# Accelerating Biomolecular Nuclear Magnetic Resonance Assignment with A\*

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## Overview

- Introduction
  - Motivation
  - Nuclear Magnetic Resonance Spectroscopy
- NMR Assignment Background
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Motivation

Introduction

#### 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 Spectroscopy

Introduction

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# Nuclear Magnetic Resonance (NMR)

- Used to obtain structural information
  - Chemical shift values
- HNCACB experiment
  - Generates  $C_{\alpha}$  and  $C_{\beta}$  residue i and i-1
- CBCA(CO) NH experiment
  - Generates  $C_{\alpha}$  and  $C_{\beta}$  for residue i
  - Confirms residue data

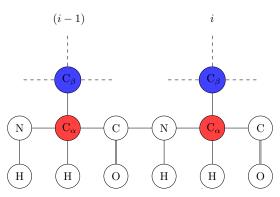
Nuclear Magnetic Resonance Spectroscopy

Introduction

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#### Chemical Shift Values

## HNCACB

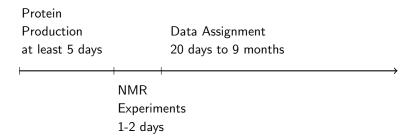


Data Collection and Manual Assignment

#### Manual Methods

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

#### **Timeline**



Preprocessing

# Automating Assingment

- Initialization
- Generating child nodes
- Goal State
- Solution State

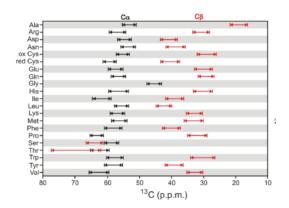
Preprocessing

#### Initialization

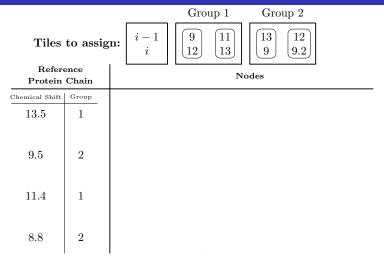
- Expected amino acid sequence
  - Converted to expected chemical shift values
  - Stored as the reference protein chain
- NMR experiment's chemical shift data
  - $C_{\alpha}$  and  $C_{\beta}$  for residue i and i-1
  - Stored in a tile
- Missing data
  - Place holder tile generation
- Grouping

Preprocessing

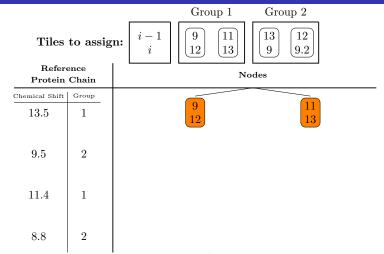
# Grouping



# Starting the assignment

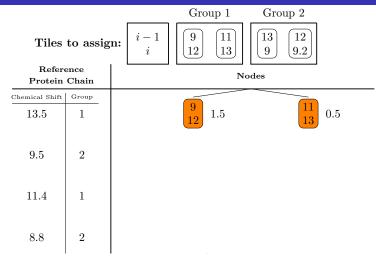


# Starting the assignment

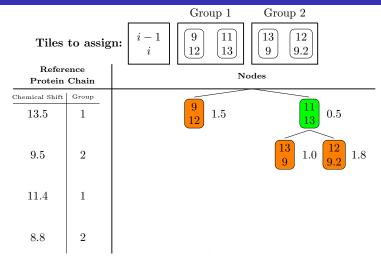


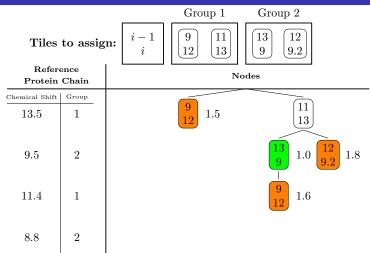
#### Cost Calculation

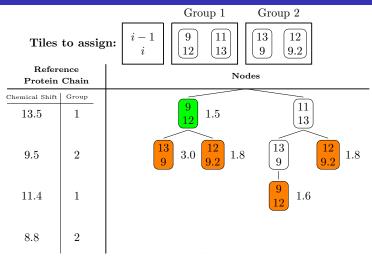
- Accuracy matching the protein chain residue
- Accuracy matching the tile above current tile
- Cost of placing all previous tiles



Automation Algorithm 0000000





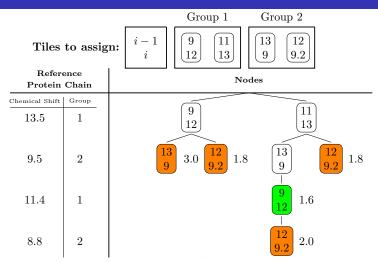


Automation Algorithm

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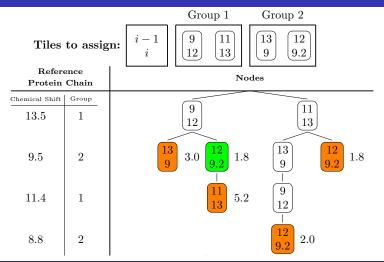
Goal State

#### Goal State



Goal State

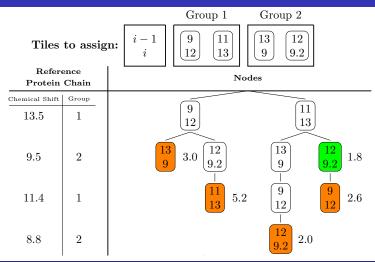
## Goal State



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Goal State

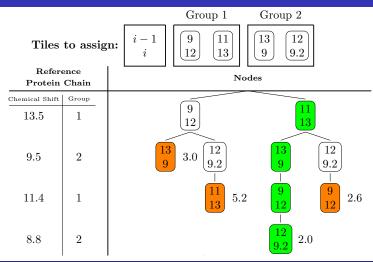
#### Goal State



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Goal State

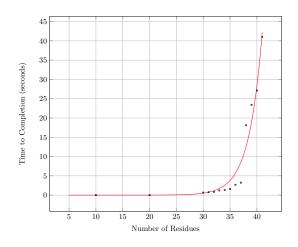
#### Solution State



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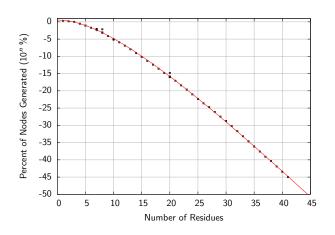
Results

# Time of Assignment



Results

#### Child Nodes Generated



#### Future Goals

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

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## Thank You

