,036	<u>0,042</u>	0,036
-02	0,035	0,036	0,035	-02	0,036	0,042	0,036
-10	0,029	0,034	0,035	-10	0,033	0,038	0,033
-11	0,038	0,040	0,038	-11	0,033	0,039	0,033
-12	0,035	0,034	0,029	-12	0,033	0,038	0,033
-20	0,035	0,036	0,035	-20	0,036	0,042	0,036
-21	0,038	0,036	0,035	-21	0,036	<u>0,042</u>	0,036
-22	<u>0,069</u>	0,057	0,000	-22	0,036	0,042	0,036

IMPORTANT REGULARITIES IN THE FUNCTION



EDAs for the H-P model

Probabilistic models used

- Markov model (only parameter learning required):

$$p_{MK}(\mathbf{x}) = p(x_1, \dots, x_{k+1}) \prod_{i=k+2}^n p(x_i \mid x_{i-1}, \dots, x_{i-k})$$

- Tree model (structure and parameter learning):

$$p_{Tree}(\mathbf{x}) = \prod_{i=1}^n p(x_i \mid pa(x_i))$$



EDAs for the H-P model

Probabilistic models used

- Mixture of trees (structure and parameter learning):

$$p_{MT}(\mathbf{x}) = \sum_{j=1}^m \lambda_j p_{Tree}^j(\mathbf{x})$$

con $\lambda_j > 0, j = 1, \dots, m, \sum_{j=1}^m \lambda_j = 1$



EDAs for the H-P model

Experimental results in 2-d

<i>inst.</i>	<i>BestEDA</i> $H(\mathbf{x})$	<i>GA</i> $H(\mathbf{x})$	<i>MMA</i> $H(\mathbf{x})$	<i>ACO</i> $H(\mathbf{x})$	<i>NewACO</i> $H(\mathbf{x})$	<i>PERM</i> $H(\mathbf{x})$
s1(20)	-9	-9	-9	-9	-9	-9
s2(24)	-9	-9	-9	-9	-9	-9
s3(25)	-8	-8	-8	-8	-8	-8
s4(36)	-14	-14	-14	-14	-14	-14
s5(48)	-23	-22	-22	-23	-23	-23
s6(50)	-21	-21		-21	-21	-21
s7(60)	-35	-34		-34	-36	-36
s8(64)	-42	-37		-32	-42	-38
s9(85)	-52				-51	-53
s10(100)	-47				-47	-50
s11(100)	-48				-47	-48

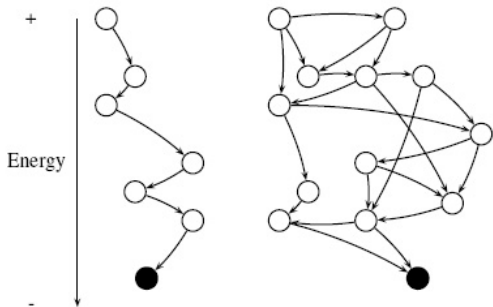
EDAs for the H-P model

Experimental results in 3-d

	hybrid GA		MK-EDA ₂		TreeEDA		MT-EDA ₄	
	$H(\mathbf{x})$	<i>mean</i>	$H(\mathbf{x})$	<i>mean</i>	$H(\mathbf{x})$	<i>mean</i>	$H(\mathbf{x})$	<i>mean</i>
s1	-11	-10,5	-11	-10,8	-11	-10,6	-11	-10,8
s2	-13	-11,2	-13	-12,0	-13	-11,3	-13	-11,8
s3	-9	-8,5	-9	-8,9	-9	-8,9	-9	-9,0
s4	-18	-15,7	-18	-16,4	-18	-16,2	-18	-16,5
s5	-28	-24,6	-29	-27,2	-29	-26,8	-29	-27,0
s6	-26	-23,0	-29	-25,7	-31	-25,9	-28	-25,7
s7	-49	-41,1	-49	-46,3	-49	-43,7	-48	-42,0
s8	-46	-40,4	-52	-46,7	-49	-43,7	-50	-45,6



EDAs as a model for protein folding



- Classical and new approaches to protein folding
- We postulate that EDAs can be considered as a model of protein folding in the new view

EDAs as a model of protein folding

General considerations

- EDAs model: At each step t the probability of being in a particular folded structure is given by the probabilistic model
- Similarities between both models:
 - Both models, define a sampling of the space of configurations
 - The probability of sampling a configuration depends on the quality of its energy function
 - Both entities tend to preserve local favorable conformational features through successive generations (time steps)



EDAs as a model of protein folding

General considerations

- EDAs model: At each step t the probability of being in a particular folded structure is given by the probabilistic model
- Similarities between both models:
 - Both models, define a sampling of the space of configurations
 - The probability of sampling a configuration depends on the quality of its energy function
 - Both entities tend to preserve local favorable conformational features through successive generations (time steps)



EDAs as a model of protein folding

General considerations

- EDAs model: At each step t the probability of being in a particular folded structure is given by the probabilistic model
- Similarities between both models:
 - Both models, define a sampling of the space of configurations
 - The probability of sampling a configuration depends on the quality of its energy function
 - Both entities tend to preserve local favorable conformational features through successive generations (time steps)



EDAs as a model of protein folding

General considerations

- EDAs model: At each step t the probability of being in a particular folded structure is given by the probabilistic model
- Similarities between both models:
 - Both models, define a sampling of the space of configurations
 - The probability of sampling a configuration depends on the quality of its energy function
 - Both entities tend to preserve local favorable conformational features through successive generations (time steps)



EDAs as a model of protein folding

General considerations

- EDAs model: At each step t the probability of being in a particular folded structure is given by the probabilistic model
- Similarities between both models:
 - Both models, define a sampling of the space of configurations
 - The probability of sampling a configuration depends on the quality of its energy function
 - Both entities tend to preserve local favorable conformational features through successive generations (time steps)



EDAs as a model of protein folding

General considerations

- EDAs model: At each step t the probability of being in a particular folded structure is given by the probabilistic model
- Similarities between both models:
 - Both models, define a sampling of the space of configurations
 - The probability of sampling a configuration depends on the quality of its energy function
 - Both entities tend to preserve local favorable conformational features through successive generations (time steps)



EDAs as a model of protein folding

New view of protein folding

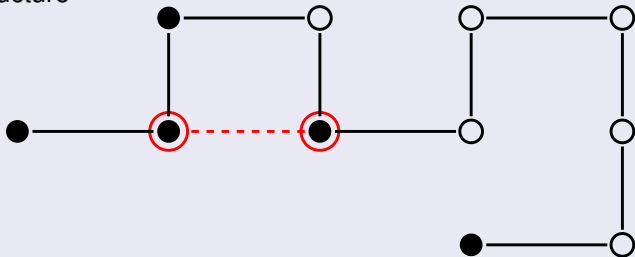
- Several parameters are used to describe a protein and the folding degree:
 - **Contact order**: Average sequence separation between residues that make contact in the native three-dimensional structure



EDAs as a model of protein folding

New view of protein folding

- Several parameters are used to describe a protein and the folding degree:
 - **Contact order**: Average sequence separation between residues that make contact in the native three-dimensional structure



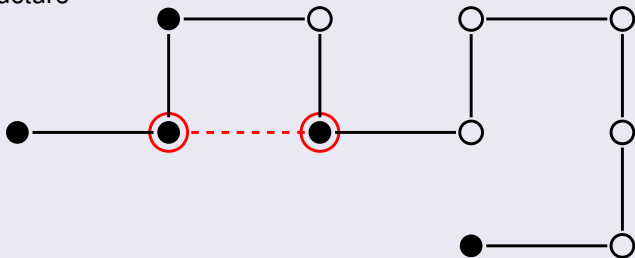
Contact Order=



EDAs as a model of protein folding

New view of protein folding

- Several parameters are used to describe a protein and the folding degree:
 - **Contact order**: Average sequence separation between residues that make contact in the native three-dimensional structure



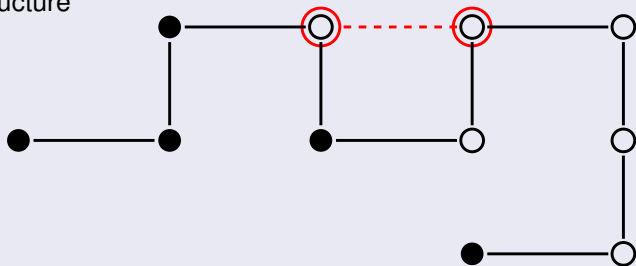
Contact Order= 3



EDAs as a model of protein folding

New view of protein folding

- Several parameters are used to describe a protein and the folding degree:
 - **Contact order**: Average sequence separation between residues that make contact in the native three-dimensional structure



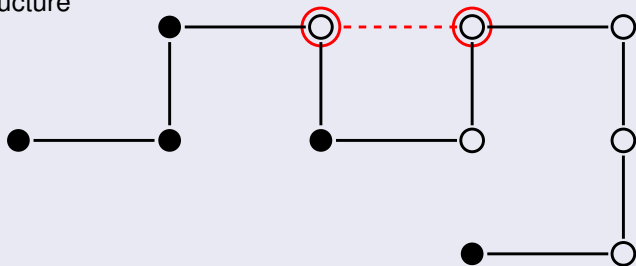
Contact Order= 3



EDAs as a model of protein folding

New view of protein folding

- Several parameters are used to describe a protein and the folding degree:
 - **Contact order**: Average sequence separation between residues that make contact in the native three-dimensional structure



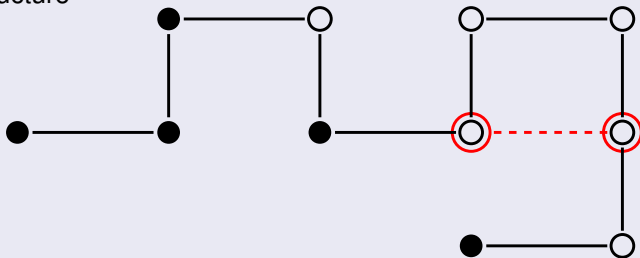
Contact Order = 3 + 3



EDAs as a model of protein folding

New view of protein folding

- Several parameters are used to describe a protein and the folding degree:
 - **Contact order**: Average sequence separation between residues that make contact in the native three-dimensional structure



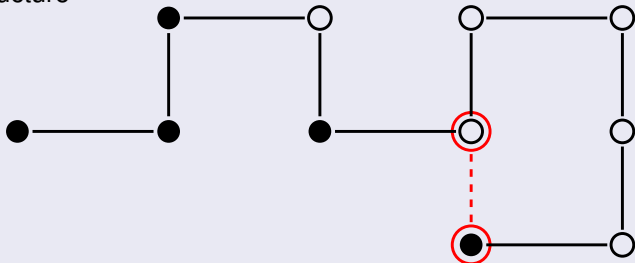
Contact Order = 3 + 3 + 3



EDAs as a model of protein folding

New view of protein folding

- Several parameters are used to describe a protein and the folding degree:
 - **Contact order**: Average sequence separation between residues that make contact in the native three-dimensional structure



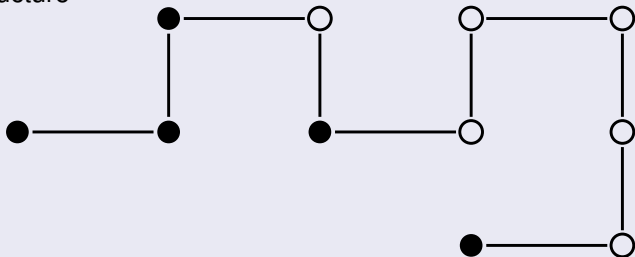
$$\text{Contact Order} = 3 + 3 + 3 + 5$$



EDAs as a model of protein folding

New view of protein folding

- Several parameters are used to describe a protein and the folding degree:
 - **Contact order**: Average sequence separation between residues that make contact in the native three-dimensional structure



$$\text{Contact Order} = \frac{3+3+3+5}{4} = 3.5$$



EDAs as a model of protein folding

New view of protein folding

- Several parameters are used to describe a protein and the folding degree:
 - **Contact order**: Average sequence separation between residues that make contact in the native three-dimensional structure
 - **Folding rate**: Amount of time the protein takes to fold



EDAs as a model of protein folding

New view of protein folding

- Several parameters are used to describe a protein and the folding degree:
 - **Contact order**: Average sequence separation between residues that make contact in the native three-dimensional structure
 - **Folding rate**: Amount of time the protein takes to fold
 - **Fraction of native contacts** (in the current folding)



EDAs as a model of protein folding

New view of protein folding

- Facts commonly accepted and explained in the new view of protein folding:
 - Folding rates of small proteins correlate with their contact order: small contact order means small folding rate



EDAs as a model of protein folding

New view of protein folding

- Facts commonly accepted and explained in the new view of protein folding:
 - Folding rates of small proteins correlate with their contact order: small contact order means small folding rate



EDAs as a model of protein folding

Experiments

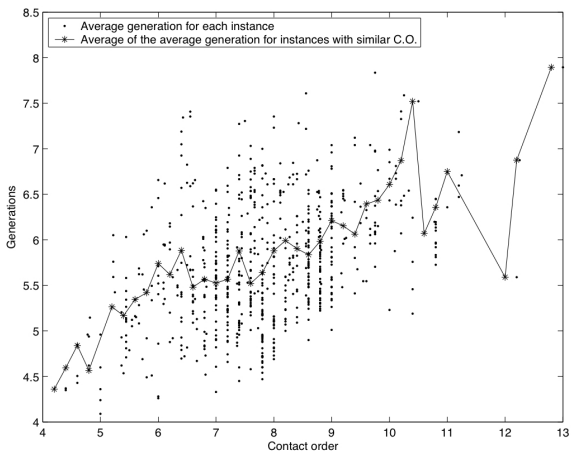
- The EDA used is MK-EDA₂ with probabilistic model:

$$p_{MK}(\mathbf{x}) = p(x_1, x_2, x_3) \prod_{i=4}^n p(x_i \mid x_{i-1}, x_{i-2})$$

- Experiments are carried out with 15545 instances of the functional model
- 100 experiments are performed with each sequence



EDAs as a model of protein folding



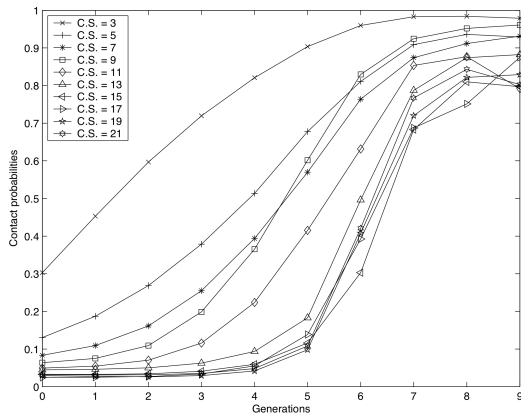
EDAs as a model of protein folding

New View of Protein Folding

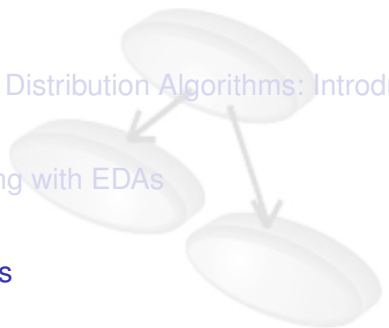
- Facts commonly accepted and explained in the new view of protein folding:
 - Folding rates of small proteins correlate with their contact order: small contact order means small folding rate
 - Local interactions are more likely to form early in folding than non-local interactions



EDAs as a model of protein folding



Outline of the presentation

- 1 Estimation of Distribution Algorithms: Introduction
 - 2 Protein Folding with EDAs
 - 3 Miscellaneous**
 - 4 Conclusions
- 

Parallel EDAs

- The structure of EDAs are very suitable for parallelization
- Two main approaches:
 - Parallelization maintaining the whole behavior of the algorithm
 - Island models: migration of models, different probabilistic models at each island

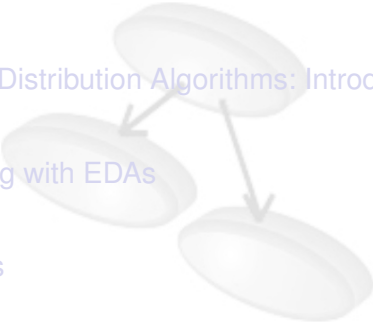


More stuff

- EDAs in multimodal problems: clustering methods, probabilistic model for clustering
- EDAs in multiobjective problems
- Memetic EDAs
- Incorporation of a priori information of the function in EDAs without fixed probabilistic model



Outline of the presentation

- 
- 1 Estimation of Distribution Algorithms: Introduction
 - 2 Protein Folding with EDAs
 - 3 Miscellaneous
 - 4 Conclusions**



Conclusions

- EDAs are an attractive field of research in Evolutionary Computation
- EDAs are encouraging cross-fertilization with other fields
- They are founded in mathematical basis
- Many, many things to be done



From a practical point of view

- They offer competitive alternatives for many problems
- The possibility of incorporating knowledge of the function is the key point in applications
- In the case of ADF: use algorithms with fixed probabilistic model
- In the case of no knowledge about the function: use EDAs without fixed structure

