# Advanced SASSIE-web

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SASSIE CCP-SAS Workshop
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# Overview

- Torsion Angle Molecular Dynamics (TAMD)
- Torsion Angle Monte Carlo (TAMC)
- Lab VII

# Torsion Angle Molecular Dynamics

- Monte Carlo sampling provides efficient coarse sampling with no dynamic (time) knowledge

- Molecular Dynamics provides dynamic knowledge and high resolution sampling

    - The larger the system the more inefficient the sampling!

$$U_{tot} = \xcancel{U_{bonds}} + \xcancel{U_{angles}} + \boxed{U_{diheds}} + U_{nonbond}$$

# Torsion Angle Molecular Dynamics

Torsion Angle MD

run name: run_0
reference pdb: Choose File No file chosen or Browse server
input filename (dcd or pdb): Choose File No file chosen or Browse server
output file name (dcd): tamd_output.dcd
number of preliminary minimization steps: 2000
number of TAMD steps: 100
temperature (K): 300.0
check box to keep output files: ☑
Rg force: 0
Rg value: 0

Complex Specific Input

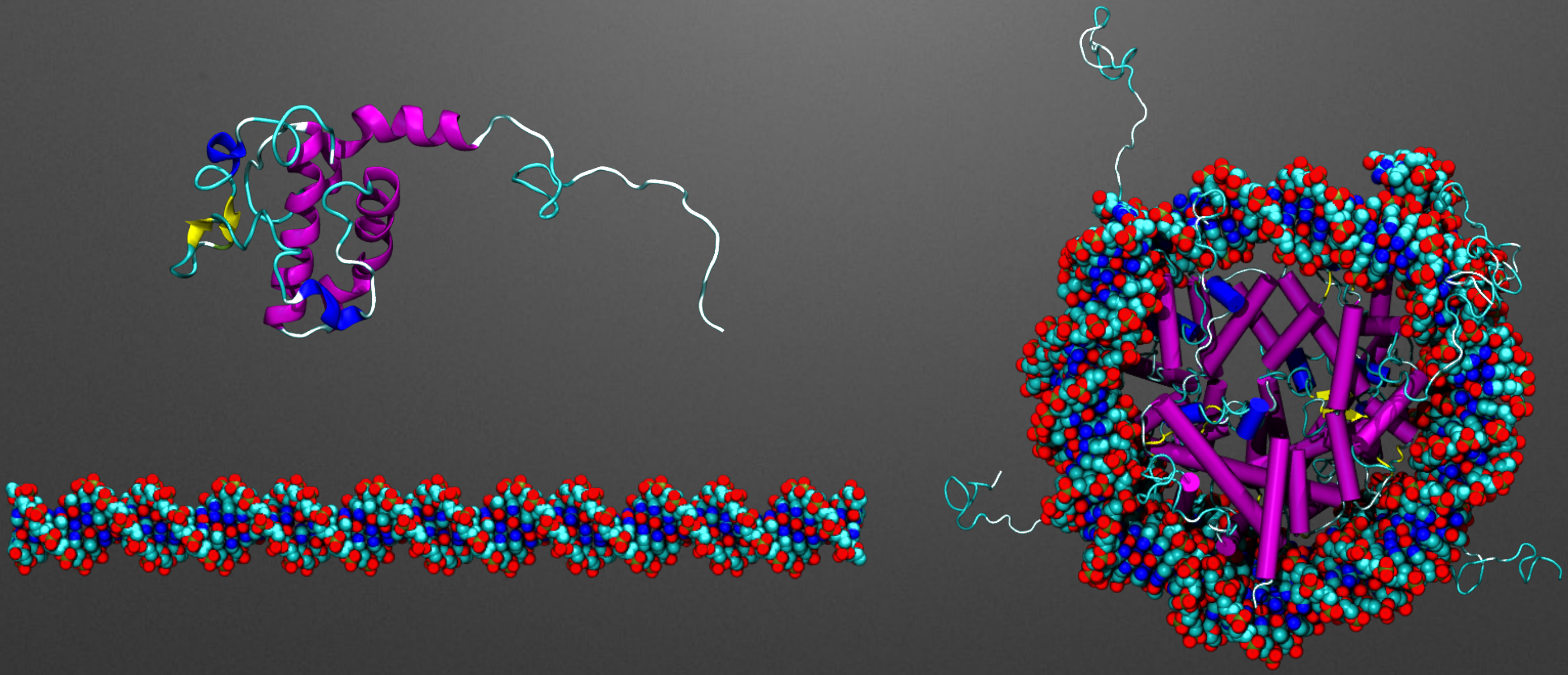
number of flexible segments: 1
molecule type [1] protein flexible segment name [1] GAG number of fleible region(s) [1] 2 flexible residue range(s) [1] 123-144, 277-282
check box if system has ds DNA: ☐

Advanced Input

Check Box for Advanced Input: ☐

# Torsion Angle Monte Carlo

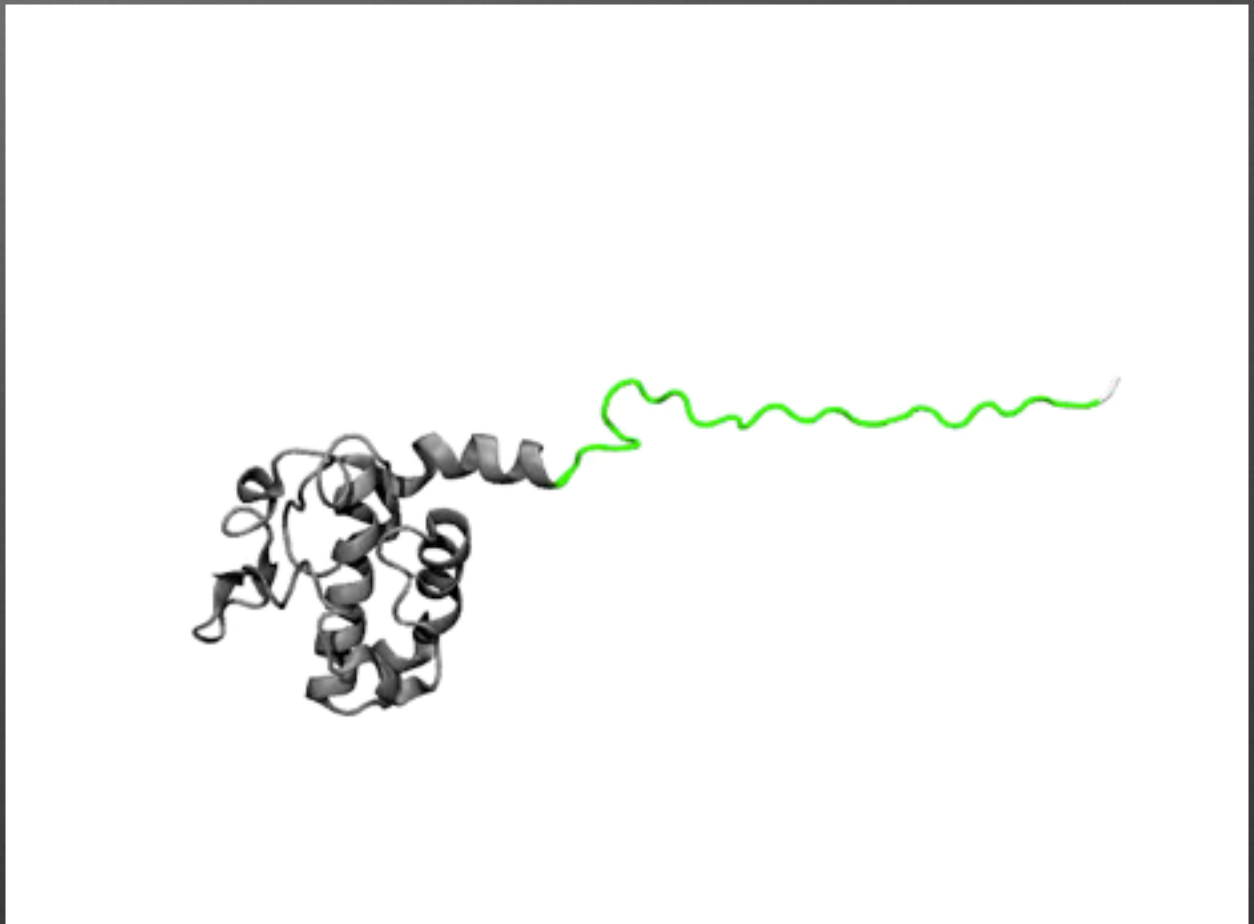
- “Biomolecules” encompass a diverse range of complexes



- Single strand backbone twists may not completely describe flexibility!

# Torsion Angle Monte Carlo

- More diverse torsion sets:
  - Protein Backbone
  - Single-Stranded Nucleic Acid Backbone
  - Double-Stranded Nucleic Acid Worm-like Chain
  - Protein Isopeptide



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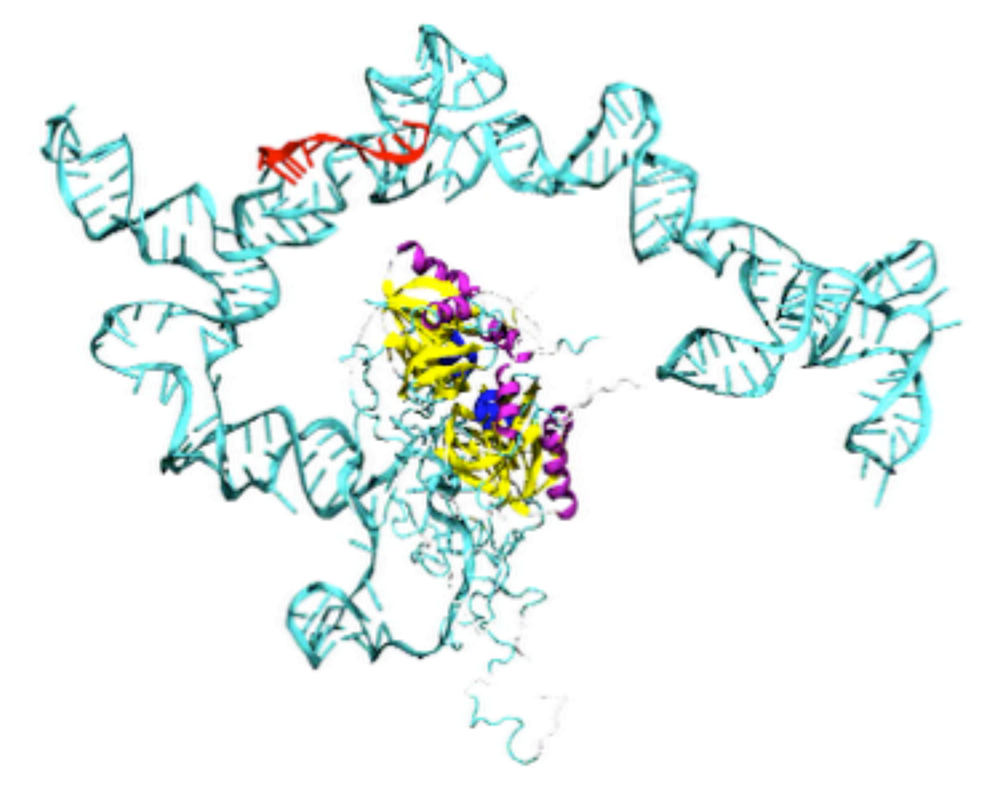

# Torsion Angle Monte Carlo

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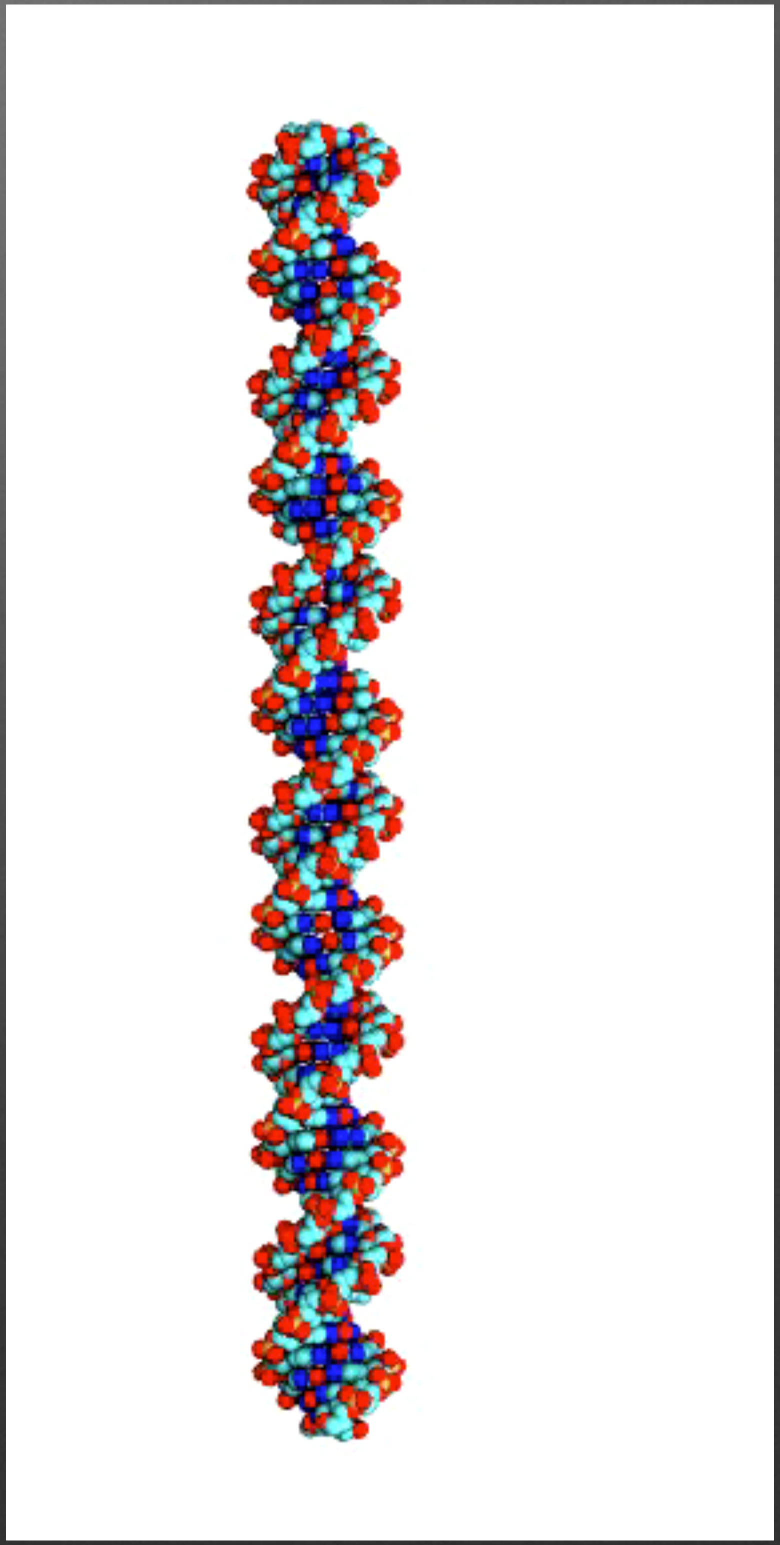

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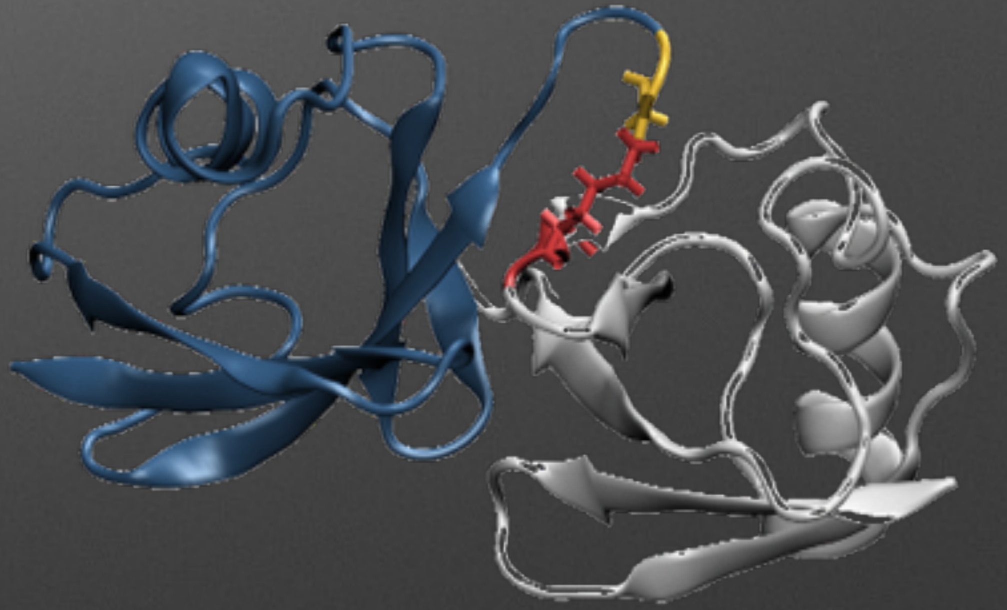

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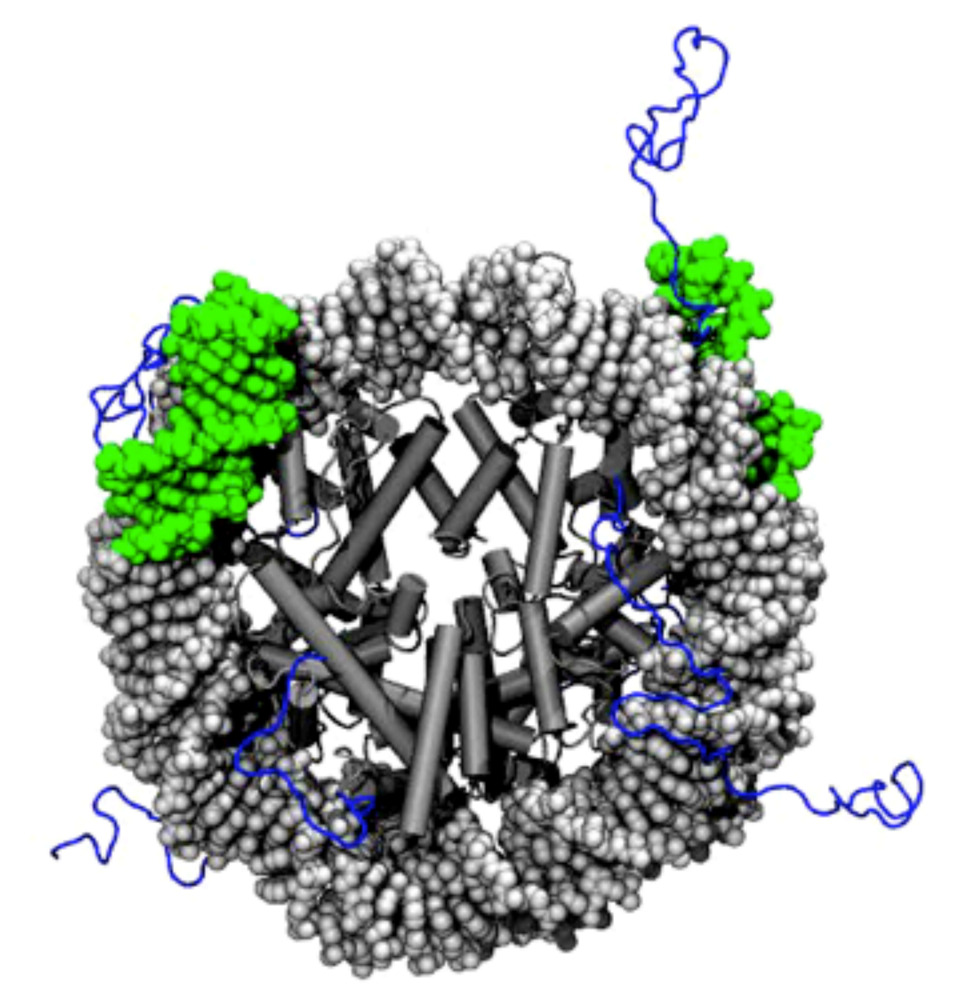
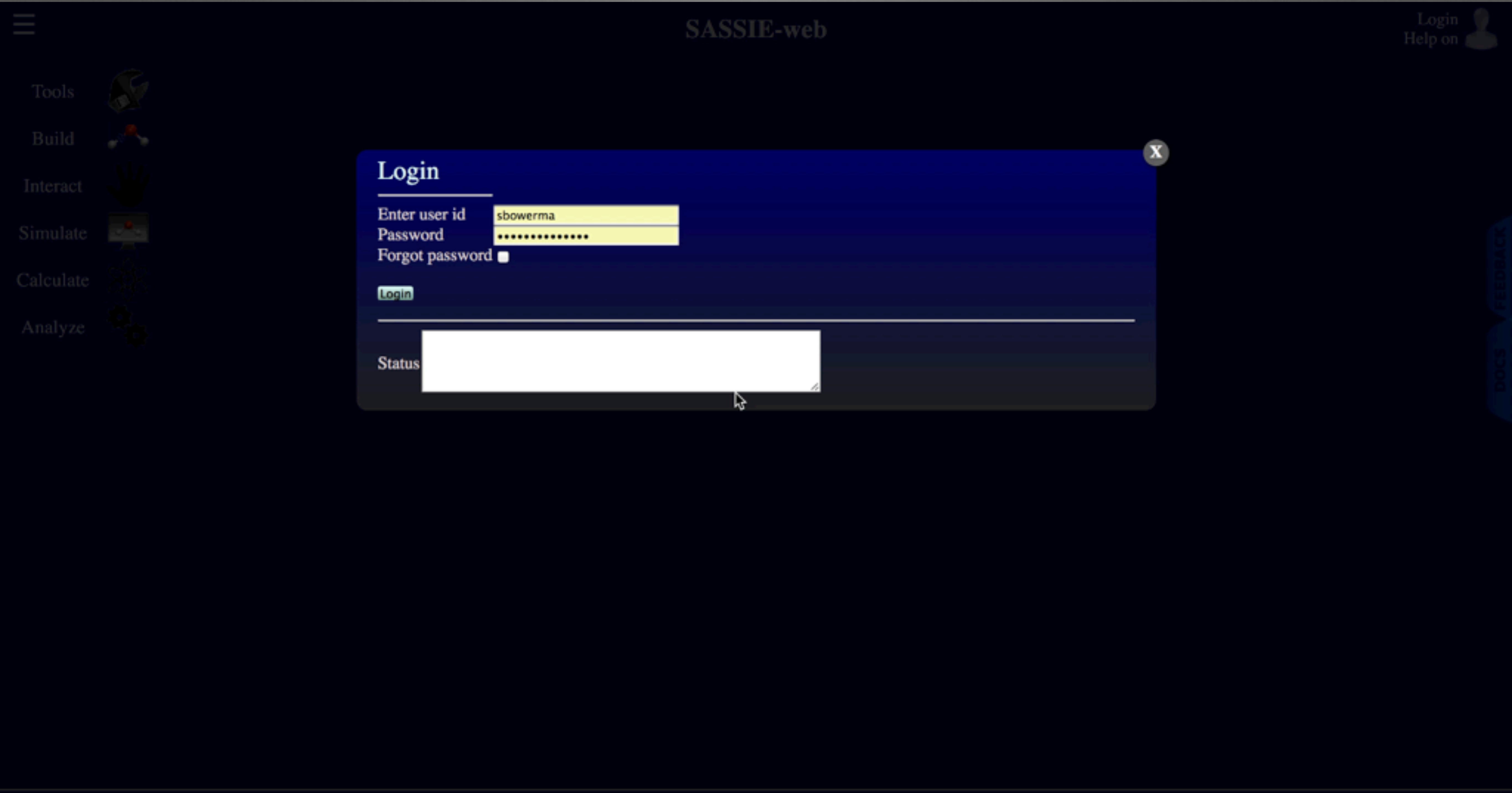
  - Protein Isopeptide



# Torsion Angle Monte Carlo

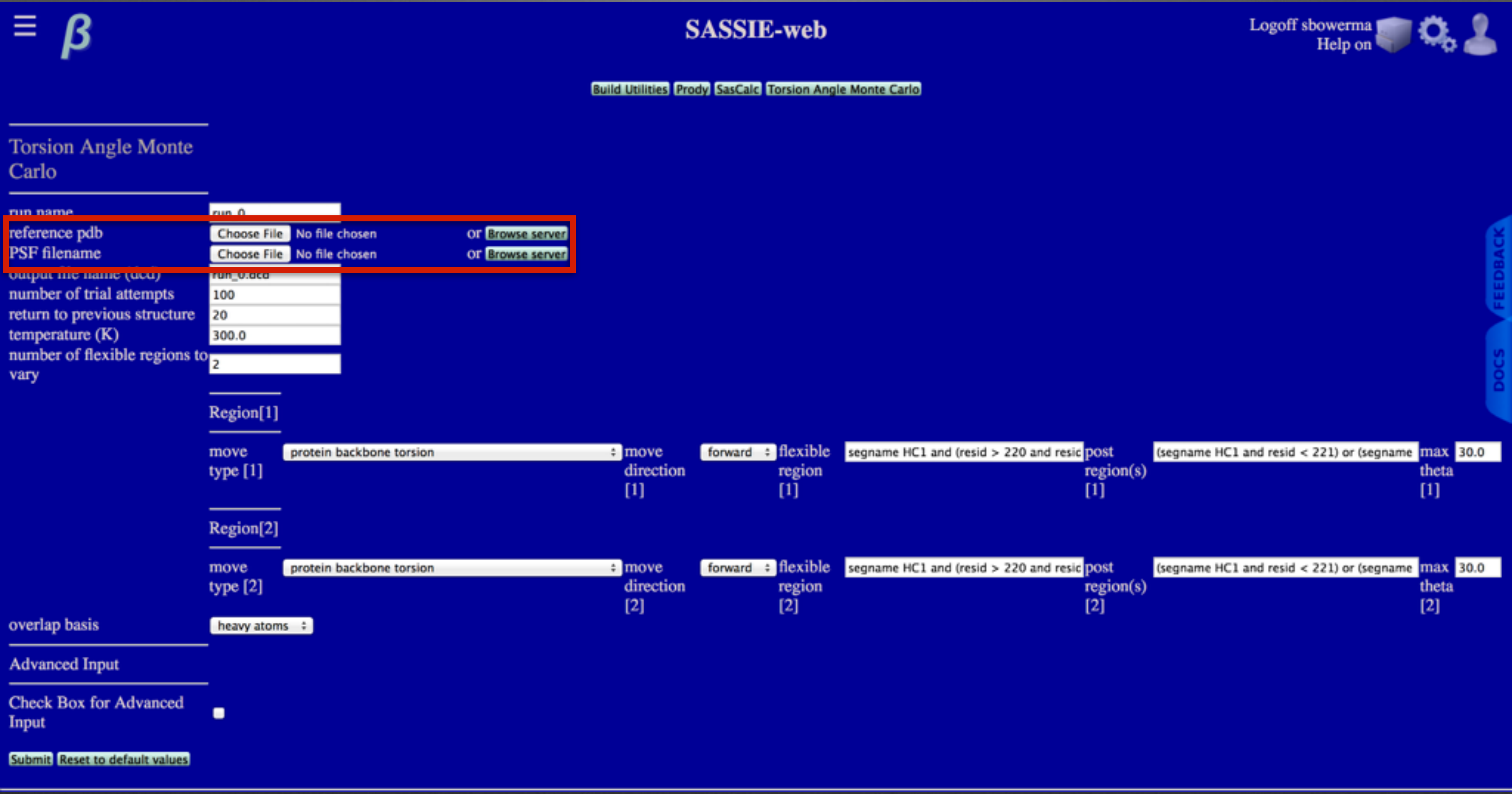


Enter user id: sbowerma

Password: •••••••••••••••

Forgot password ☐

# Torsion Angle Monte Carlo



Torsion Angle Monte Carlo

run name: run_0

reference pdb: Choose File No file chosen or Browse server

PSF filename: Choose File No file chosen or Browse server

output file name (dcd): run_0.dcd

number of trial attempts: 100

return to previous structure: 20

temperature (K): 300.0

number of flexible regions to vary: 2

Region[1]

move type [1]: protein backbone torsion

move direction [1]: forward

flexible region [1]: segname HC1 and (resid > 220 and resic

post region(s) [1]: (segname HC1 and resid < 221) or (segname

max theta [1]: 30.0

Region[2]

move type [2]: protein backbone torsion

move direction [2]: forward

flexible region [2]: segname HC1 and (resid > 220 and resic

post region(s) [2]: (segname HC1 and resid < 221) or (segname

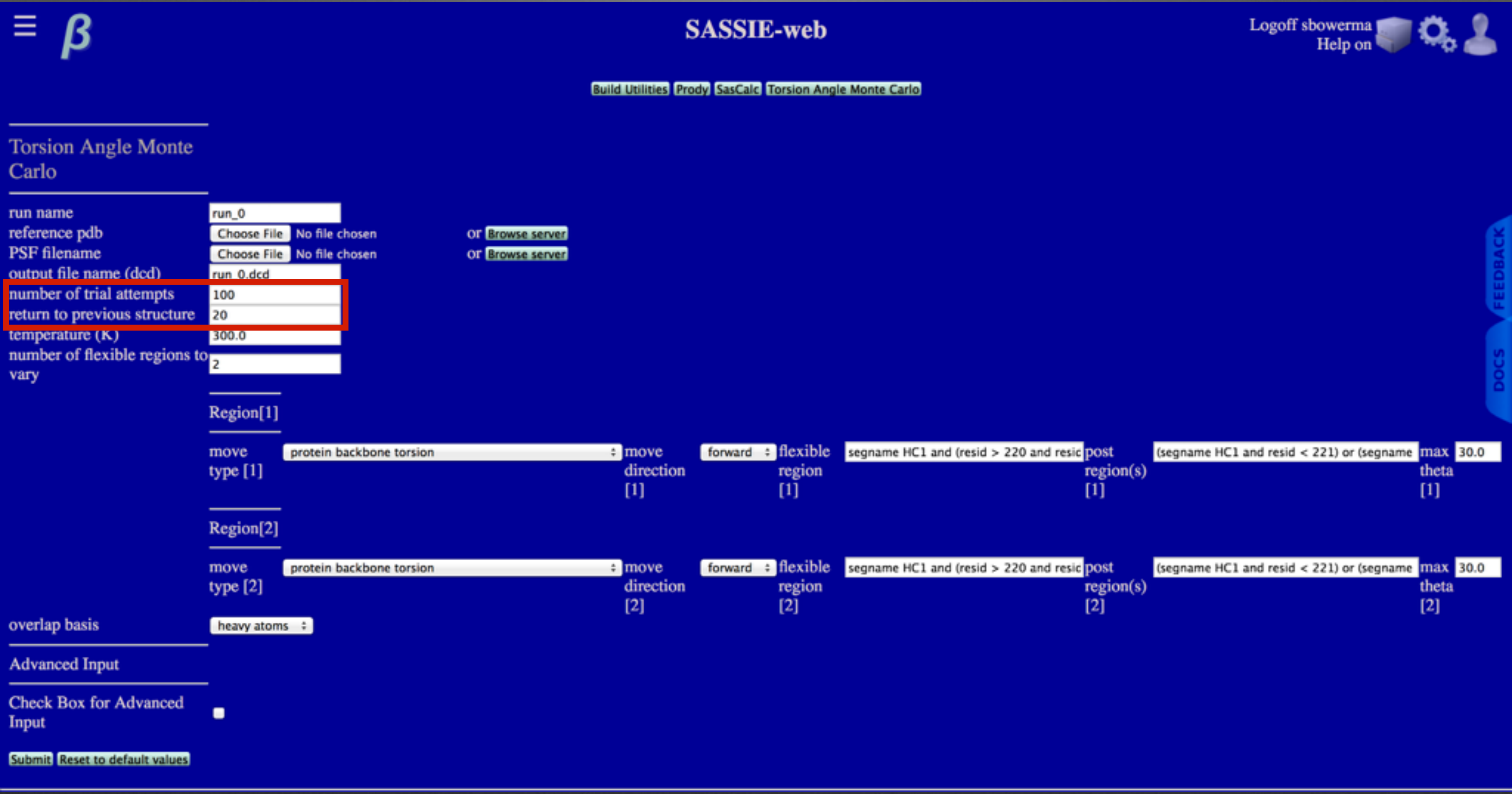
max theta [2]: 30.0

overlap basis: heavy atoms

Advanced Input

Check Box for Advanced Input ☐

# Torsion Angle Monte Carlo



Torsion Angle Monte Carlo

run name: run_0
reference pdb: Choose File No file chosen or Browse server
PSF filename: Choose File No file chosen or Browse server
output file name (dcd): run_0.dcd
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max theta [1]: 30.0

Region[2]

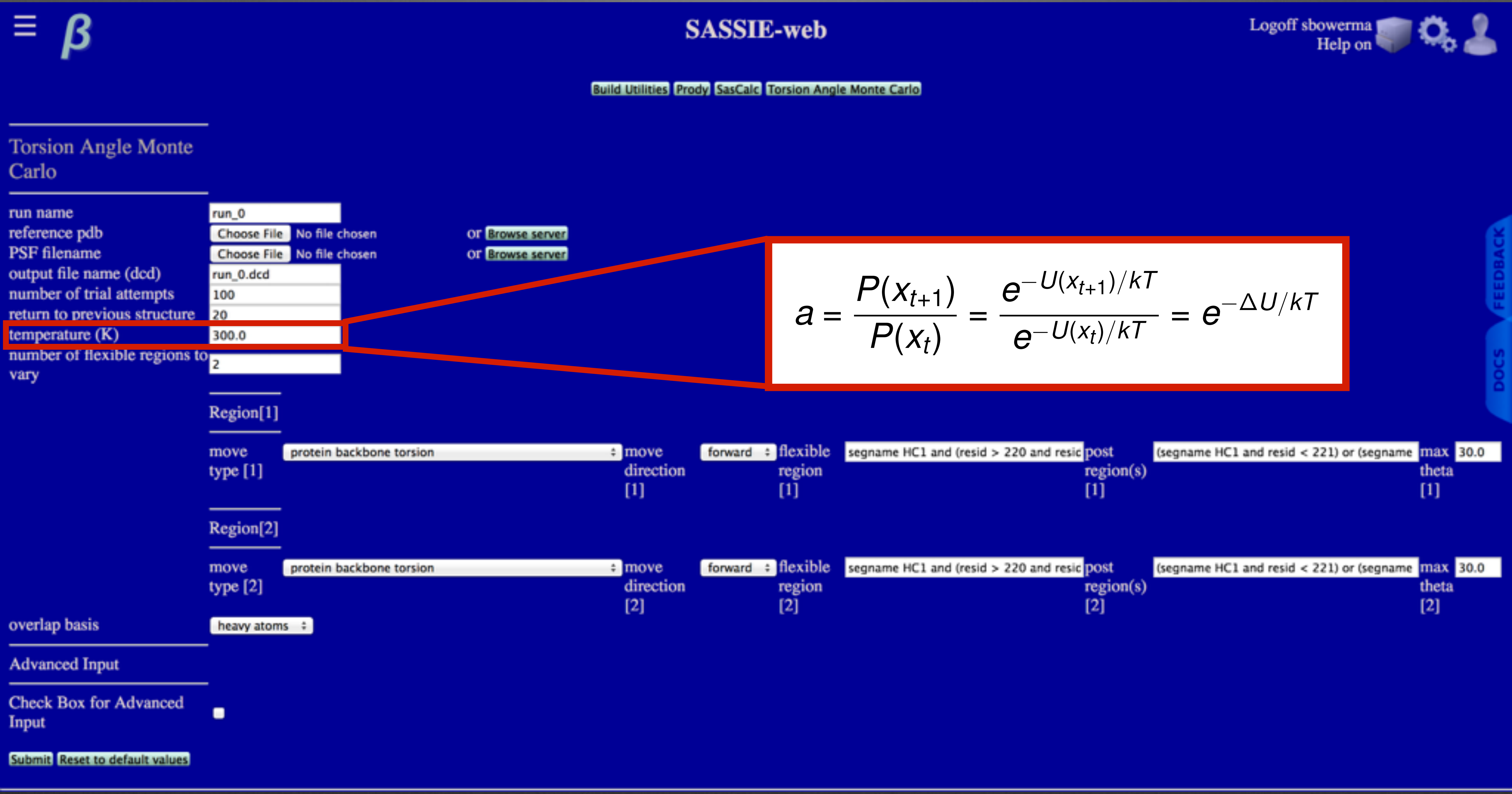
move type [2]: protein backbone torsion
move direction [2]: forward
flexible region [2]: segname HC1 and (resid > 220 and resic
post region(s) [2]: (segname HC1 and resid < 221) or (segname
max theta [2]: 30.0

overlap basis: heavy atoms

Advanced Input

Check Box for Advanced Input ☐

# Torsion Angle Monte Carlo



Torsion Angle Monte Carlo

| | | |
|---|---|---|
| run name | run_0 | |
| reference pdb | No file chosen | or Browse server |
| PSF filename | No file chosen | or Browse server |
| output file name (dcd) | run_0.dcd | |
| number of trial attempts | 100 | |
| return to previous structure | 20 | |
| temperature (K) | 300.0 | |
| number of flexible regions to vary | 2 | |

Region[1]

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| move type [1] | protein backbone torsion | move direction [1] | forward | flexible region [1] | segname HC1 and (resid > 220 and resic | post region(s) [1] | (segname HC1 and resid < 221) or (segname | max theta [1] | 30.0 |

Region[2]

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| move type [2] | protein backbone torsion | move direction [2] | forward | flexible region [2] | segname HC1 and (resid > 220 and resic | post region(s) [2] | (segname HC1 and resid < 221) or (segname | max theta [2] | 30.0 |

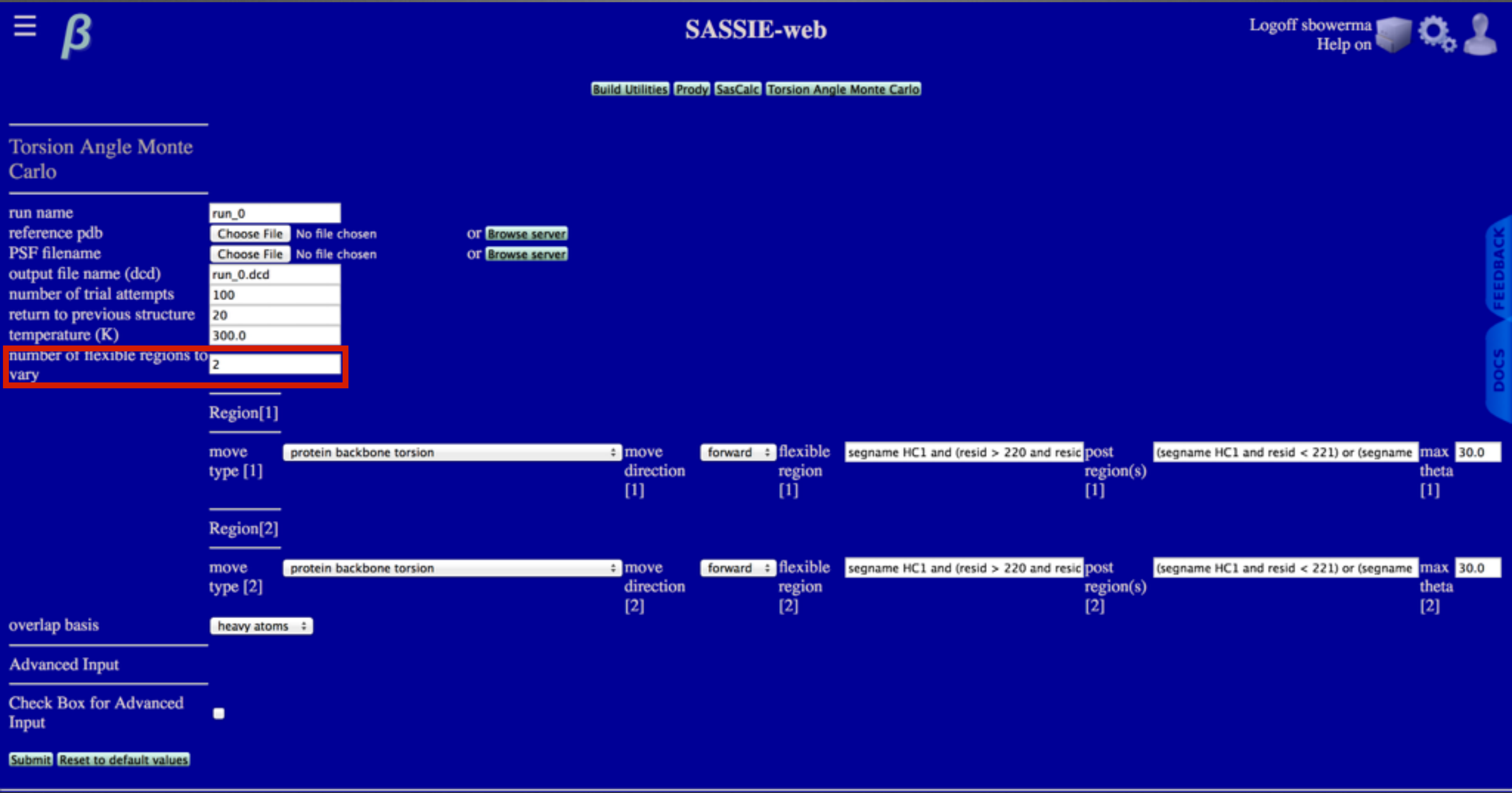
overlap basis: heavy atoms

Advanced Input

Check Box for Advanced Input ☐

$$a = \frac{P(x_{t+1})}{P(x_t)} = \frac{e^{-U(x_{t+1})/kT}}{e^{-U(x_t)/kT}} = e^{-\Delta U/kT}$$

# Torsion Angle Monte Carlo



Torsion Angle Monte Carlo

run name: run_0
reference pdb: Choose File No file chosen or Browse server
PSF filename: Choose File No file chosen or Browse server
output file name (dcd): run_0.dcd
number of trial attempts: 100
return to previous structure: 20
temperature (K): 300.0
number of flexible regions to vary: 2

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move direction [1]: forward
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post region(s) [1]: (segname HC1 and resid < 221) or (segname
max theta [1]: 30.0

Region[2]

move type [2]: protein backbone torsion
move direction [2]: forward
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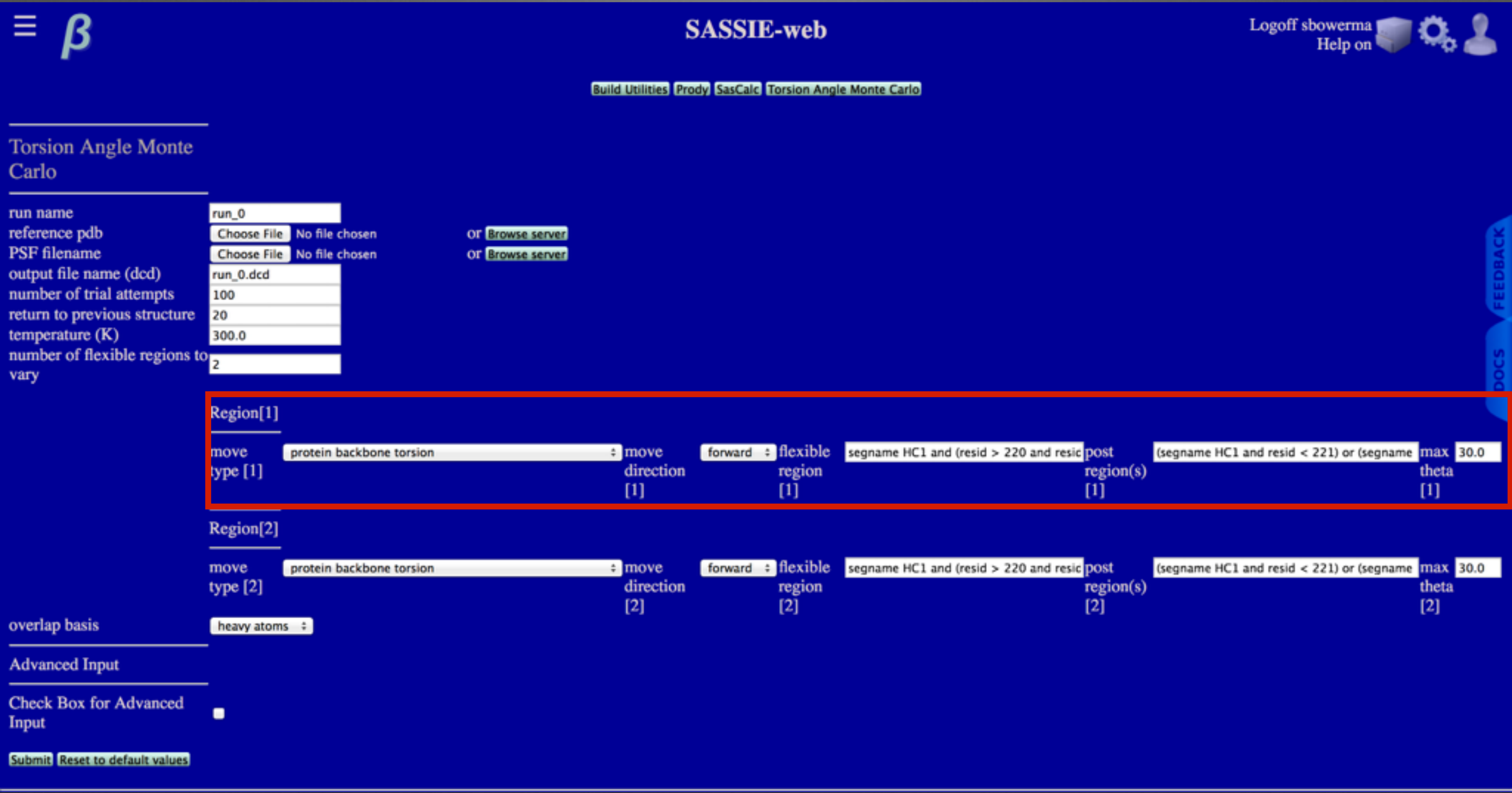
overlap basis: heavy atoms

Advanced Input

Check Box for Advanced Input ☐

# Torsion Angle Monte Carlo



Torsion Angle Monte Carlo

| | |
|---|---|
| run name | run_0 |
| reference pdb | Choose File No file chosen or Browse server |
| PSF filename | Choose File No file chosen or Browse server |
| output file name (dcd) | run_0.dcd |
| number of trial attempts | 100 |
| return to previous structure | 20 |
| temperature (K) | 300.0 |
| number of flexible regions to vary | 2 |

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| max theta [1] | 30.0 |

Region[2]

| | |
|---|---|
| move type [2] | protein backbone torsion |
| move direction [2] | forward |
| flexible region [2] | segname HC1 and (resid > 220 and resic |
| post region(s) [2] | (segname HC1 and resid < 221) or (segname |
| max theta [2] | 30.0 |

overlap basis: heavy atoms

Advanced Input

Check Box for Advanced Input ☐

# Torsion Angle Monte Carlo

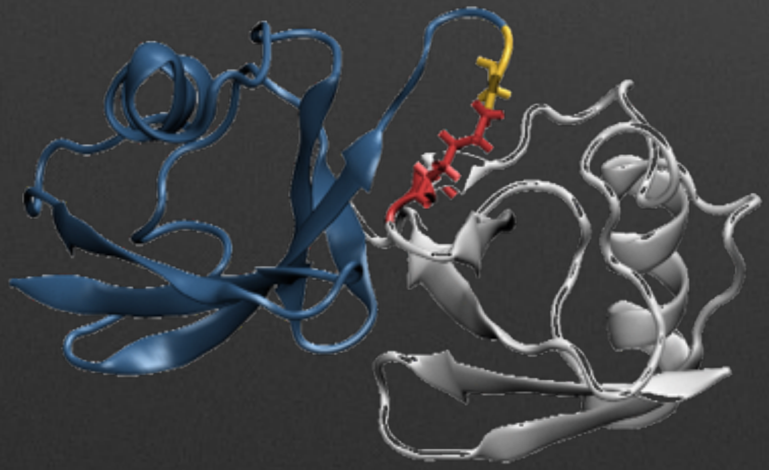
“Forward”

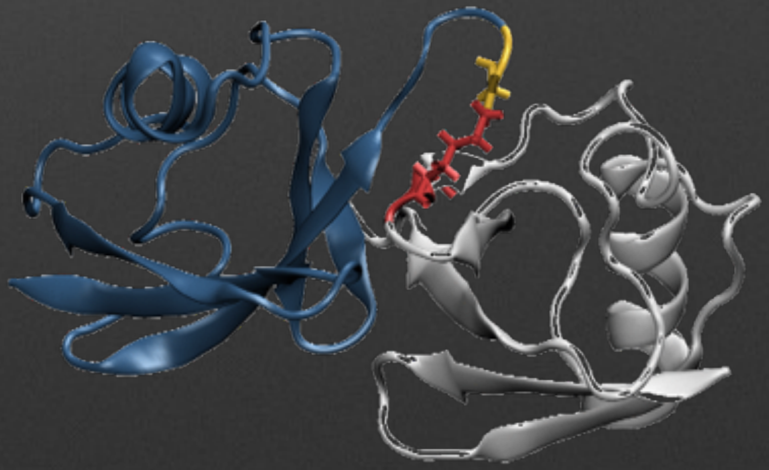
- Backbone - “post” region follows flexible region
- Isopeptide - “post” region is the Lys side of the bond

or

“Reverse”?

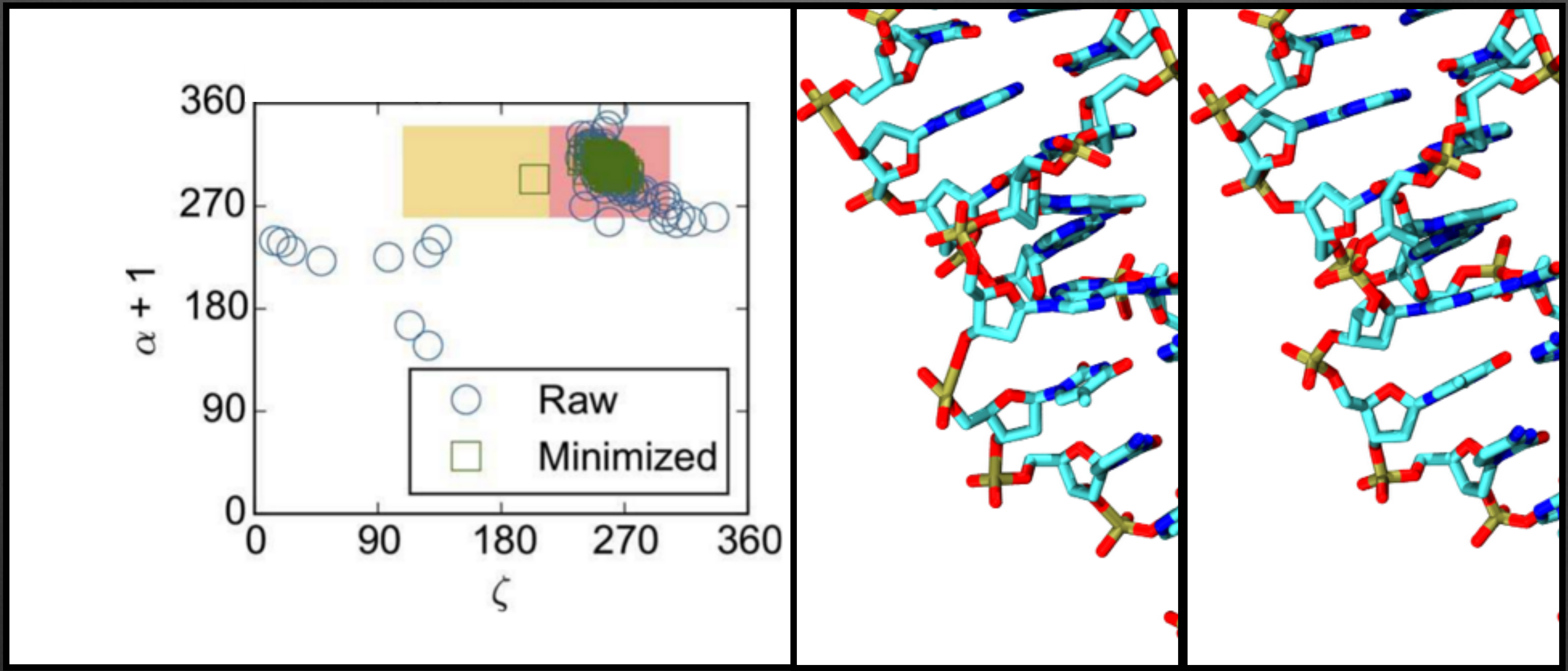
- Backbone - “post” region precedes flexible region
- Isopeptide - “post” region is the C-term side of the bond





# Torsion Angle Monte Carlo

- Because Monte Carlo sampling is a coarse method, further refinement is typically necessary.



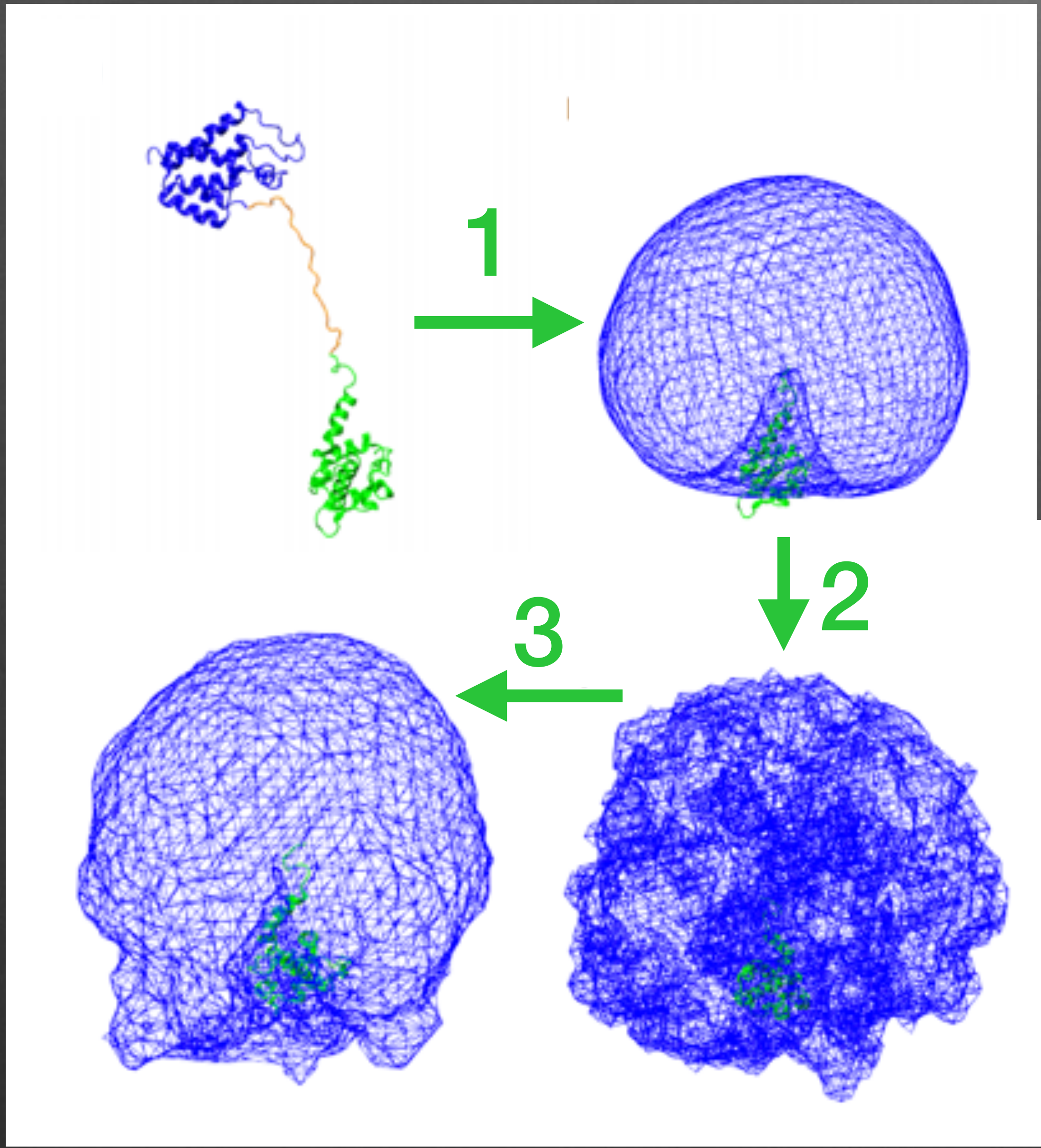
S.C. Howell, X. Qiu, and J.E. Curtis. “Monte Carlo Simulation Algorithm for B-DNA.” *J. Comput. Chem.* 37:2553-2563 (2016)

# Closing Remarks

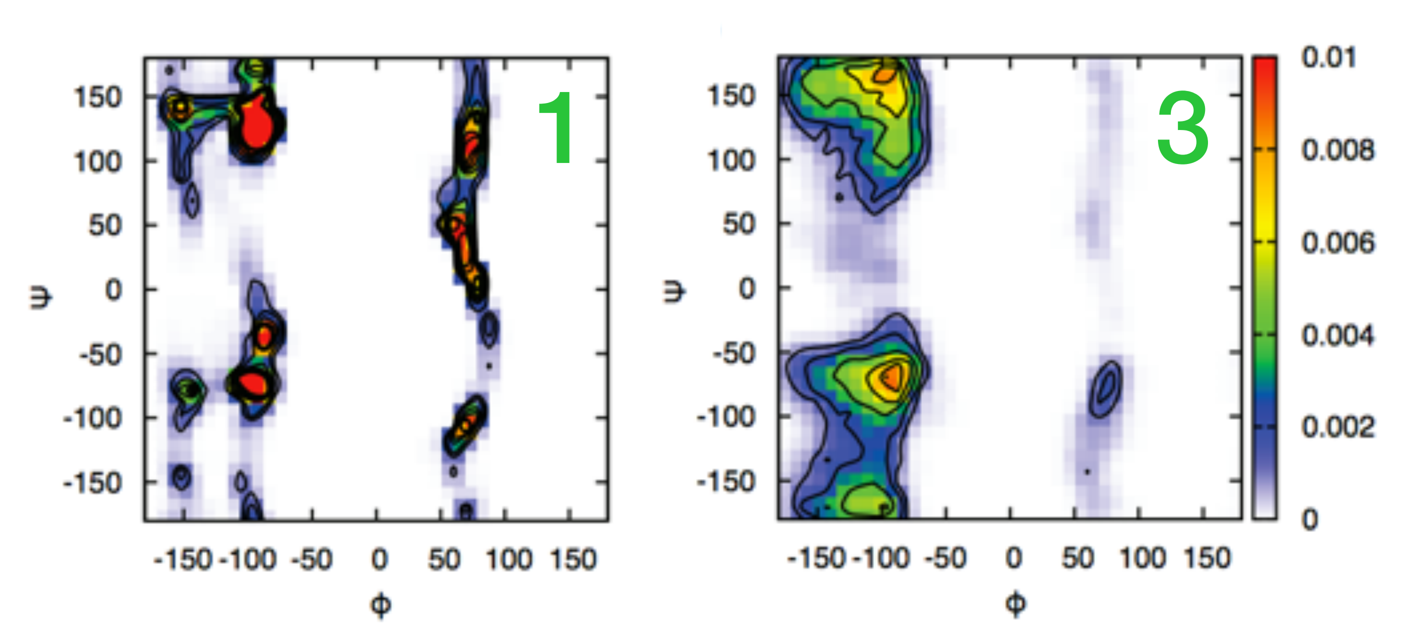
- The Torsion Angle Molecular Dynamics (TAMD) samples dynamics in a reduced phase-space
- The Torsion Angle Monte Carlo (TAMC) module creates a vast structure library from a variety of possible motions
- SASSIE-web allows us to combine methods as parts of a larger workflow!

# Summary

- SASSIE-web allows us to combine methods as parts of a larger workflow!



1. Coarse structure search using TAMC
2. Structurally cluster
3. TAMD each cluster rep to get a smoother landscape



W. Zhang, S.C. Howell, D.W. Wright, *et al.* “Combined Monte Carlo / Torsion-Angle Molecular Dynamics for Ensemble Modeling of Proteins, Nucleic Acids, and Carbohydrates.” *J. Mol. Graph. Model.* (In-press).

# Lab VII:
# Advanced SASSIE-web