

Accelerating Biomolecular Nuclear Magnetic Resonance Assignment with A*

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Overview

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Motivation

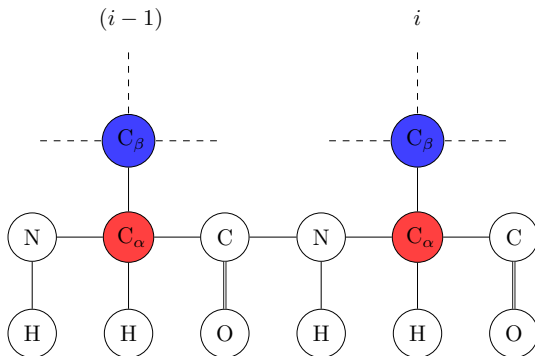
- Nuclear Magnetic Resonance Spectroscopy
 - Gain knowledge about protein structure
 - Study how mutations lead to diseases
- Problems
 - Generates large amounts of data
 - Data analysis is slow and error prone
- Goal
 - Automate the assignment process
 - Decrease human error
 - Increase productivity

Nuclear Magnetic Resonance (NMR)

- Used to obtain structural information
 - Chemical shift values
- HNCACB experiment
 - Generates C_α and C_β residue i and $i - 1$
- CBCA(CO) NH experiment
 - Generates C_α and C_β for residue i
 - Confirms residue data

Chemical Shift Values

HNCACB



Timeline

Protein
Production
at least 5 days

Data Assignment
20 days to 9 months

NMR
Experiments
1-2 days

[1]

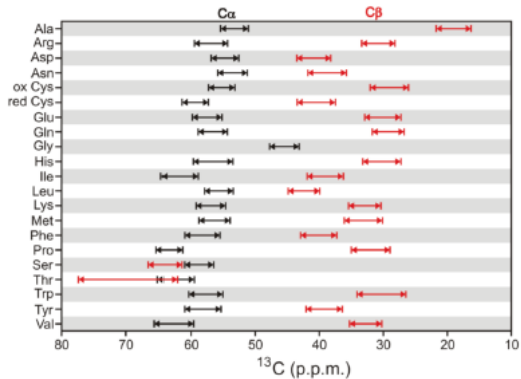
Manual Methods

- Most time consuming part
- Prone to human error
- Missing and ambiguous data forces chunks to be skipped

Initialization

- Expected amino acid sequence
 - Converted to expected chemical shift values
 - Stored as the reference protein chain
- NMR experiment's chemical shift data
 - C_α and C_β for residue i and $i - 1$
 - Stored in a tile
- Missing data
 - Place holder tile generation
- Grouping

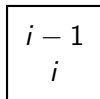
Grouping



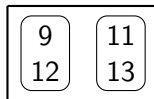
[2]

Starting the assignment

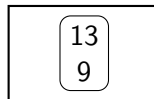
Tiles to assign:



Group 1



Group 2



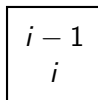
**Reference
Protein Chain**

Nodes

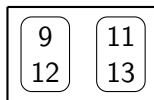
Chemical Shift	Group
13.5	1
9.5	2
11.4	1

Starting the assignment

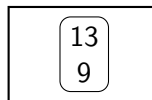
Tiles to assign:



Group 1



Group 2



Reference
Protein Chain

Nodes

Chemical Shift	Group
13.5	1
9.5	2
11.4	1



Cost Calculation

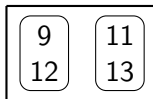
- Accuracy matching the protein chain residue
- Accuracy matching the tile above current tile
- Cost of all tiles place before current tile

Generating child nodes

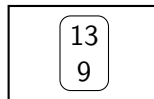
Tiles to assign:



Group 1



Group 2



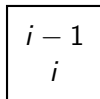
Reference
Protein Chain

Nodes

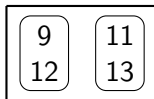
Chemical Shift	Group		
13.5	1	<div>9 12</div> 1.5	<div>11 13</div> 0.5
9.5	2		
11.4	1		

Generating child nodes

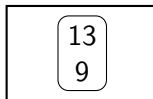
Tiles to assign:



Group 1



Group 2



Reference
Protein Chain

Nodes

Chemical Shift	Group
13.5	1
9.5	2
11.4	1



1.5



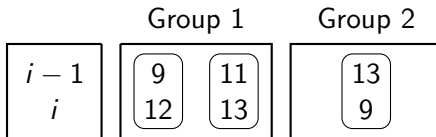
0.5



1.0

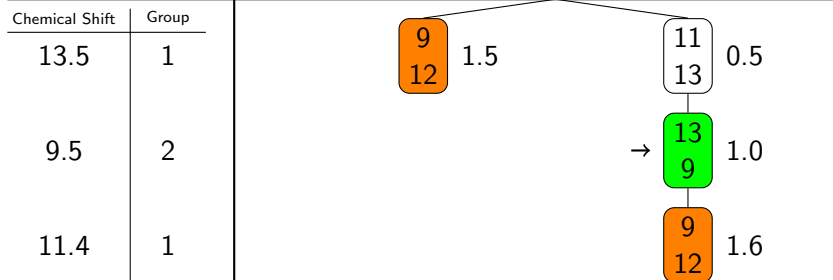
Goal State

Tiles to assign:



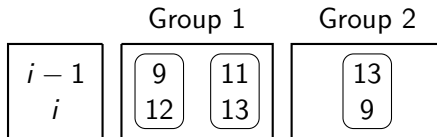
Reference
Protein Chain

Nodes



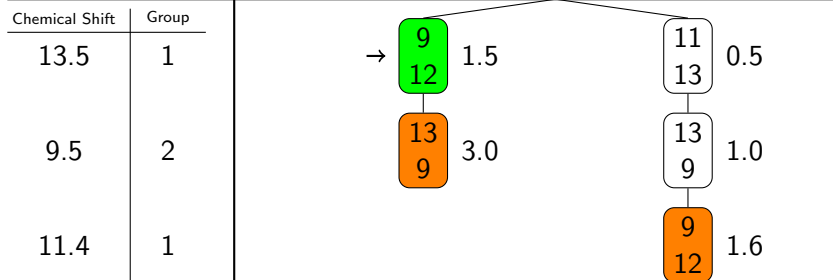
Goal State

Tiles to assign:



Reference
Protein Chain

Nodes

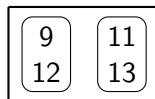


Solution State

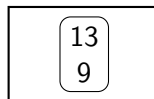
Tiles to assign:



Group 1

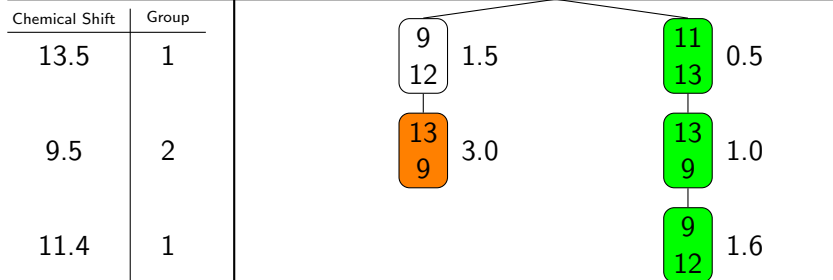


Group 2

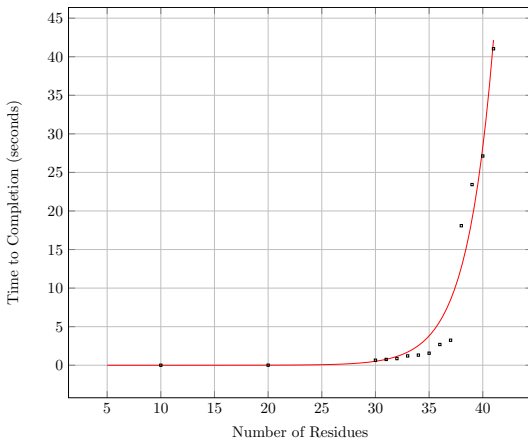


Reference
Protein Chain

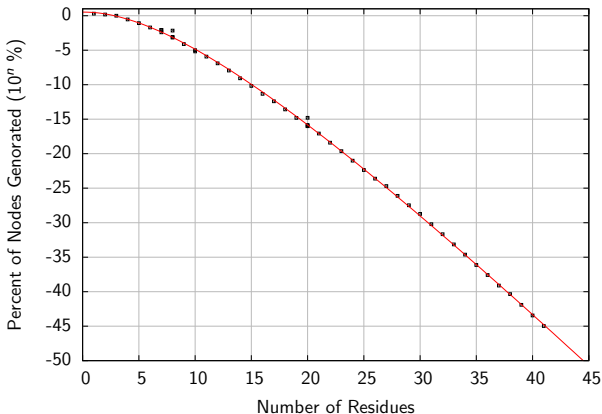
Nodes



Time of Assignment



Child Nodes Generated



Future Goals

- Parallelization
 - Decrease assignment time
 - Allow for larger data sets
- Machine learning
 - Increase accuracy of assignment
 - Optimize cost calculation

Acknowledgments

- Dr. Tim Urness (Mathematics and Computer Science)
- Dr. Adina Kilpatrick (Physics)
- Rachel Davis (research colleague)
- John Emmons (research colleague)
- Katherine Roth (research colleague)
- David Mascharka (research colleague)
- Leah Robison (research colleague)

Bibliography



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Thank You

