Universidad Nacional de San Agustín

Artificial Intelligence

Multiple Sequence Alignment using Particle Swarm Optimization

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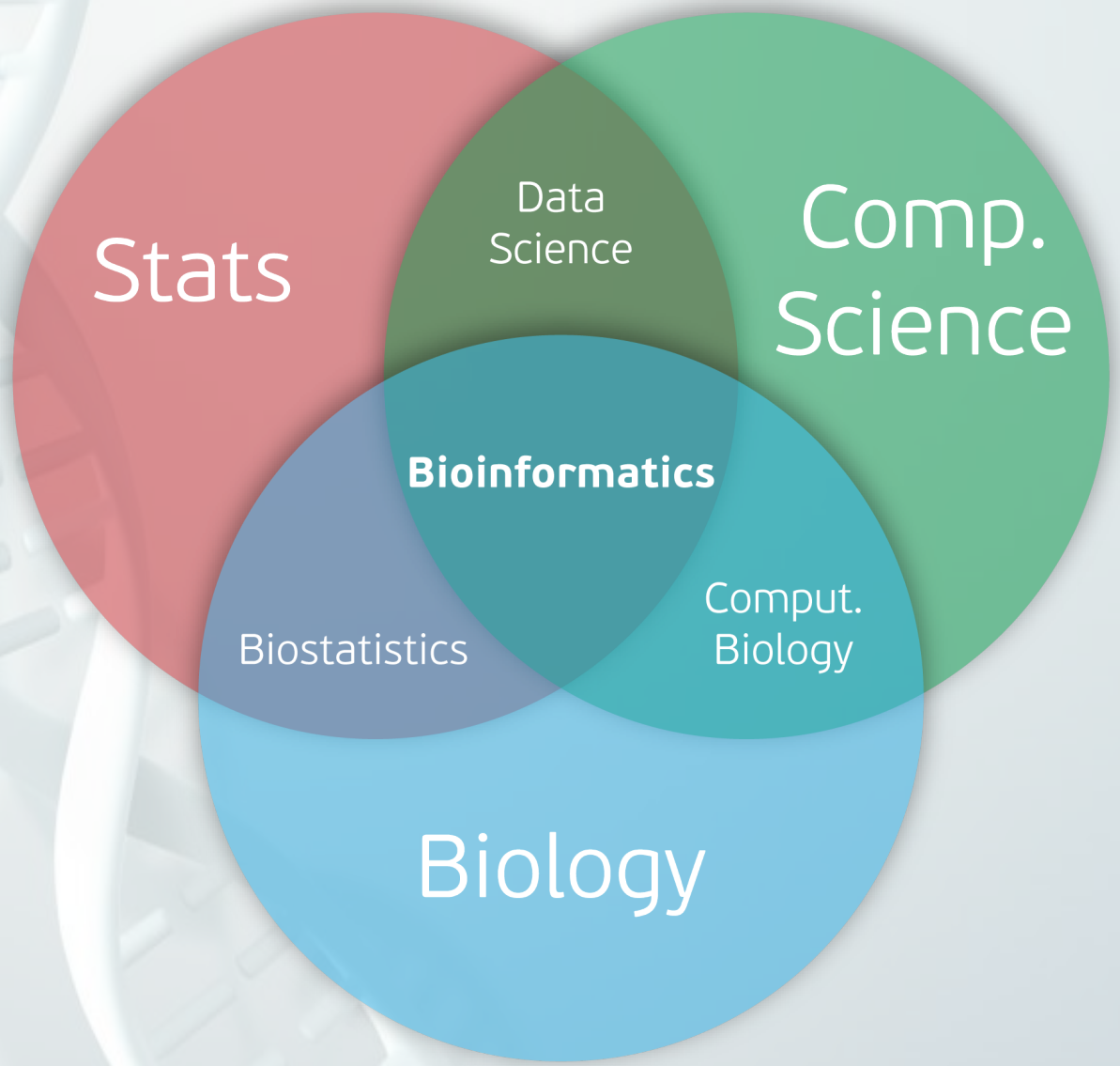
2021

Content

Overview

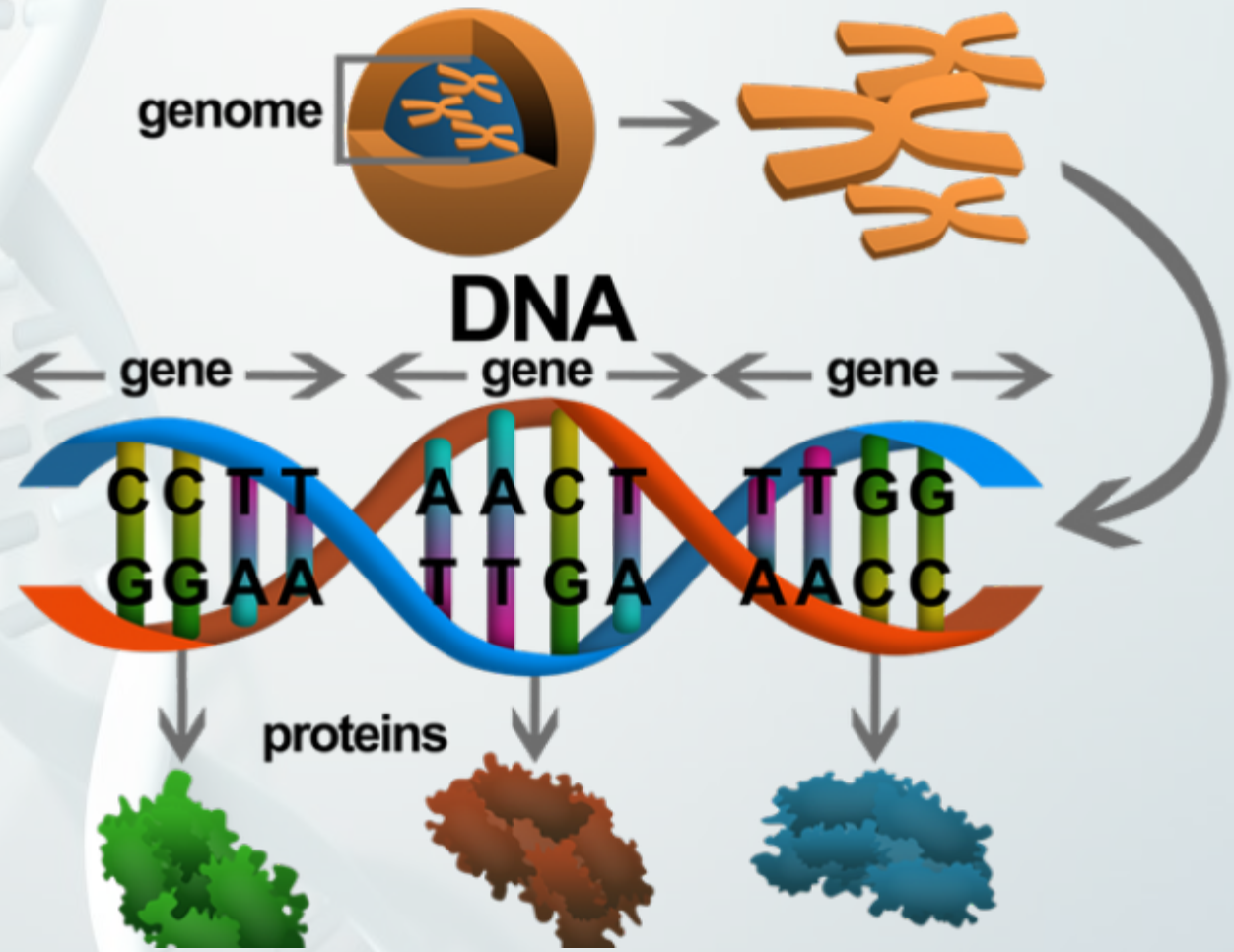
Bioinformatics



According to Luscombe et al.: **Bioinformatics** involves the technology that uses computers for storage, retrieval, manipulation, and distribution of information related to biological macromolecules such as DNA, RNA, and proteins [1].

Bioinformatics is limited to sequence, structural, and functional analysis of genes and genomes and their corresponding products and is often considered **Computational molecular biology**. However, **Computational Biology** encompasses all biological areas that involve computation [2].

Bioinformatics



Bioinformatics

Example of DNA sequence


```
>J01859.1 Escherichia coli 16S ribosomal RNA, complete sequence
AAATTGAAGAGTTTGATCATGGCTCAGATTGAACGCTGGCGGCAGGCCTAACACATGCAAGTCGAACGGT
AACAGGAAGAAGCTTGCTCTTTGCTGACGAGTGGCGGACGGGTGAGTAATGTCTGGGAAACTGCCTGATG
GAGGGGGATAACTACTGGAAACGGTAGCTAATACCGCATAACGTCGCAAGACCAAAGAGGGGGACCTTCG
GGCCTCTTGCCATCGGATGTGCCCAGATGGGATTAGCTAGTAGGTGGGGTAACGGCTCACCTAGGCGACG
ATCCCTAGCTGGTCTGAGAGGATGACCAGCCACACTGGAACTGAGACACGGTCCAGACTCCTACGGGAGG
CAGCAGTGGGGAATATTGCACAATGGGCGCAAGCCTGATGCAGCCATGCCGCGTGTATGAAGAAGGCCTT
CGGGTTGTAAAGTACTTTCAGCGGGGAGGAAGGGAGTAAAGTTAATACCTTTGCTCATTGACGTTACCCG
CAGAAGAAGCACCGGCTAACTCCGTGCCAGCAGCCGCGGTAATACGGAGGGTGCAAGCGTTAATCGGAAT
TACTGGGCGTAAAGCGCACGCAGGCGGTTTGTTAAGTCAGATGTGAAATCCCCGGGCTCAACCTGGGAAC
TGCATCTGATACTGGCAAGCTTGAGTCTCGTAGAGGGGGGTAGAATTCCAGGTGTAGCGGTGAAATGCGT
AGAGATCTGGAGGAATACCGGTGGCGAAGGCGGCCCCCTGGACGAAGACTGACGCTCAGGTGCGAAAGCG
TGGGGAGCAAACAGGATTAGATACCCTGGTAGTCCACGCCGTAAACGATGTCGACTTGGAGGTTGTGCCC
TTGAGGCGTGGCTTCCGGAGCTAACGCGTTAAGTCGACCGCCTGGGGAGTACGGCCGCAAGGTTAAAACT
CAAATGAATTGACGGGGGCCCGCACAAGCGGTGGAGCATGTGGTTTAATTCGATGCAACGCGAAGAACCT
TACCTGGTCTTGACATCCACGGAAGTTTTCAGAGATGAGAATGTGCCTTCGGGAACCGTGAGACAGGTGC
TGCATGGCTGTCGTCAGCTCGTGTTGTGAAATGTTGGGTTAAGTCCCGCAACGAGCGCAACCCTTATCCT
TTGTTGCCAGCGGTCCGGCCGGGAACTCAAAGGAGACTGCCAGTGATAAACTGGAGGAAGGTGGGGATGA
CGTCAAGTCATCATGGCCCTTACGACCAGGGCTACACACGTGCTACAATGGCGCATACAAAGAGAAGCGA
CCTCGCGAGAGCAAGCGGACCTCATAAAGTGCGTCGTAGTCCGGATTGGAGTCTGCAACTCGACTCCATG
AAGTCGGAATCGCTAGTAATCGTGGATCAGAATGCCACGGTGAATACGTTCCCGGGCCTTGTACACACCG
CCCGTCACACCATGGGAGTGGGTTGCAAAAGAAGTAGGTAGCTTAACCTTCGGGAGGGCGCTTACCACTT
TGTGATTCATGACTGGGGTGAAGTCGTAACAAGGTAACCGTAGGGGAACCTGCGGTTGGATCACCTCCTT
```

Figure: 16S ribosomal DNA of Escherichia coli with FASTA Format.

Overview

Problem

Sequence alignment


```
No alignment

 CGATGCTAGCGTATCGTAGTCTATCGTAC
               |     ||
 ACGATGCTAGCGTTTCGTATCATCGTA

Alignned

 -CGATGCTAGCGTATCGTAGTCTATCGTAC
  |||||||||||| |||||||||||||||
 ACGATGCTAGCGTTTCGTA-TC-ATCGTA-
```

Figure: No alignment versus alignment.

In the alignment process there could be substitutions, changes of residues and gaps. Gaps could cause by insertions or deletions.

Problem

Sequence alignment


```
No gaps (10 matches)

 a:  ATATTGCTACGTATATCAT
         ||||||||||
 b: ATATATGCTACGTATCAT

With one gap (14 matches)

 a: ATAT-TGCTACGTATATCAT
    |||| ||||||||||
 b: ATATATGCTACGTATCAT

With two gaps (16 matches)
 a: ATAT-TGCTACGTATATCAT
    |||| |||||||  ||||||
 b: ATATATGCTACG--TATCAT
```

Figure: Alignment and gaps.

Algorithms should take into account the possibility of introducing gaps. **Several alignments can be constructed** between two sequences.

Problem

Multiple Sequence alignment


```
RLA0_METVA --MIDAKSEHKIAPWKIEEVNALKELLKSANVIALIDMMEVPAVQLQEIRDK
RLA0_METJA ---METKVKAHVAPWKIEEVKTLKGLIKSKPVVAIVDMMDVPAPQLQEIRDK
RLA0_PYRAB --------MAHVAEWKKKEVEELANLIKSYPVIALVDVSSMPAYPLSQMRRL
RLA0_PYRHO --------MAHVAEWKKKEVEELAKLIKSYPVIALVDVSSMPAYPLSQMRRL
RLA0_PYRFU --------MAHVAEWKKKEVEELANLIKSYPVVALVDVSSMPAYPLSQMRRL
RLA0_PYRKO --------MAHVAEWKKKEVEELANIIKSYPVIALVDVAGVPAYPLSKMRDK
RLA0_HALMA MSAESERKTETIPEWKQEEVDAIVEMIESYESVGVVNIAGIPSRQLQDMRRD
RLA0_HALVO MSESEVRQTEVIPQWKREEVDELVDFIESYESVGVVGVAGIPSRQLQSMRRE
RLA0_HALSA MSAEEQRTTEEVPEWKRQEVAELVDLLETYDSVGVVNVTGIPSKQLQDMRRG
RLA0_THEAC --------MKEVSQQKKELVNEITQRIKASRSVAIVDTAGIRTRQIQDIRGK
RLA0_THEVO --------MRKINPKKKEIVSELAQDITKSKAVAIVDIKGVRTRQMQDIRAK
RLA0_PICTO --------MTEPAQWKIDFVKNLENEINSRKVAAIVSIKGLRNNEFQKIRNS
```

Figure: Example of Multiple Sequence Alignment (MSA) in amino acid sequences.

Overview

Objective

Propose Particle Swarn Optimization (PSO) to solve the Multiple Sequence Alignment (MSA) [3].

Overview

Proposal
Particle definition

	W	G	K	V	-	-	N	V	D
Leader:	W	D	K	V	-	-	N	-	-
	S	-	K	V	G	G	N	-	-
	W	G	K	-	-	V	N	V	D
Particle:	-	W	D	K	-	-	-	V	N
	S	-	K	V	G	G	-	N	-

	5	6		
Leader:	5	6	8	9
	2	8	9	
	4	5		
Particle:	1	5	6	7
	2	7	9	

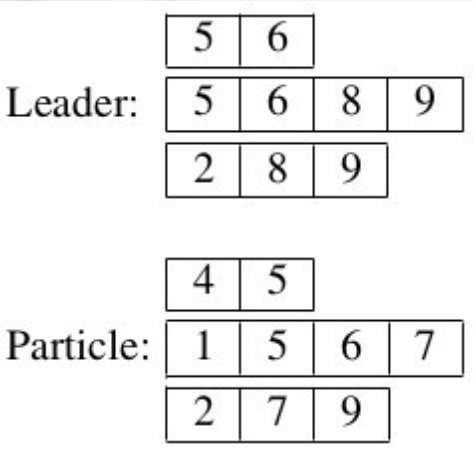
Figure: Example of particle representation.

Overview

Proposal
Movements

$$distance = \frac{matchingGaps}{totalGaps} \tag{1}$$

$$crossPoint = rand(1, distance * length) \tag{2}$$



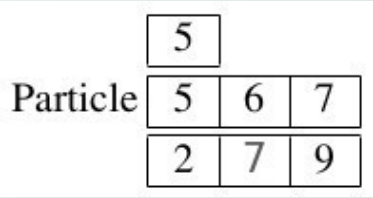


Figure: Example of particle movement.

Overview

Proposal
Objective function


```
ACGTCTGATACGCCGTATAGTCTATCT
     ||||| |||    || ||||||||
----CTGATTCGC---ATCGTCTATCT
```

Matches: 18 × (+1)

Mismatches: 2 × 0

Gaps: 7 × (– 1)

Score = +11

Figure: Example of score in sequence alignment.

Overview

Proposal
Mutations

The mutation operator inserts a gap in a random position in a random sequence inside a particle.

Overview

Experiments
Datasets

Table: Dataset used in the experiments.

Dataset	min. length	max. length	num. bases
S6	8	17801	153
S7	457	457	8
S8	7	10	5

Experiments

Datasets S8

1	A	T	G	C	A	A	G			
2	T	A	A	G	T	C	A	A	G	T
3	A	T	G	C	A	A	C	T		
4	T	A	A	G	T	C	A	T	A	
5	A	T	G	G	A	T	T	C		

Figure: Sequences of S8 dataset.

Experiments
Params

Table: Params used in the experiments.

Param	Value
Iterations	30
Num. of particles	25
Mutation probability	0.2
Gaps	30%
Num. of experiments test	10

Overview

Results
PSO vs CLUSTALW

Table: Score comparison of PSO and CLUSTALW.

Dataset	**PSO-mutation**	**PSO**	**CLUSTALW**
S6	12678	10012	18045
S7	11105	9054	12564
S8	32	28	49

Results
PSO vs CLUSTALW


```
1  -ATG-C-AAG
2  TAAGTCAAGT
3  -A-TGCAACT
4  TAAGTCAT-A
5  -ATGGATTC-
```

```
1  ATGCAAG----
2  -TAAGTCAAGT
3  ATGCAACT---
4  -TAAGTCATA-
5  ATGGATTC---
```

Figure: Left: S8 alignment with PSO-mutation. Right: S8 alignment with CLUSTALW.

Results
PSO


```
1 --ACTTCAGGACGGGGACAACAGTTGGAAACGACTGCTAATACCCGATGTGCCGCAAGGTGAAACCTAATTGGCCTGGAGAAGAGCTTGCGTCTGATTAGCTAGT
2 ACTTCAGGACGGGGACAACAGTTGGAAACGA-CTGCTAATACCCGATGTGCCGCAAGGTGAAACCTAATTGGCCTGAAGAAGAGCTTGCGTCTGATTAGCTAGT-
3 ACTTCAGGACGGGGACA-ACAGTTGGAA-ACGACTGCTAATACCCGATGTGCCGCAAGGTGAAACCTAATTGGCCTGAAGAAGAGCTTGCGTCTGATTAGCTAGT
4 ACTTC-AGGACGGGGACAACAGTTGGAAACGACTGCTAATACCCGATGTGCCGCAAGGTGAAACCTAATTGGCCTGGAGAAGAGCT-TGCGTCTGATTAGCT-AG
5 -ACTTCAGGACGGGGACAACAGTTGGAAACGACTGCTAATA-CCCGATGTGCCGAAAGGTGAAACCTAATTGGCCTGAAGAAGAGCTTGCGTCTGATTAGCTAGT
6 -ACTTCAGGACGGGGACAACAGTTGGAAACGACTGCTAATACCCGATGTGCCGAAAGGTGAAACCTAATTGGCCTGAAGAAGAGCTTGCGTCTGATTAGCTAGTT
7 --ACTTCAGGAC-GGGGACAACAGTTGGAAACGACTGCTAATACCCGATGTGCCGCGAGGTGAAACCTAATTGGCCTGAAGAAGAGCTTGCGTCTGATTAGCTAG
8 ACTTCAGGACGGGGACAA-CAGTTGGAAACGACTGCTAATACCCGATGTGCCGCAAGGTGAAACCTAATTGGCCTGAAGAAGAGCTTGCGTCTGATTAGCTAGTT
```

Figure: Extract of S7 alignment using PSO-mutation

Conclusions

This thesis proposed the use of PSO to solve the MSA problem. The author used a set of datasets from NCBI.

The author proposed a mutation operator to avoid local solutions. This operator just inserts a gap.

The score of PSO was accepatble and very similar to CLUSTALW. Currently, there is more research on this topic.

References I

[1] N. M. Luscombe, D. Greenbaum, and M. Gerstein, “What is bioinformatics? a proposed definition and overview of the field,” *Methods of information in medicine*, vol. 40, no. 04, pp. 346–358, 2001.

[2] J. Xiong, *Essential bioinformatics*. Cambridge University Press, 2006.

[3] F. B. R. Zablocki *et al.*, “Multiple sequence alignment using particle swarm optimization,” Ph.D. dissertation, University of Pretoria, 2009.