Well-supported phylogenies using largest subsets of core-genes by discrete particle swarm optimization

Reem Alsrraj, Bassam AlKindy, Christophe Guyeux, Laurent Philippe, and Jean-François Couchot

June 28, 2017

Abstract

The number of complete chloroplastic genomes increases day after day, making it possible to rethink plants phylogeny at the biomolecular era. Given a set of close plants sharing in the order of one hundred of core chloroplastic genes, this article focuses on how to extract the largest subset of sequences in order to obtain the most supported species tree. Due to computational complexity, a discrete and distributed Particle Swarm Optimization (DPSO) is proposed. It is finally applied to the core genes of Rosales order.

1 Introduction

Given a set of biomolecular sequences or characters, various well-established approaches have been developed in recent years to deduce their phylogenetic relationship, encompassing distance-based matrices, Bayesian inference, or maximum likelihood [1]. Robustness aspects of the produced trees can be evaluated too, for instance through bootstrap analyses. However the relationship between this robustness, the real accuracy of the phylogenetic tree, and the amount of data used for this reconstruction is not yet completely understood. More precisely, if we consider a set of species reduced to lists of gene sequences, we have an obvious dependence between the chosen subset of sequences and the obtained tree (its topology or robustness). This dependence is usually regarded by the mean of gene trees merged into a phylogenetic network.

This article investigates the converse approach: it starts by the union of whole core genes, and tries to remove the ones that blur the phylogenetic signals. More precisely, the objective is to find the largest part of the genomes that produces a phylogenetic tree as supported as possible, reflecting by doing so the relationship of the largest part of the sequences under consideration. Due to overwhelming number of combinations to investigate, a brute force approach is a nonsense, which explains why heuristics have been considered. The proposal of this research work is
thus the application of a Discrete Particle Swarm Optimization (DPSO) that aims at finding the largest subset of core genes producing a phylogenetic tree as supported as possible. A new algorithm has been proposed and applied, in a distributive manner, to investigate the phylogeny of Rosales order.

The remainder of this article is constituted as follows. The DPSO metaheuristic is recalled in the next section. The way to apply it for resolving problematic supports in biomolecular based phylogenies is detailed in Section 3. The proposed methodology is then applied to the particular case of Rosales in Section 4. This article ends by a conclusion section, in which the article is summarized and intended future work is outlined.

2 Discrete Particle Swarm Optimization

Particle Swarm Optimization (PSO) is a stochastic optimization technique developed by Eberhart and Kennedy in 1995 [2]. PSOs have been successfully applied in function optimization, artificial neural network training, and fuzzy system control. In this metaheuristic, particles follow a very simple behavior that is to learn from the success of neighboring individuals. An emergent behavior enables individual swarm members to take benefit from the discoveries or from previous experiences of the other members that have obtained more accurate solutions. In the case of the standard binary PSO model [3], the particle position is a vector of \( N \) parameters that can be set as “yes” or “no”, “true” or “false”, “include” or “not include”, etc. (binary values). A function associates to such kind of vector a real number score according to the optimization problem. The objective is then to define a way to move the particles in the \( N \)-dimensional binary search space so that they produce the optimal binary vector w.r.t. the scoring function.

In details, each particle \( i \) is thus represented by a binary vector \( X_i \) (its position). Its length \( N \) corresponds to the dimension of the search space, that is, the number of binary parameters to investigate. An 1 in coordinate \( j \) in this vector means that the associated \( j \)-th parameter is selected. A swarm of \( n \) particles is then a list of \( n \) vectors of positions \( (X_1, X_2, \ldots, X_n) \) together with their associated velocities \( V = (V_1, V_2, \ldots, V_n) \), which are \( N \)-dimensional vectors of real numbers between 0 and 1. These latter are initially set randomly. At each iteration, the new velocity is computed as follows:

\[
V_i(t + 1) = w V_i(t) + \phi_1 (P_{i_{best}} - X_i) + \phi_2 (P_{g_{best}} - X_i)
\]

where \( w \), \( \phi_1 \), and \( \phi_2 \) are weighted parameters setting the level of each 3 trends for the particle, which are respectively to continue in its adventurous direction, to move in the direction of its own best position \( P_{i_{best}} \), or to follow the gregarious instinct to the global best known solution \( P_{g_{best}} \). Both \( P_{i_{best}} \) and \( P_{g_{best}} \) are computed according to the scoring function.

The new position of the particle is then obtained using the equation below:

\[
X_{ij}(t + 1) = \begin{cases} 1, & \text{if } r_{ij} \leq \text{Sig}(V_{ij}(t + 1)), \\ 0, & \text{otherwise}, \end{cases}
\]
where $r_{ij}$ is a chosen threshold that depends on both the particle $i$ and the parameter $j$, while the $\text{Sig}$ function operating as selection criterion is the sigmoid one \[3\], that is:

$$\text{Sig}(V_{ij}(t)) = \frac{1}{1 + e^{-V_{ij}(t)}}.$$ (3)

### 3 PSO applied to phylogeny

Let us consider, for illustration purpose, a set of chloroplast genomes of *Rosales*, which has already been analyzed in \[4\] using an hybrid genetic algorithm and Lasso test approach. We sampled 9 ingroup species and 1 outgroup (*Mollissima*), see Table 1 for details, which have been annotated using DOGMA \[5\]. We can then compute the core genome (genes present everywhere), whose size is equal to 82 genes, by using for instance the method described in \[6, 7\]. After having aligned them using MUSCLE, we can infer a phylogenetic tree with RAxML \[1\] (for a general presentation on phylogenetic tree construction see, e.g., \[8\]). If all bootstrap values are larger than 95, then we can reasonably consider that the *Rosales* phylogeny is resolved, as the largest possible number of genes has led to a very well supported tree.

| Species     | Accession  | Seq.length | Family | Genus |
|-------------|------------|------------|--------|-------|
| Chiloensis  | NC_019601  | 155603 bp  | Rosaceae | Fragaria |
| Bracteata   | NC_018766  | 129788 bp  | Rosaceae | Fragaria |
| Vesca       | NC_015206  | 155691 bp  | Rosaceae | Fragaria |
| Virginiana  | NC_019602  | 155621 bp  | Rosaceae | Fragaria |
| Kansuensis  | NC_023956  | 157736 bp  | Rosaceae | Prunus |
| Persica     | NC_014697  | 157790 bp  | Rosaceae | Prunus |
| Pyrifolia   | NC_015996  | 159922 bp  | Rosaceae | Pyrus |
| Rupicola    | NC_016921  | 156612 bp  | Rosaceae | Pentactina |
| Indica      | NC_008359  | 158484 bp  | Moraceae | Morus |
| Mollissima  | NC_014674  | 160799 bp  | Fagaceae | Castanea |

Table 1: Genomes information of *Rosales* species under consideration

In case where some branches are not well supported, we can wonder whether a few genes can be incriminated in this lack of support, for a large variety of reasons encompassing homoplasy, stochastic errors, undetected paralogy, incomplete lineage sorting, horizontal gene transfers, or even hybridization. If so, we face an optimization problem: to find the most supported tree using the largest subset of core genes. Obviously, a brute force approach investigating all possible combinations of genes is intractable ($2^N$ phylogenetic trees for $N$ core genes, with $N = 82$ for *Rosales*).

More precisely, genes of the core genome are supposed to be lexicographically ordered. Each subset $s$ of the core genome is thus associated with a unique binary word $w$ of length $n$: for each $i$, $1 \leq i \leq n$, $w_i$ is 1 if the $i$-th core gene is in $s$ and 0 otherwise. Any $n$-length binary word $w$
can be associated with its percentage \( p \) of 1’s and the lowest bootstrap \( b \) of the phylogenetic tree we obtain when considering the subset of genes associated to \( w \). Each word \( w \) is thus associated with a fitness score value \( b + p \).

Let us be back in the PSO context. The search space is then \( \{0,1\}^N \). Each node of this \( N \)-cube is associated with the set of following data: its subset of core genes, the deduced phylogenetic tree, its lowest bootstrap \( b \) and the percentage \( p \) of considered core genes, and, finally, the score \( b + p \). Notice that two close nodes of the \( N \)-cube have two close percentages of core genes. We thus have to construct two phylogenies based on close sequences, leading to a high probability to the same topology with close bootstrap. In other words, the score remains essentially unchanged when moving from a node to one of its neighbors. It allows to find optimal solutions using approaches like PSO.

Algorithm 1: PSO algorithm

```
population ← 10, maxiter ← 10
for each particle in population do
    particle[position] ← [randint(0,1) for each gene in core genome]
    particle[velocity] ← [rand(0,1) for each gene in core genome]
    particle[score] ← 0
    particle[best] ← Empty list
end for
while fitness < b + p and iter < Maxiter do
    for each particle in population do
        Calculate new_fitness
        if new_fitness > fitness then
            particle[score] ← new_fitness
            particle[best] ← particle[position]
        end if
    end for
    fitness ← max(particle[score])
    Gbest ← position[Max( Particle[score] in population )]
    for each particle in population do
        Calculate particle velocity according to Equation [1]
        Update particle position according to Equations [3] and [2]
    end for
end while
```

Initially, the \( L \) (set to 10 in our experiments) particles are randomly distributed among all the vertices (binary words) of the \( N \)-cube that have a large percentage of 1. The objective is then to move these particles in the cube, hoping that they will converge to an optimal node. At each iteration, the particle velocity is updated according to the fitness and its best position. It is influenced by constant weight factors according to Equation [1]. In this one, we have set \( c_1 = 1 \), \( c_2 = 1 \), while \( r_1, r_2 \) are random numbers between \((0.1,0.5)\), and \( w \) is the inertia weight. This
latter determines the contribution rate of a particle's previous velocity to its velocity at the current time step. To increase the number of included components in a particle, we reduced the interval of Equation (2) to [0.1, 0.5]. For instance, if the velocity $V_i$ of an element is equal to 0.511545 and $r = 0.83$, then $\text{Sig}(0.51) = 0.62$. So $r > \text{Sig}(V_i)$ and this will lead to 0 in the vector elements of the particle. By minimizing the interval we increase the probability of having $r < \text{Sig}(V_i)$, and this will lead to more 1s, which means more included elements in the particle. A large inertia weight facilitates a global search while a small inertia weight tends more to a local investigation [9]. A larger value of $w$ facilitates a complete exploration, whereas small values promote exploitation of areas. This is why Eberhart and Shi suggested to decrease $w$ over time, typically from 0.9 to 0.4, thereby gradually changing from exploration to exploitation. Finally, each particle position is updated according to Equation (2), see Algorithm 1 for further details. In this algorithm, the particle is defined by its position (a binary word) in the cube together with its velocity (a real vector).

4 Experimental results and discussions

We have implemented the proposed DPSO algorithm on the Mésocentre de calculs supercomputer facilities of the University of Franche-Comté. Investigated Rosales species are listed in Table 1. 10 swarms having a variable number of particles have been launched 10 times, with $c_1 = 1$, $c_2 = 1$, and $w$ linearly decreasing from 0.9 to 0.4. Obtained results are summarized in Table 2 that contains, for each 10 runs of each 10 swarms: the number of removed genes and the minimum bootstrap of the best tree. Remark that some bootstraps are not so far from the intended ones (larger than 95), whereas the number of removed genes are in average larger than what we desired.

7 topologies have been obtained after either convergence or maxIter iterations. Only 3 of them have occurred a representative number of times, namely the Topologies 0, 2, and 4, which are depicted in Figure 2 (see details in Table 3). These three topologies are almost well supported, except in a few branches. We can notice that the differences in these topologies are based on the sister relationship of two species named Fragaria vesca and Fragaria bracteata, and of the relation between Pentactina rupicola and Pyrus pyriformis. Due to its larger score and number of occurrences, we tend to select Topology 0 as the best representative of the Rosales phylogeny.

To further validate this choice, consel [10] software has been used on per site likelihoods of each best tree obtained using RAxML [11]. Consel ranks the trees after having computed the $p$-values of various well-known statistical tests, like the so-called approximately unbiased (au), Kishino-Hasegawa (kh), Shimodaira-Hasegawa (sh), and Weighted Shimodaira-Hasegawa (wsh) tests. Obtained results are provided in Table 4, they confirm the selection of Topology 0 as the tree reflecting the best the Rosales phylogeny.
Table 2: Best tree in each swarm

| Swarm | Removed genes | \((p + b)/2\) | b  |
|-------|---------------|---------------|----|
| 1     | 4             | 75.5          | 73 |
| 2     | 6             | 75.5          | 76 |
| 3     | 20            | 75            | 88 |
| 4     | 52            | 59.5          | 89 |
| 5     | 3             | 75.5          | 72 |
| 6     | 19            | 77.5          | 92 |
| 7     | 47            | 63.5          | 92 |
| 8     | 9             | 73.5          | 74 |
| 9     | 10            | 72.5          | 73 |
| 10    | 13            | 76.5          | 84 |

Figure 1: Average fitness of Rosales order

Table 3: Best topologies obtained from the generated trees. \(b\) is the lowest bootstrap of the best tree having this topology, while \(p\) is the number of considered genes to obtain this tree.

| Topology | Swarms       | b  | p  | Occurrences |
|----------|--------------|----|----|-------------|
| 0        | 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 | 92 | 63 | 568         |
| 1        | 1, 2, 3, 4, 5, 6, 10          | 63 | 45 | 11          |
| 2        | 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 | 76 | 67 | 55          |
| 3        | 8, 1, 2, 3, 4                 | 56 | 41 | 5           |
| 4        | 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 | 89 | 30 | 65          |
| 5        | 1, 3, 4, 5, 6                 | 71 | 33 | 9           |
| 6        | 5, 6                        | 25 | 45 | 2           |

Table 4: Consel results regarding best trees

| Rank | item | obs | au  | np  | bp  | pp  | kh  | sh  | wkh | wsh  |
|------|------|-----|-----|-----|-----|-----|-----|-----|-----|------|
| 1    | 0    | -1.4| 0.774| 0.436| 0.433| 0.768| 0.728| 0.89 | 0.672| 0.907|
| 2    | 4    | 1.4 | 0.267| 0.255| 0.249| 0.194| 0.272| 0.525| 0.272| 0.439|
| 3    | 2    | 3   | 0.364| 0.312| 0.317| 0.037| 0.328| 0.389| 0.328| 0.383|

5 Conclusion

A discrete particle swarm optimization algorithm has been proposed in this article, which focuses on the problem to extract the largest subset of core sequences with a view to obtain the most supported phylogenetic tree. This heuristic approach has then been applied to the 82 core genes of the Rosales order.

References

[1] Alexandros Stamatakis. Raxml version 8: A tool for phylogenetic analysis and post-analysis of large phylogenes. *Bioinformatics*, 2014.
[2] James Kennedy and R.C. Eberhart. Particle swarm optimization. In Proceedings of IEEE International Conference on Neural Networks, volume 4, pages 1942–1948, 1995.

[3] Mojtaba Ahmadieh Khanesar, Hassan Tavakoli, Mohammad Teshnehlab, and Mahdi Aliyari Shoorehdeli. Novel binary particle swarm

![Diagram](image)

Figure 2: The best obtained topologies for *Rosales* order
optimization. www.intechopen.com, (978-953-7619-48-0):11, 2009.

[4] Bassam AlKindy, Christophe Guyeux, Jean-François Couchot, Michel Salomon, Christian Parisod, and Jacques M. Bahi. Hybrid genetic algorithm and lasso test approach for inferring well supported phylogenetic trees based on subsets of chloroplastic core genes. *International Conference on Algorithms for Computational Biology, Al-CoB 2015*, pages 1–15, 2015.

[5] Stacia K. Wyman, Robert K. Jansen, and Jeffrey L. Boore. Automatic annotation of organellar genomes with dogma. *BIOINFORMATICS, Oxford Press*, 20(172004):3252–3255, 2004.

[6] Bassam Alkindy, Jean-François Couchot, Christophe Guyeux, Arnaud Mouly, Michel Salomon, and Jacques M. Bahi. Finding the core-genes of chloroplasts. *Journal of Bioscience, Biochemistry, and Bioinformatics*, 4(5):357–364, 2014.

[7] Bassam Alkindy, Christophe Guyeux, Jean-François Couchot, Michel Salomon, and Jacques Bahi. Gene similarity-based approaches for determining core-genes of chloroplasts. November 2014. Short paper.

[8] Jeffrey Rizzo and Eric C. Rouchka. Review of phylogenetic tree construction. *University of Louisville Bioinformatics Laboratory Technical Report Series*, (TR-ULBL-2007-01):2–7, 2007.

[9] Tim Blackwell Riccardo Poli, James Kennedy. Particle swarm optimization. *Springer Science + Business Media*, 1(10.1007/s11721-007-0002-0):33–57, 2007.

[10] Hidetoshi Shimodaira and Masami Hasegawa. Consel: for assessing the confidence of phylogenetic tree selection. *Bioinformatics*, 17(12):1246–1247, 2001.