Finding Many Stable Molecular Arrangements

Conformational Searching with Genetic Algorithms

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Outline

1. Background Information
2. The Genetic Algorithm
3. Conclusion

Background Information

The Problem

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$\Rightarrow$ We can't tell for sure if we've found the global minimum

We may need information about one or more low-energy conformations

$\Rightarrow$ Ok, let's find them all!

Possible Solutions

Many techniques are well established

method	description	implemented, e.g., in
grid-based	based on grids of selected Cartesian or internal coordinates (e.g., grids of different torsional angle values of a molecule)	CAESAR,[9] **Open Babel**,[10] **Confab**,[11] MacroModel,[12] MOE[13]
rule/knowledge-based	use known (e.g., from experiments) structural preferences of compounds	**ALFA**,[14] **CONFECT**,[15] CORINA and ROTATE,[16,17] **COSMOS**,[18,19] OMEGA[20]
population-based metaheuristic	improve candidate solutions in a guided search	**Balloon**,[21] **Cyndi**[22]
distance geometry	based on a matrix with permitted distances between pairs of atoms	**RDKit**[23]
basin-hopping[24]/ minima hopping[25]	based on moves across the PES combined with local relaxation	**ASE**,[26] **GMIN**,[27] **TINKER SCAN**[28]

[a]Names of freely available programs are highlighted in boldface.

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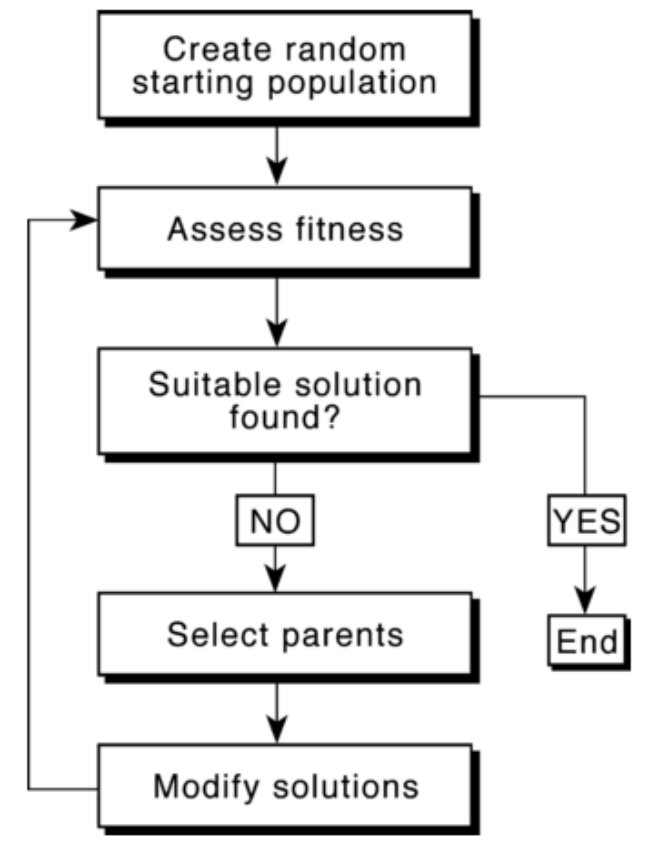
- Parallel-Scalable

The Genetic Algorithm

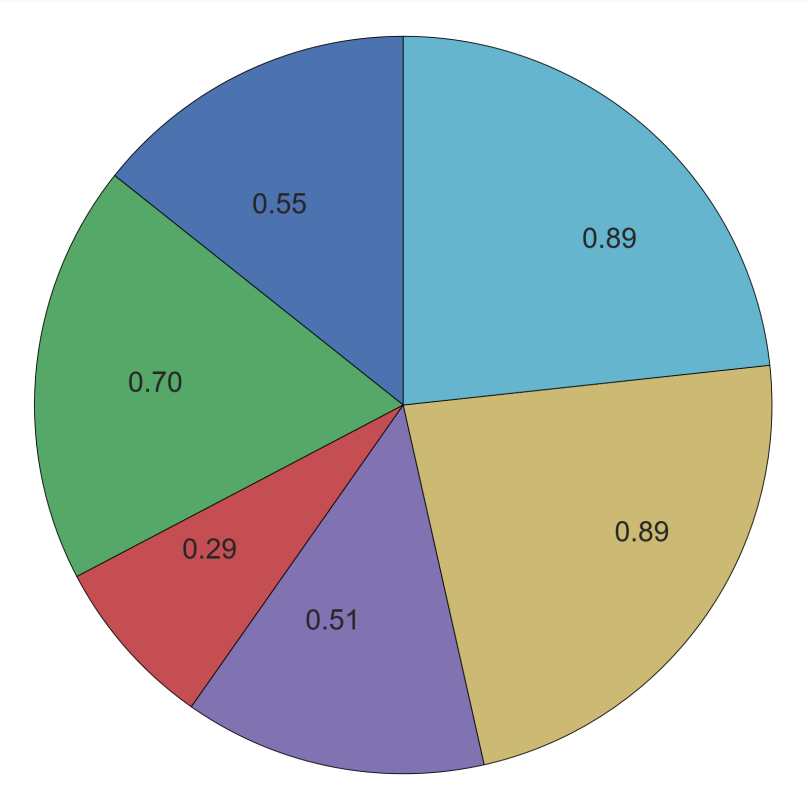
Outline

- Inspired by biological evolution
- Evolve a population over generations
- Survival of the fittest
- Requirements:
  - Represent individuals as vector
  - Fitness function
- $v = \left(x_1 \; y_1 \; z_1 \; x_2 \; y_2 \; z_2 \; \ldots \; x_N \; y_N \; z_N \right)$
- $F = \frac{E_{max} - E}{E_{max} - E_{min}}$



Selecting Parents

- Several methods are common
- Reinforce good characteristics
- Still give losers a chance
- ’Breed’ pairs of winners



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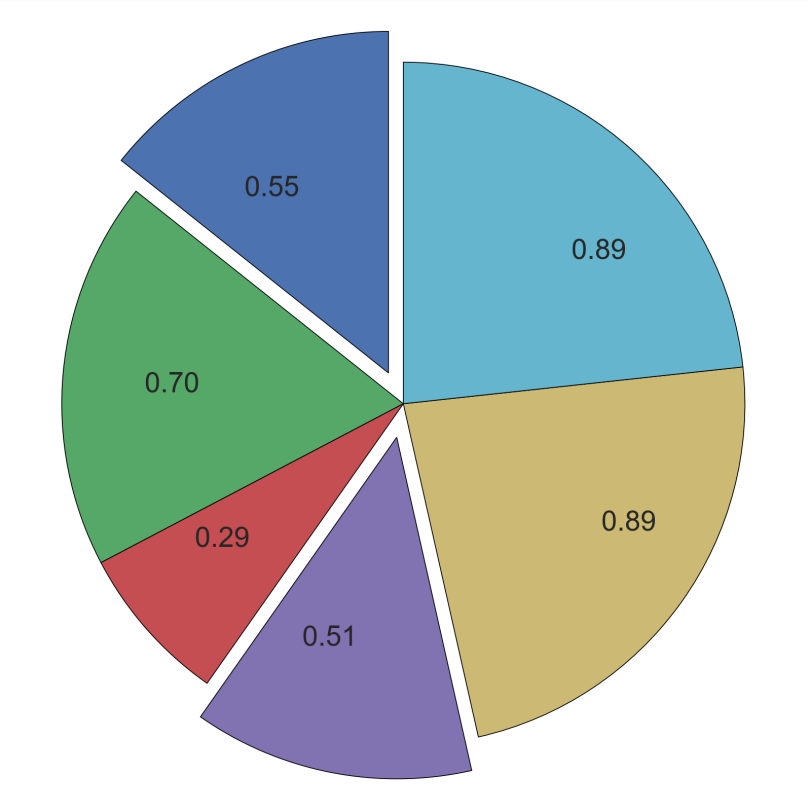
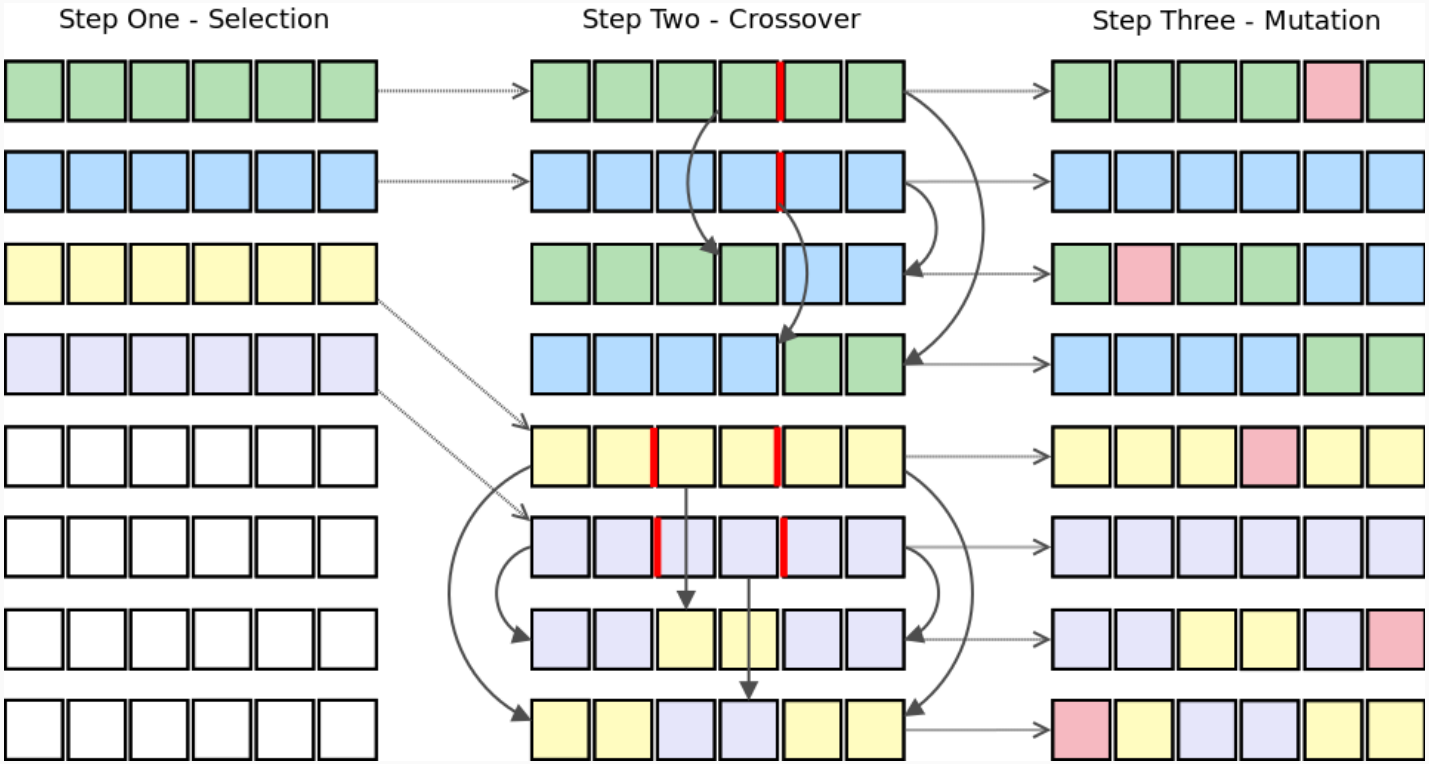


The Next Generation



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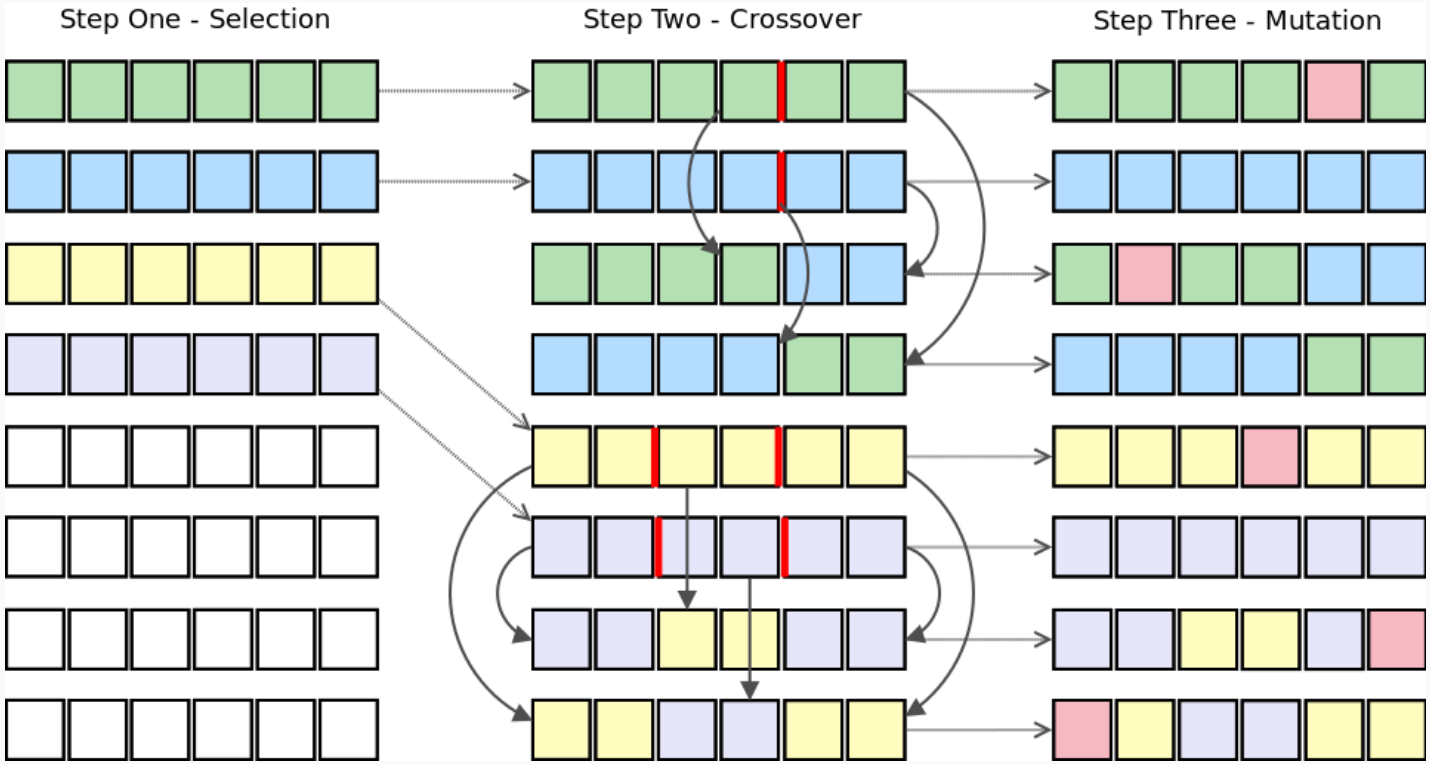

Crossover distinguishes this from Monte Carlo

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Conclusion

Questions?

Backup slides

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