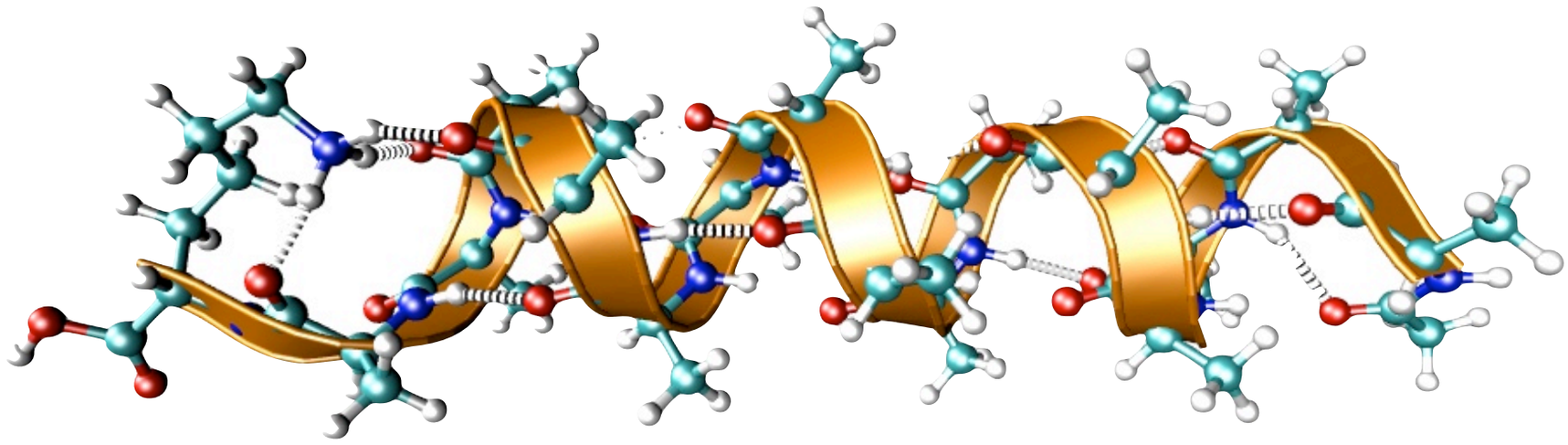
Ab initio molecular dynamics for biomolecular spectroscopy

Mariana Rossi

Fritz-Haber-Institut der MPG, Faradayweg 4-6, 14195 Berlin



DFT and beyond - FHI-aims Developers' and Users' Meeting 2012, Berlin

Polyalanine in the gas-phase

Ion mobility spectroscopy

Evidence of helical secondary structure for Ac-Ala$_n$-LysH$^+$, n=5-20 in the gas-phase

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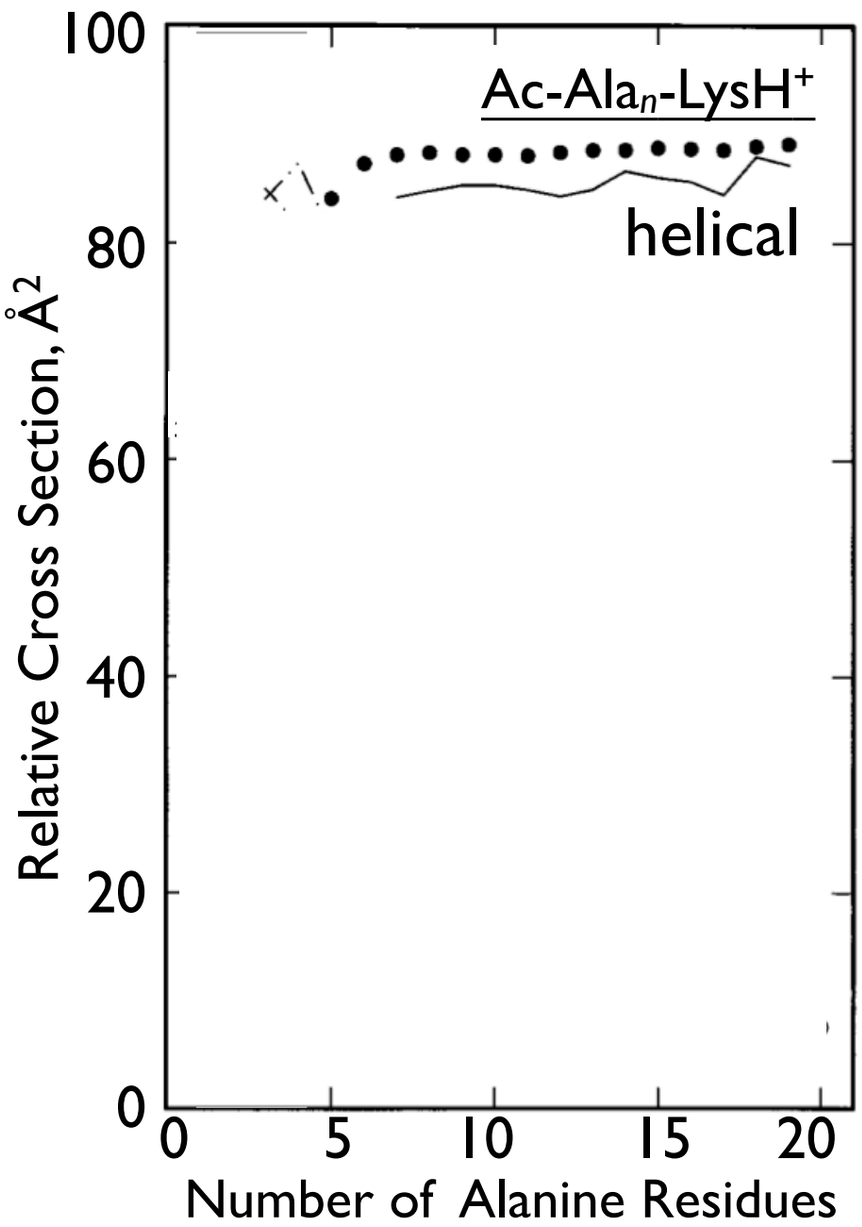

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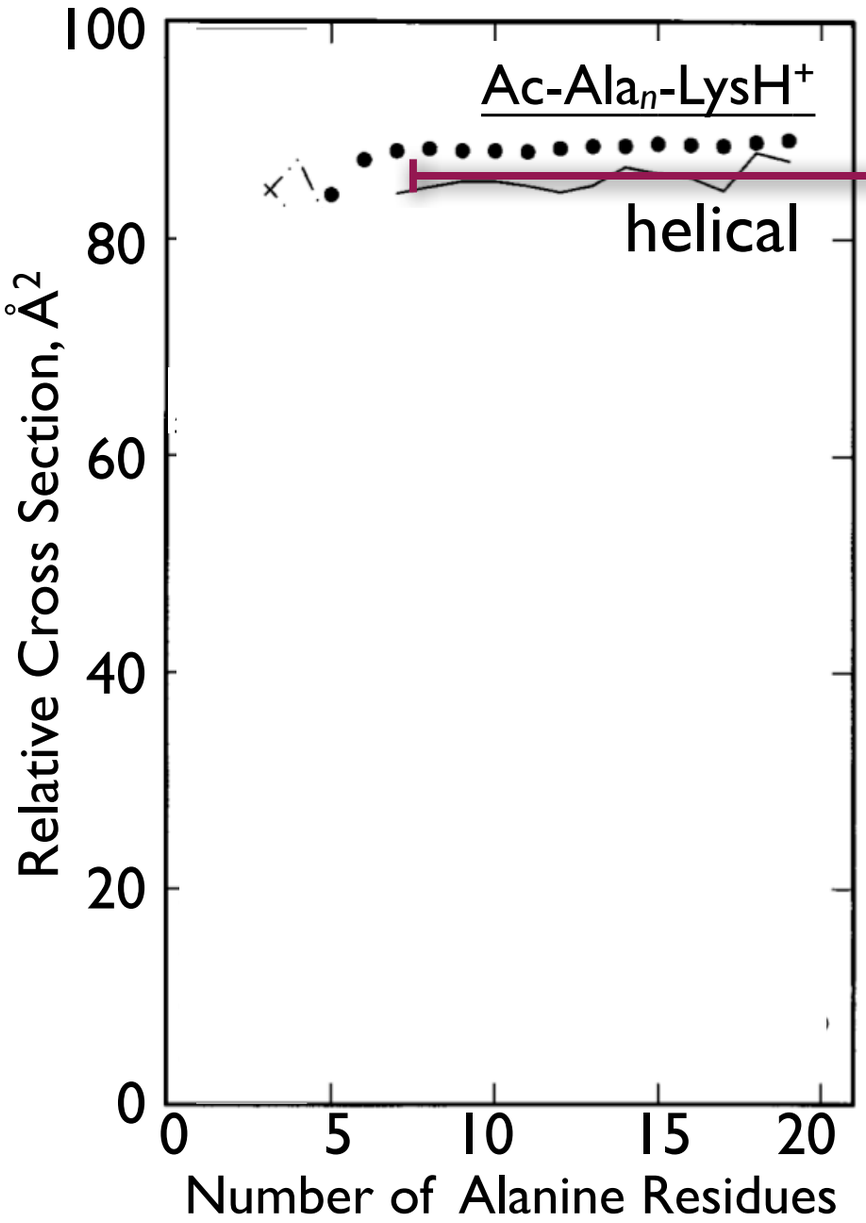

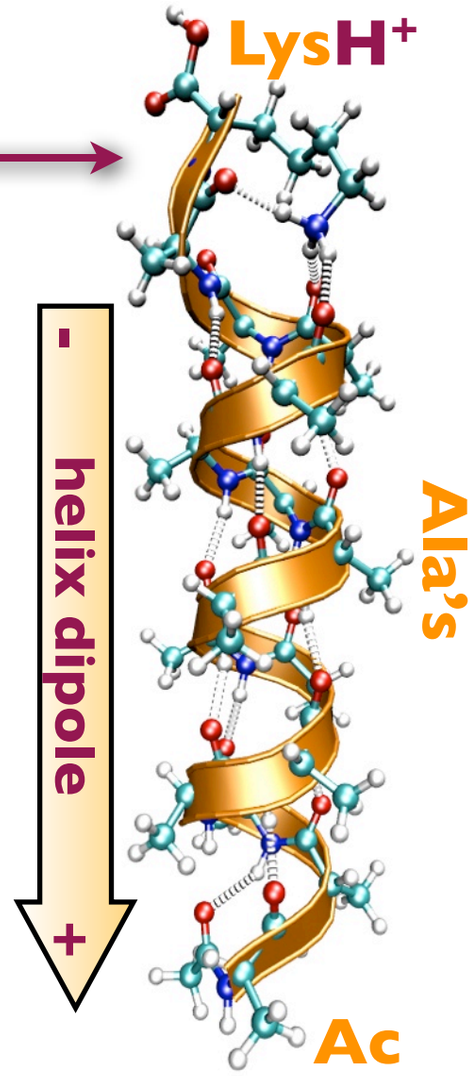

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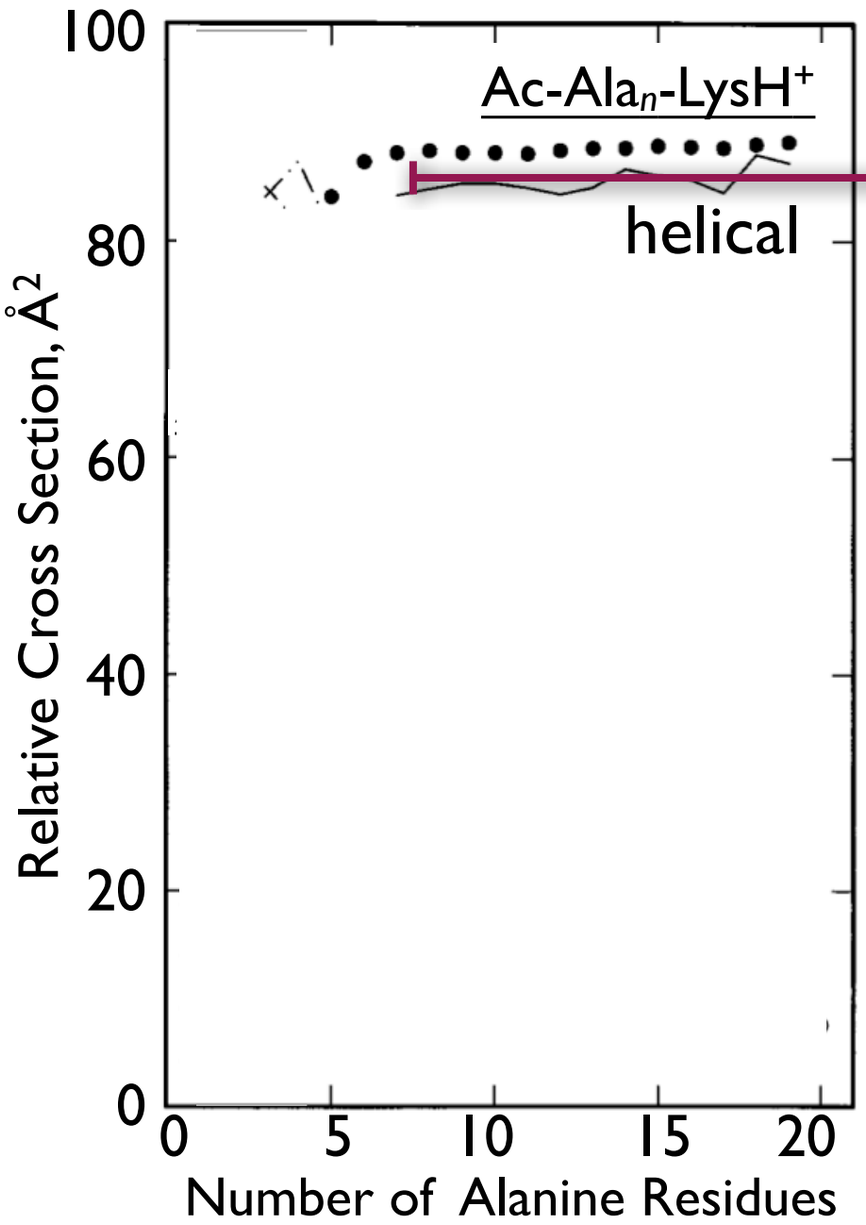

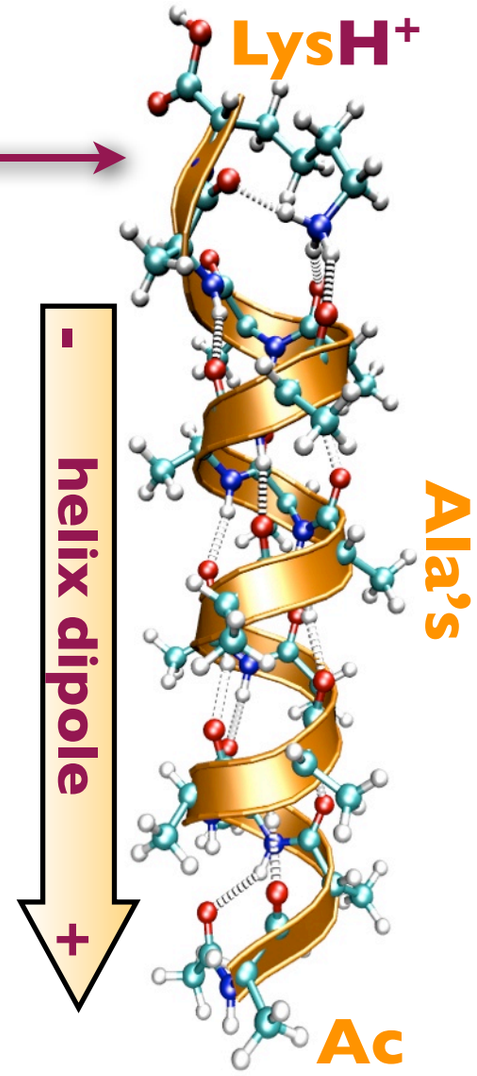

IR spectroscopy

Detailed structure sensitivity

[1] Stearns, Seaiby, Boyarkin, Rizzo, Phys. Chem. Chem. Phys. ***11****, 125 (2009)*

[2] Kupser, Pagel, Oomens, Polfer, Koksch, Meijer, von Helden, J. Am. Chem. Soc. ***132****, 2085 (2010)*

Others!

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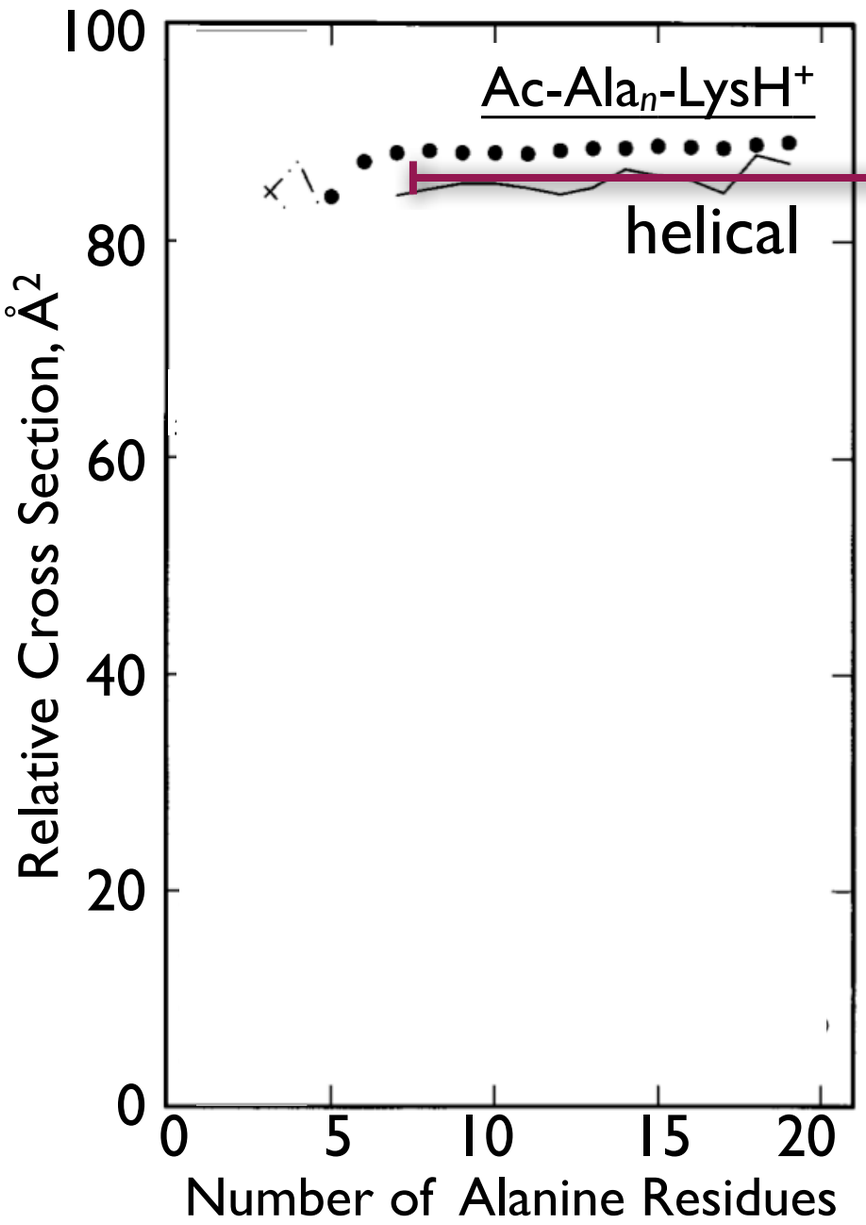

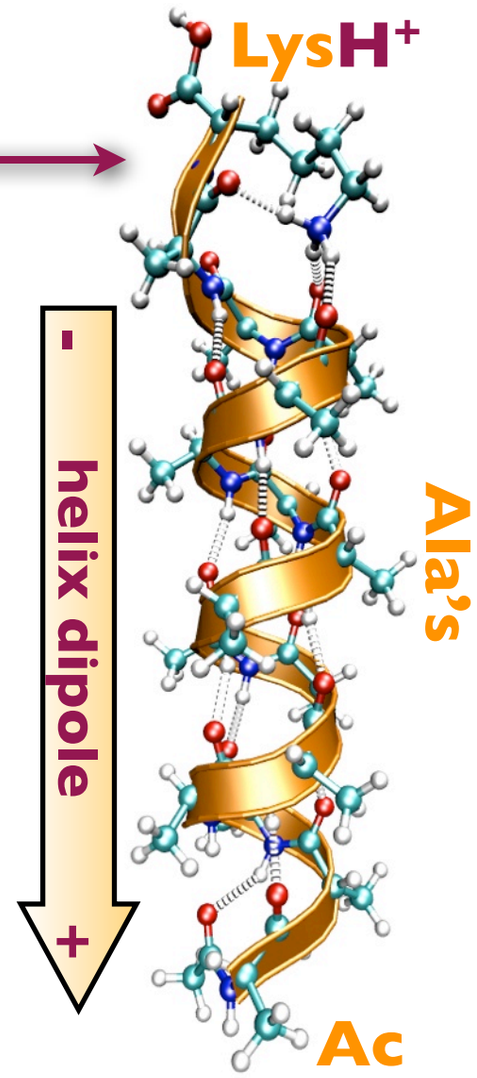

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Others!

- Clean and accurate experiments in unambiguous environment
- Good opportunity for theory vs. experiment

Outline

- Conformational search and IR spectra
- Benchmark against “beyond DFT” methods
- Including nuclear quantum effects - new features of FHI-aims

Methodology

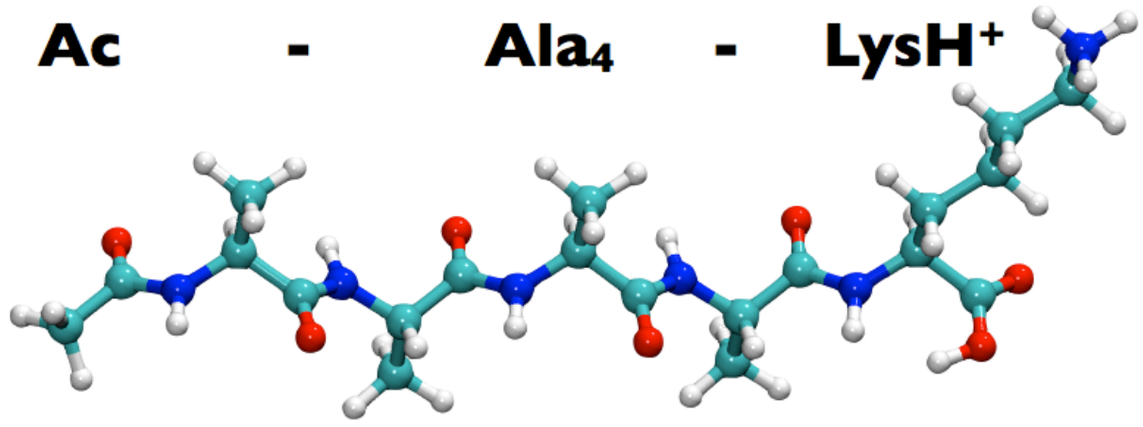
- All-electron / localized basis code (DFT and beyond) developed in the Fritz-Haber-Institut: FHI-aims[1]
- Accurate NAO basis sets for DFT
- PBE exchange correlation functional
- Inclusion of van der Waals (vdW) effects via a $C_6[n]/R^6$ term derived from self consistent electronic density[2]
  - Benchmarked against CCSD(T) for alanine based polypeptides[3]

[1] V. Blum et al. Comp. Phys. Comm. ***180****, 2175 (2009)*
[2] A. Tkatchenko and M. Scheffler, Phys. Rev. Lett. ***102****, 073005 (2009)*
[3] A. Tkatchenko, M. Rossi, V. Blum, J. Ireta, and M. Scheffler, Phys. Rev. Lett. ***106****, 118102, (2011)*

How to find your way to the relevant conformers?

Example:
(70 atoms)

Ac - Ala_4 - $LysH^+$



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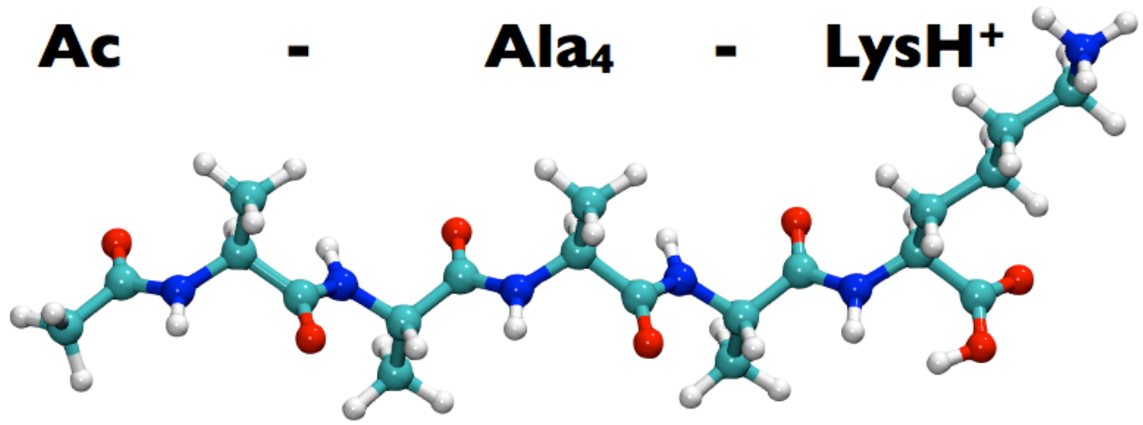

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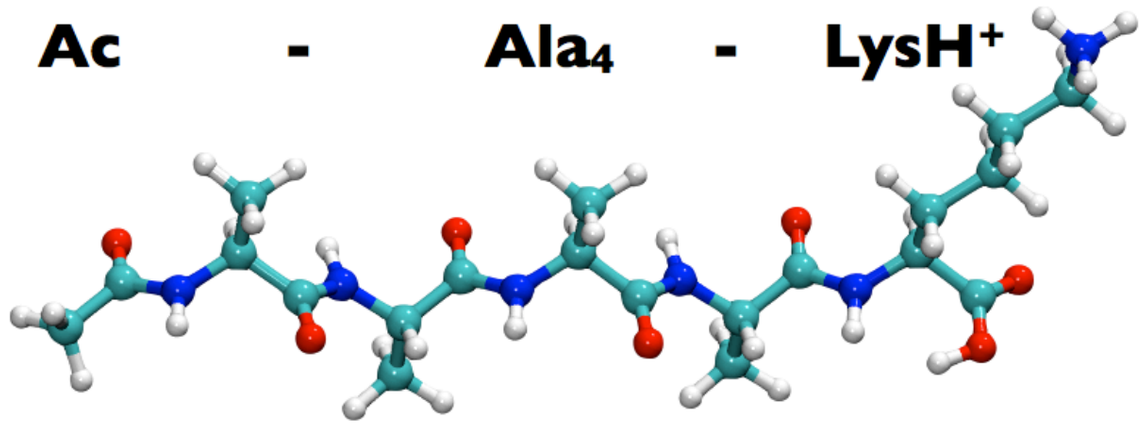

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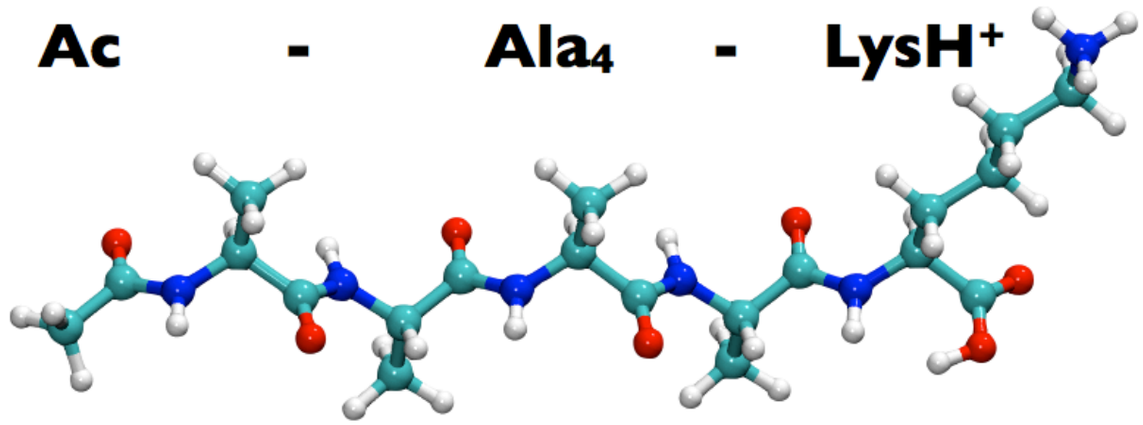

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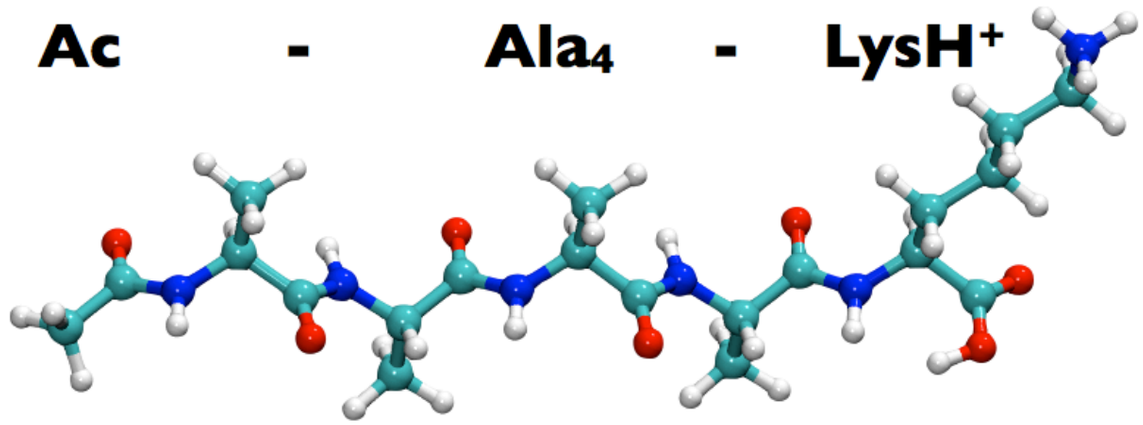

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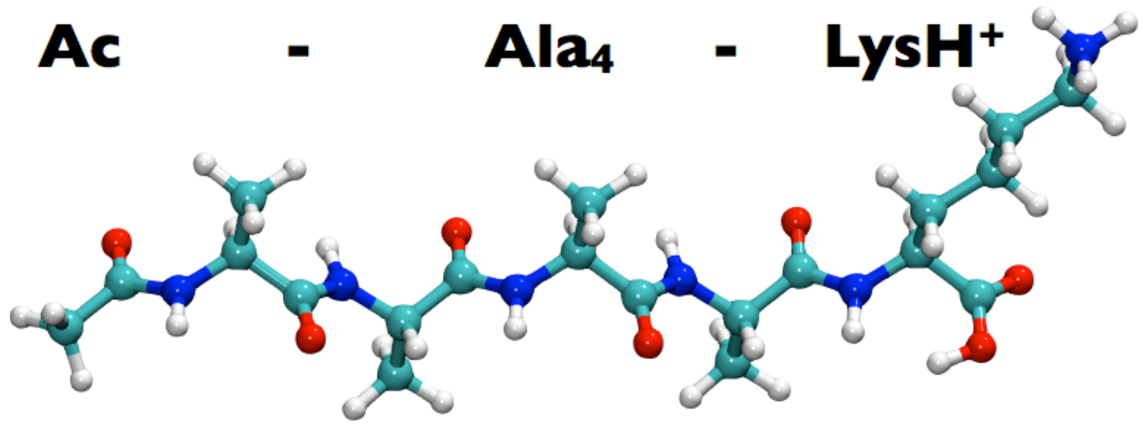

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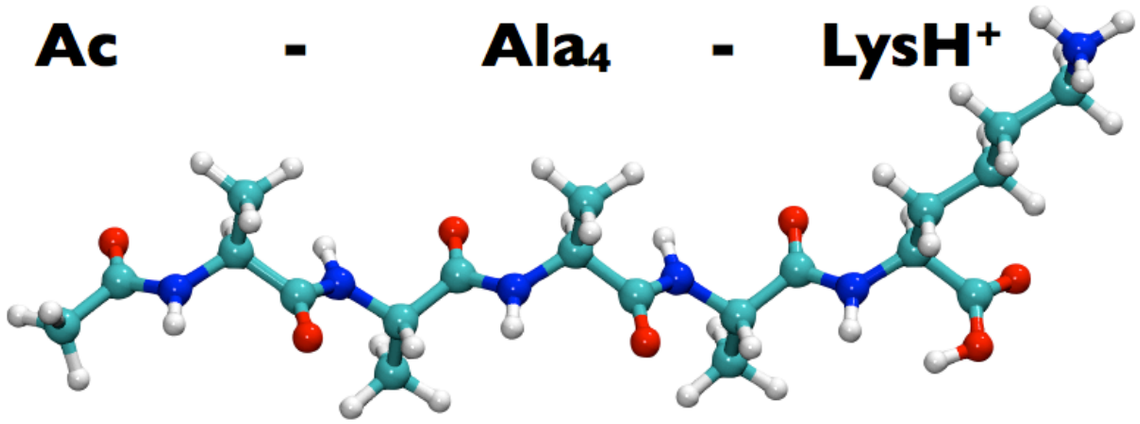

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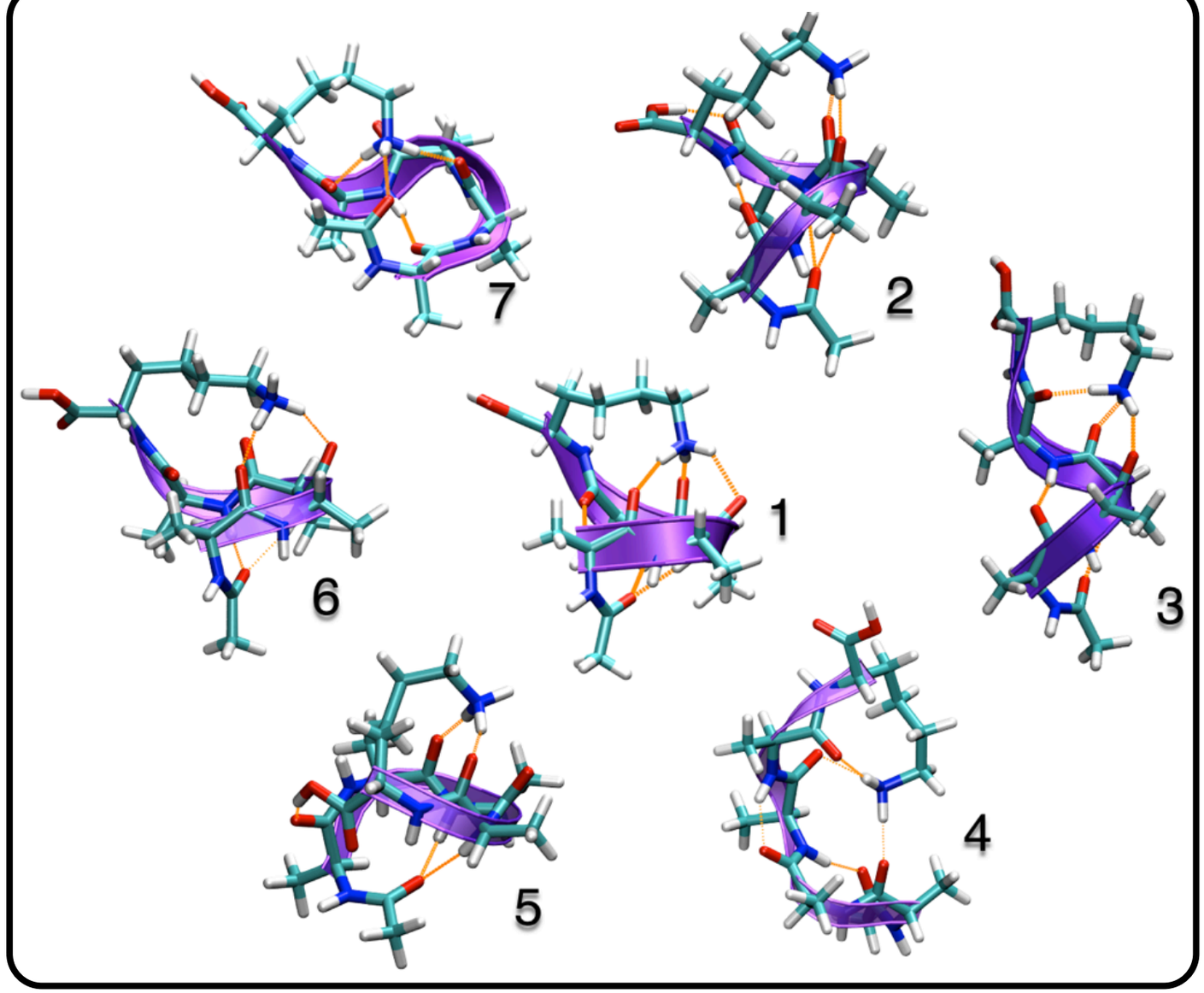

Strategy to find conformers: Ac-Ala$_n$-LysH$^+$, n=4-8

$N_{conformers}$

Input structures generation: Basin-hopping search (TINKER) with *opls-aa* force field

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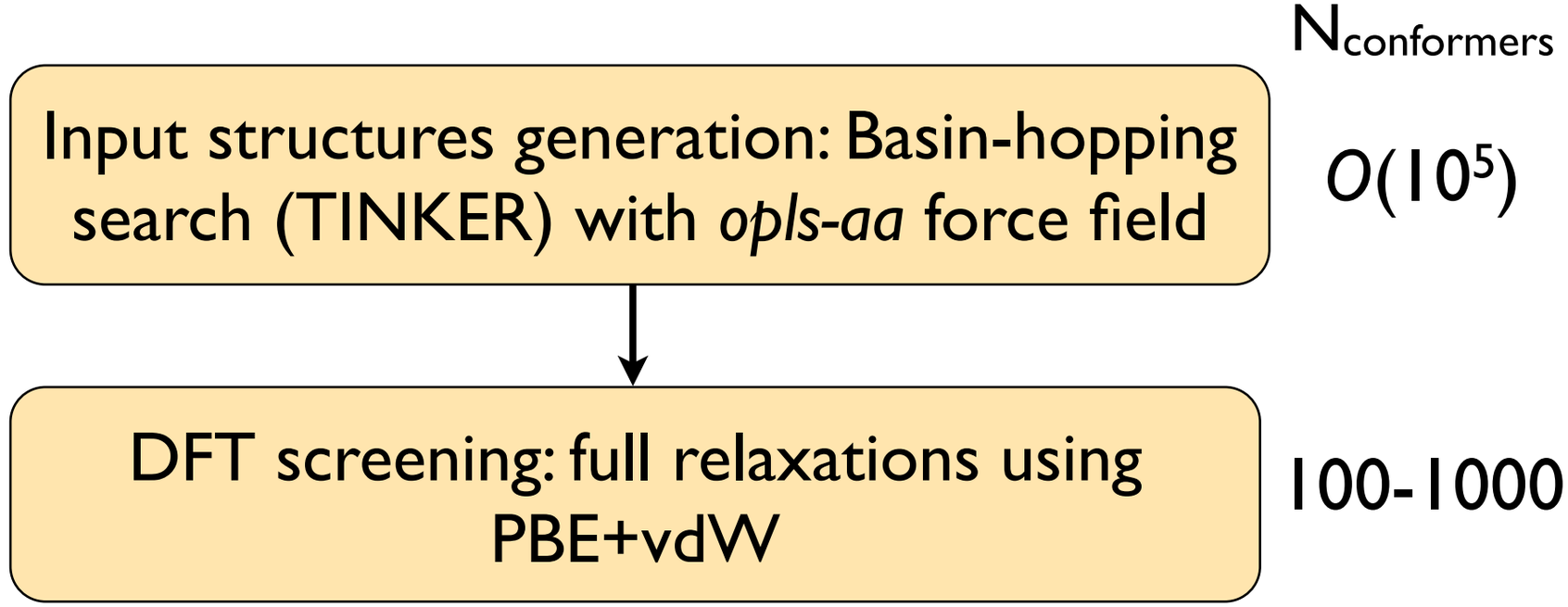

Number of PBE+vdW relaxations for Ac-Ala$_n$-LysH$^+$, n=4-8

size	# of relax.
4	1068
5	1000
6	800
7	800
8	820

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⇣

Sort conformers into families according to their H-bond connection

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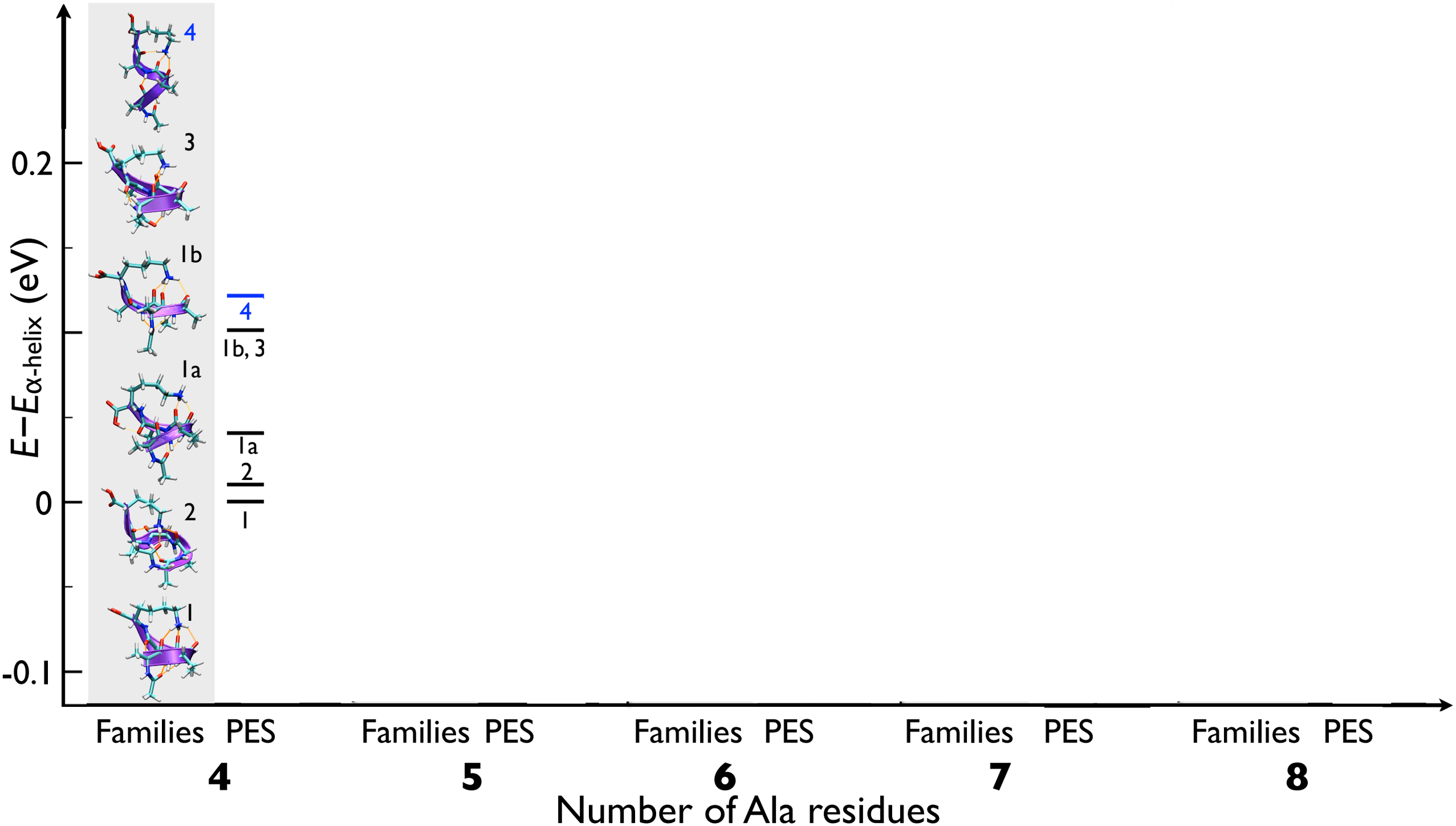
Energy hierarchies: PES and harmonic free energies

α-helix

3_{10}-helix



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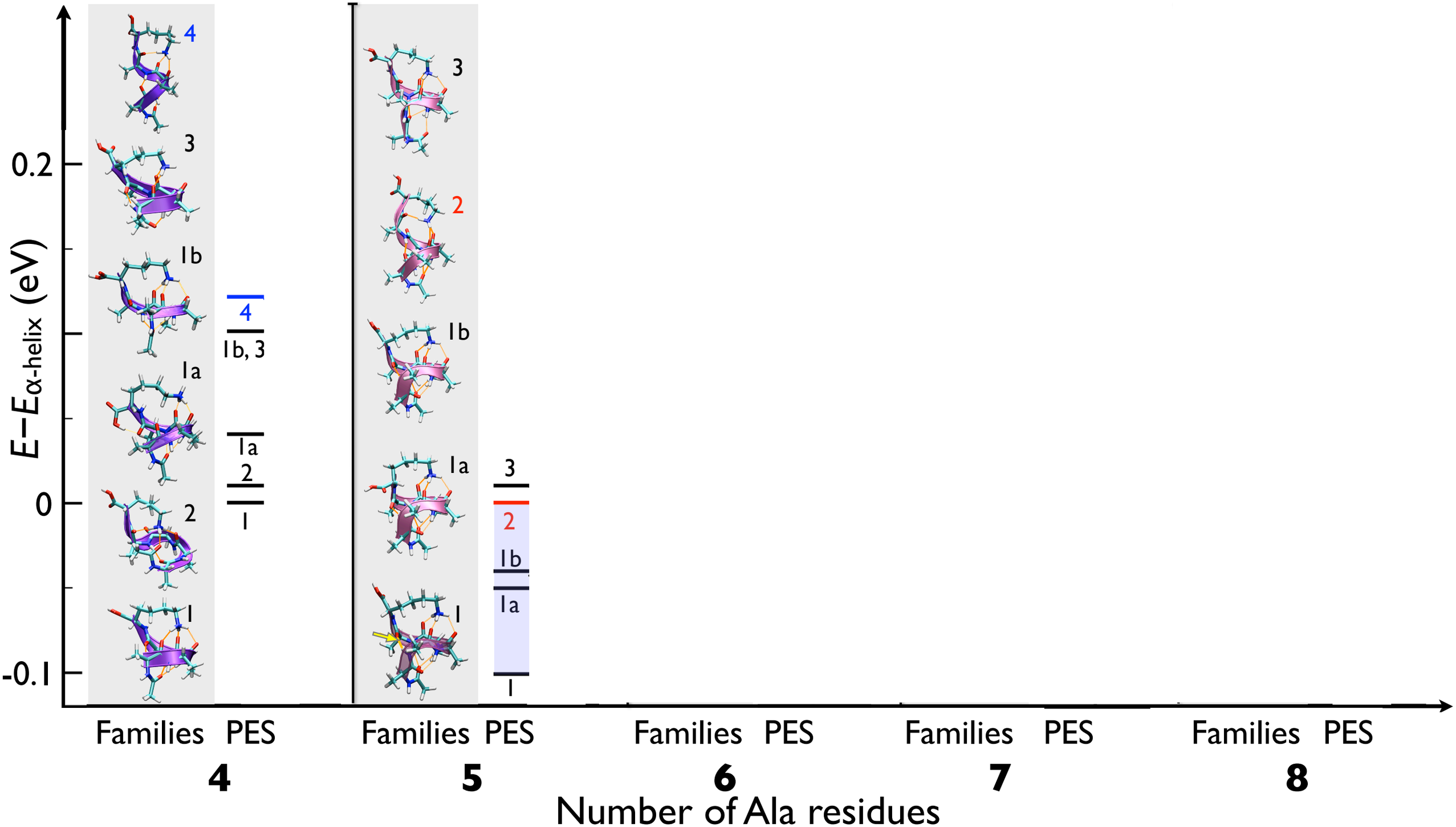

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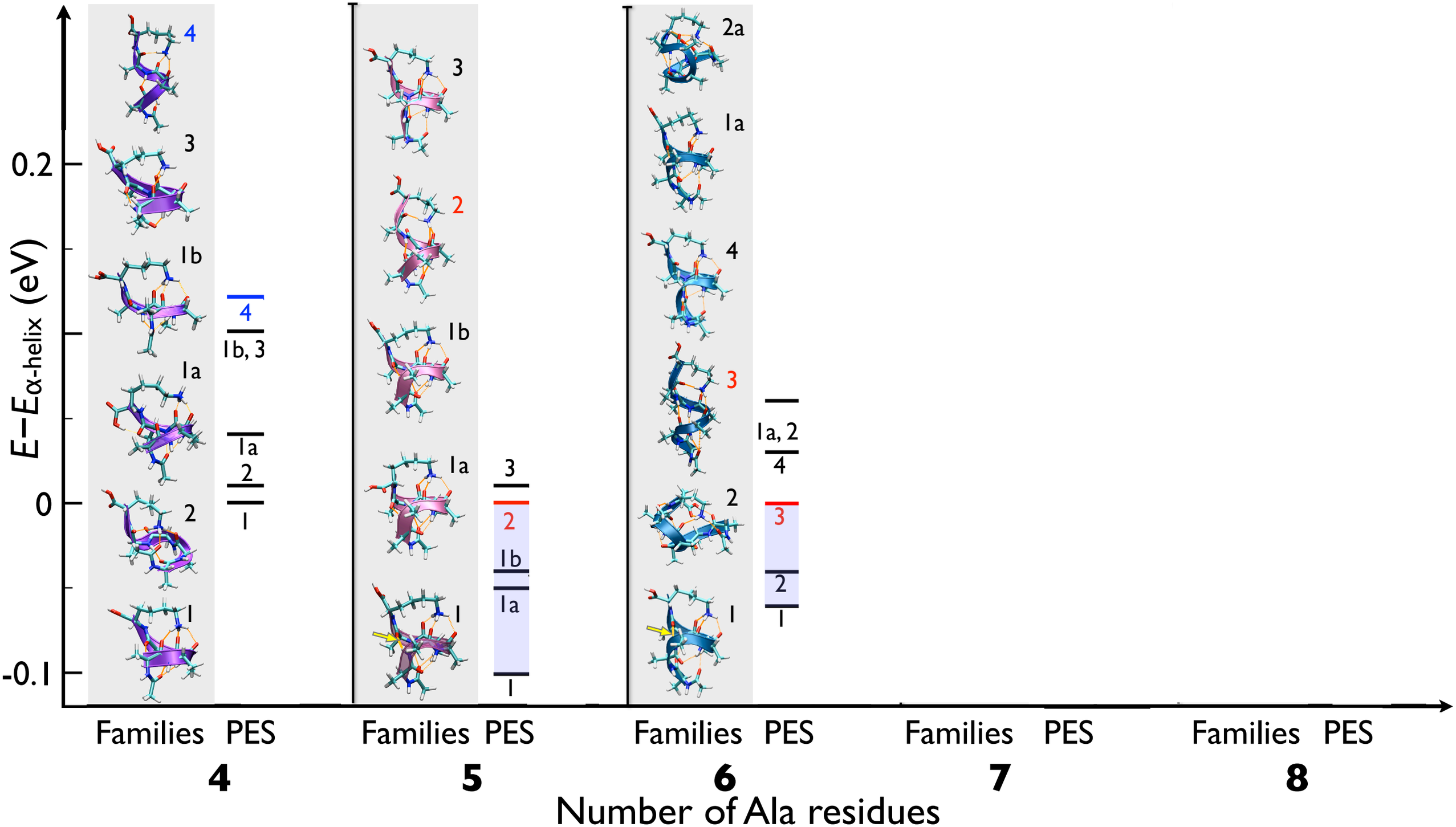

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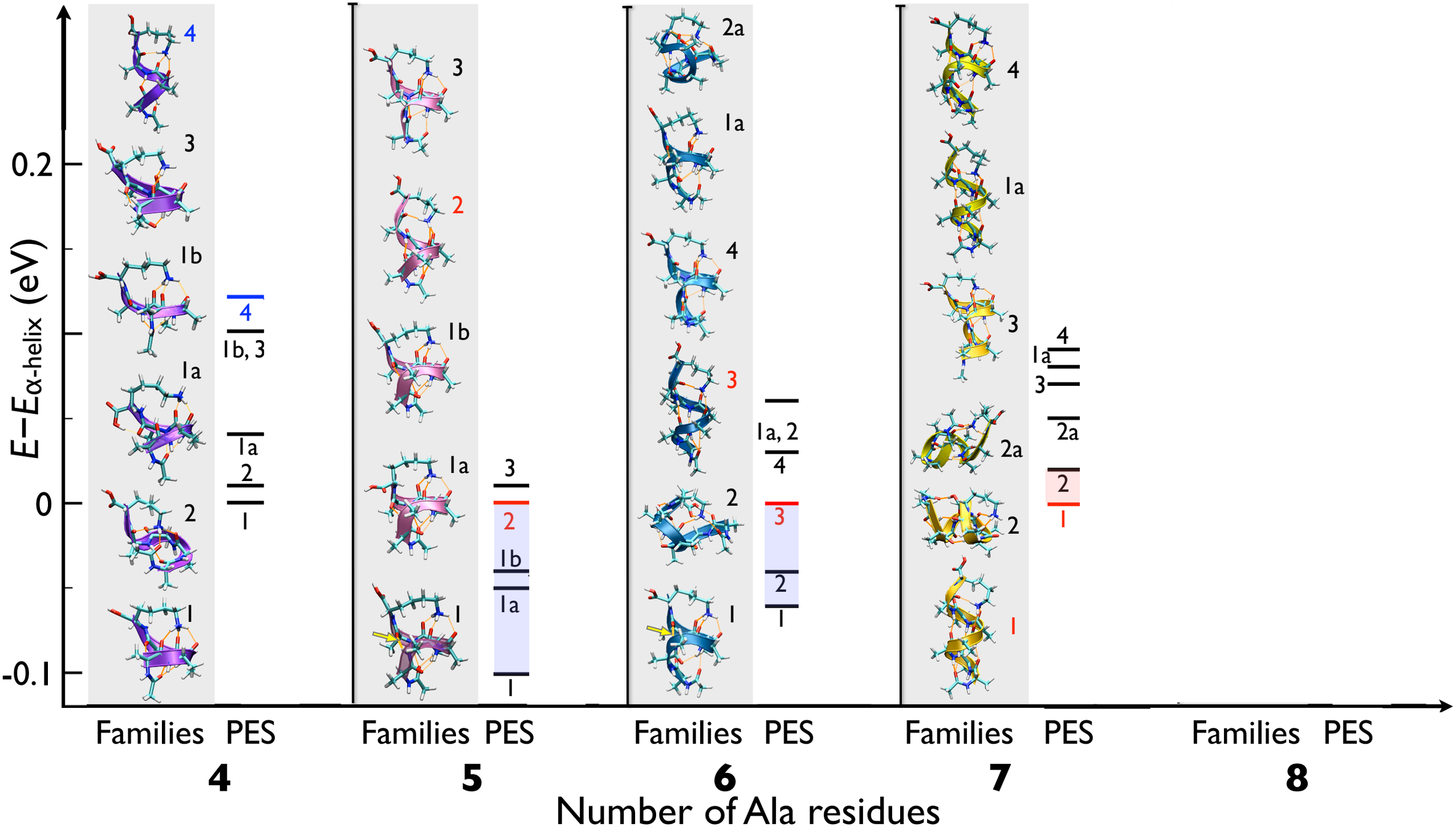

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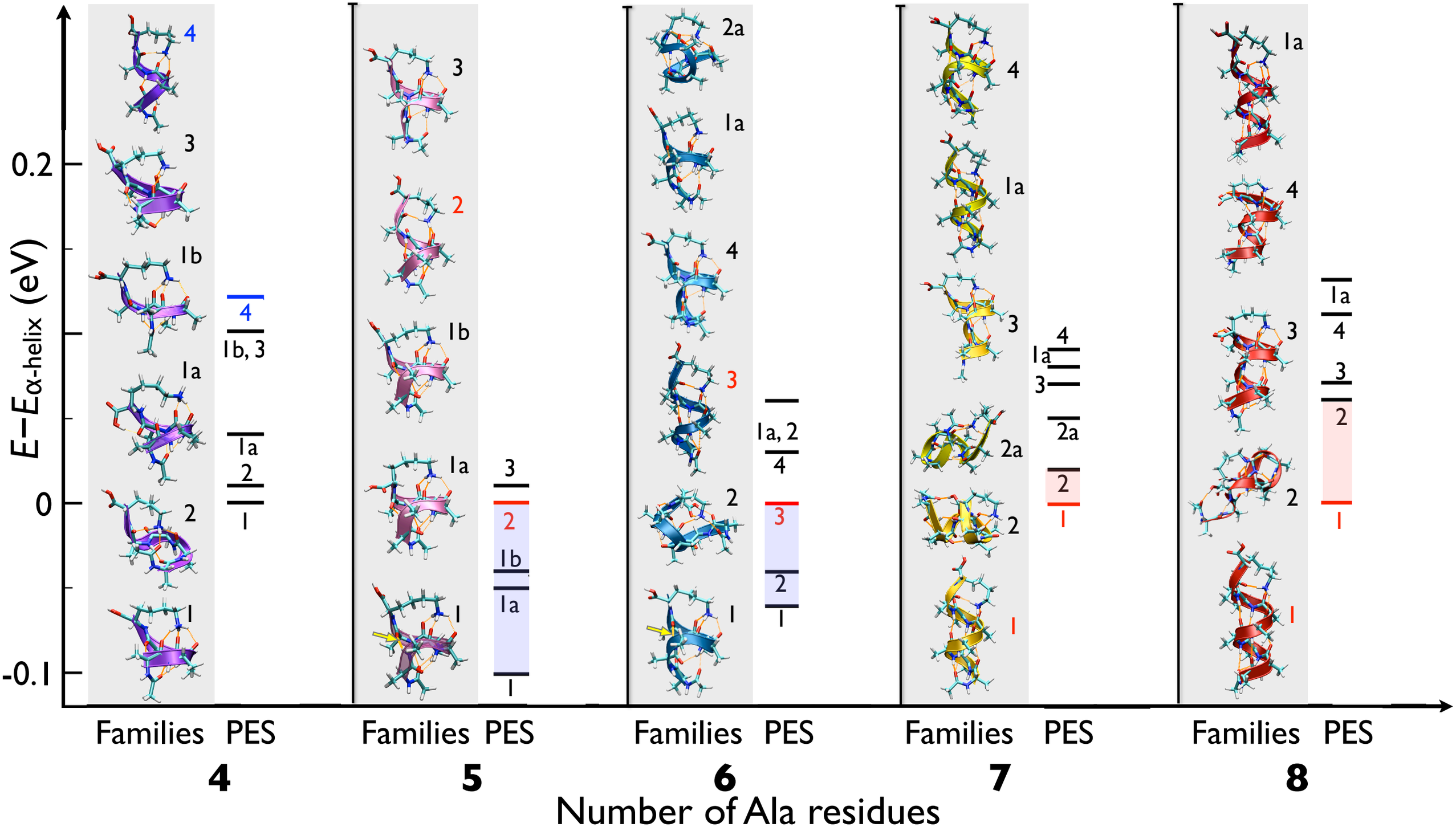

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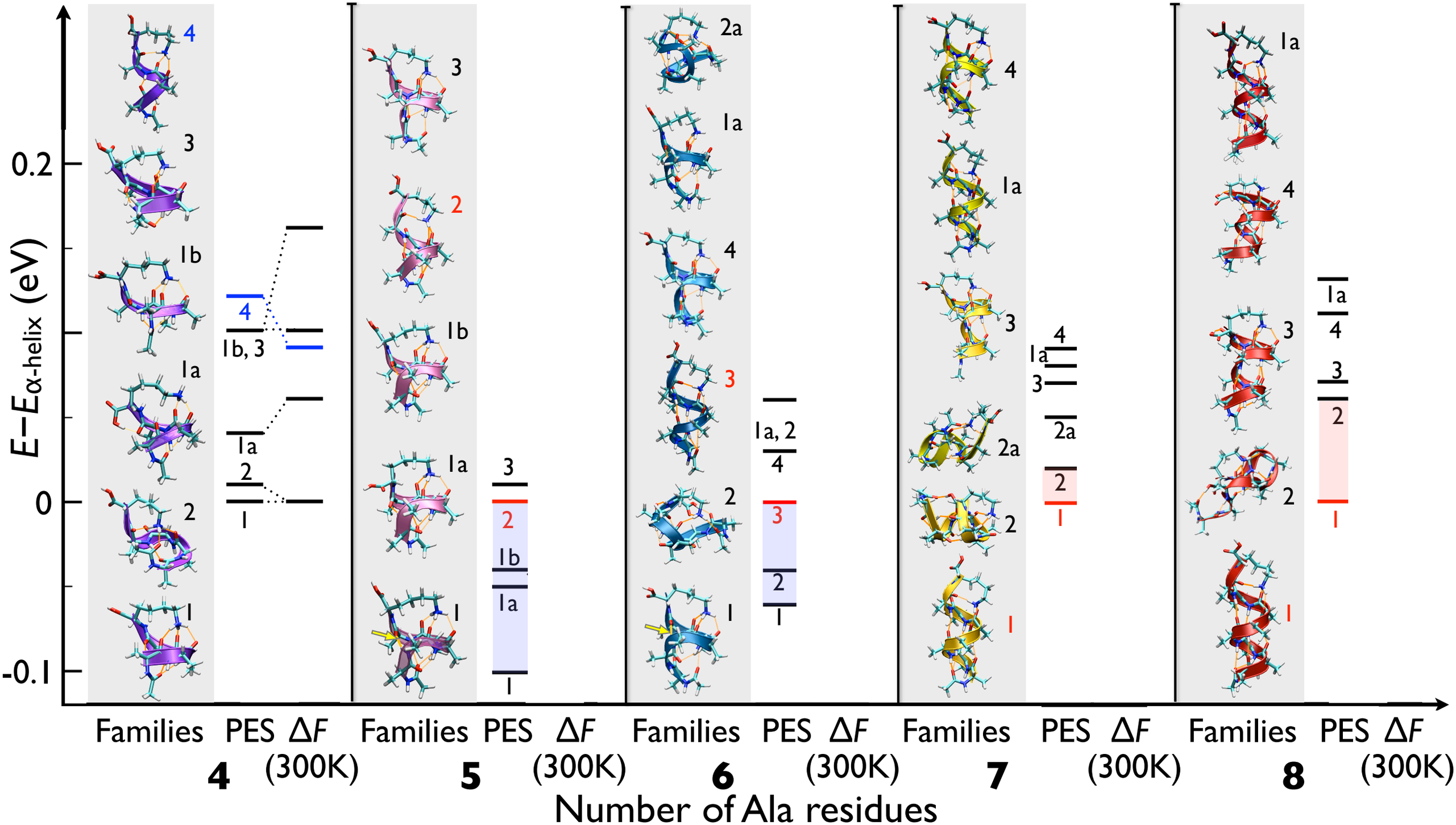

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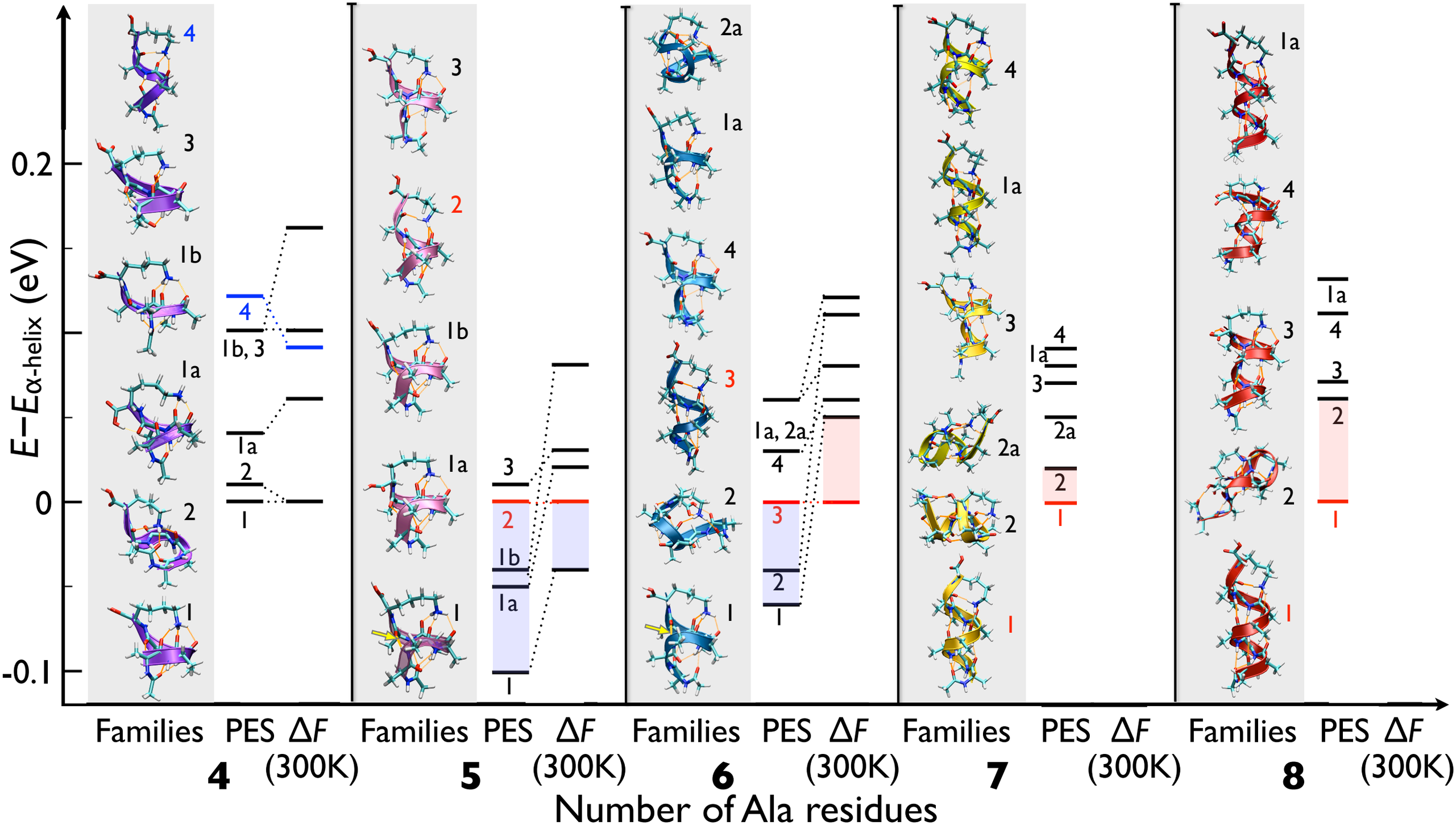

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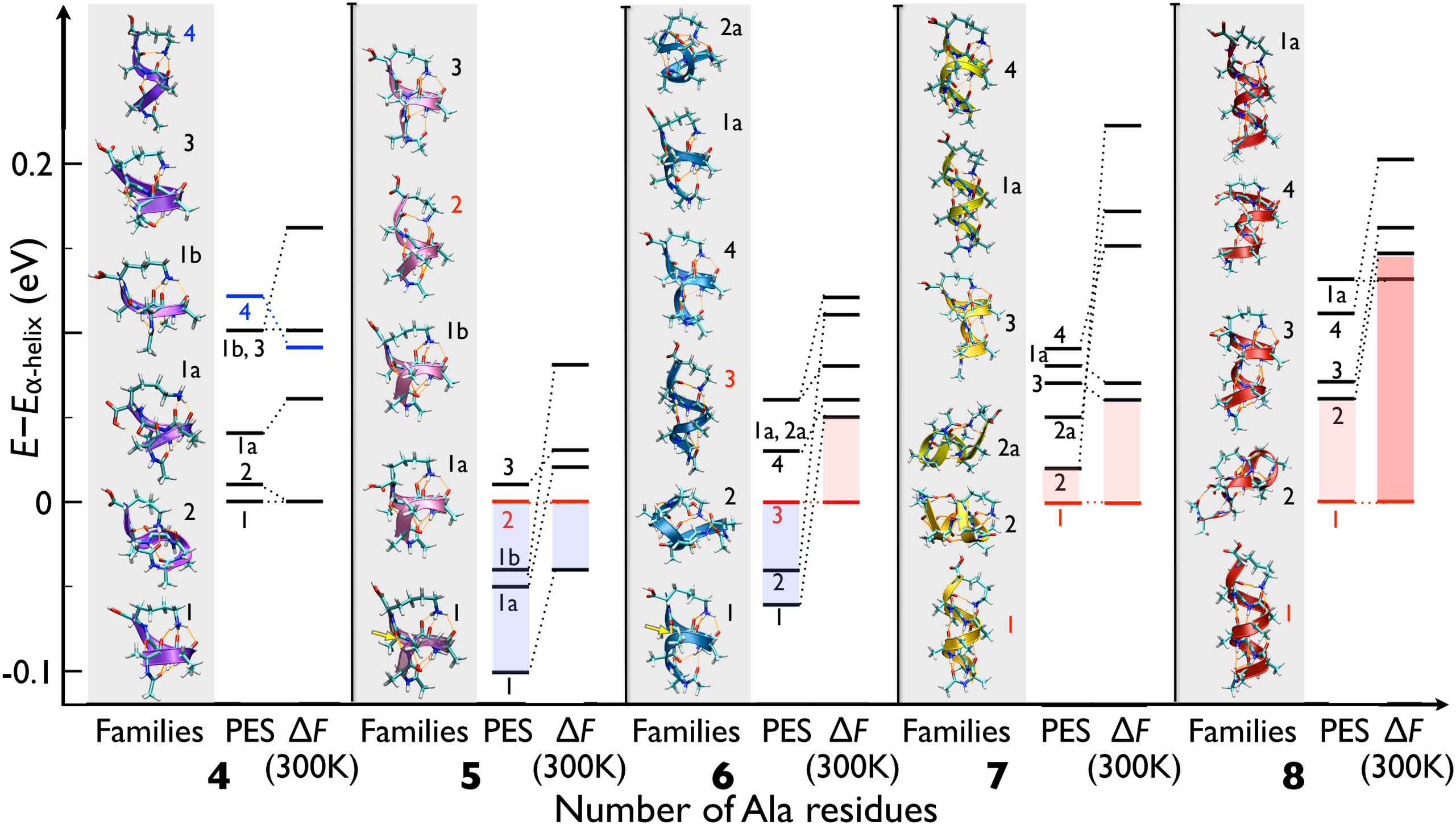

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Helices systematically stabilized over compact conformers, with increasing *T*

$E - E_{\alpha\text{-helix}}$ (eV)

0.2

0

-0.1

Families PES ΔF (300K)

4 **5** **6** **7** **8**

Number of Ala residues

Vibrational entropy favors more extended structures

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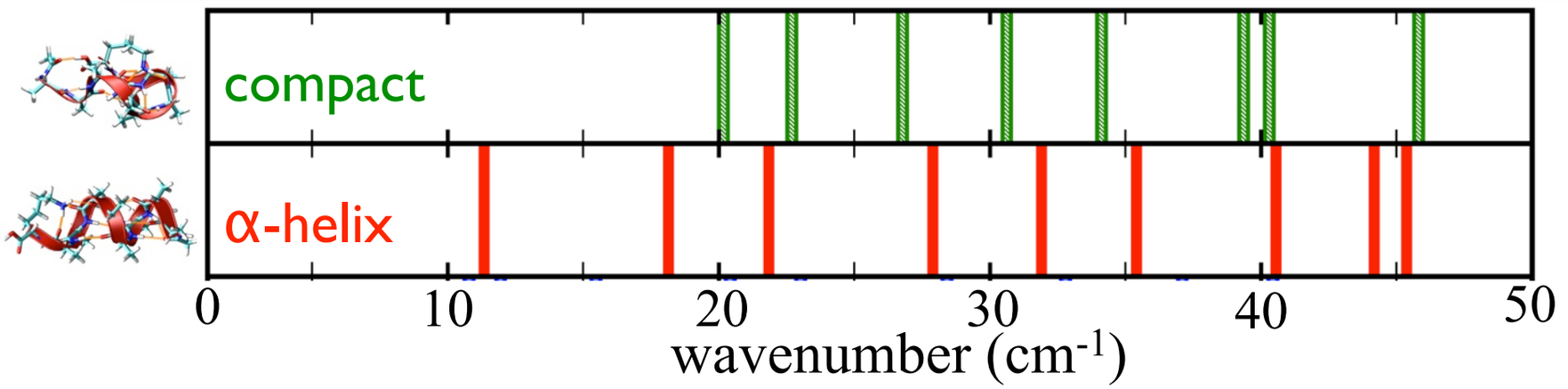

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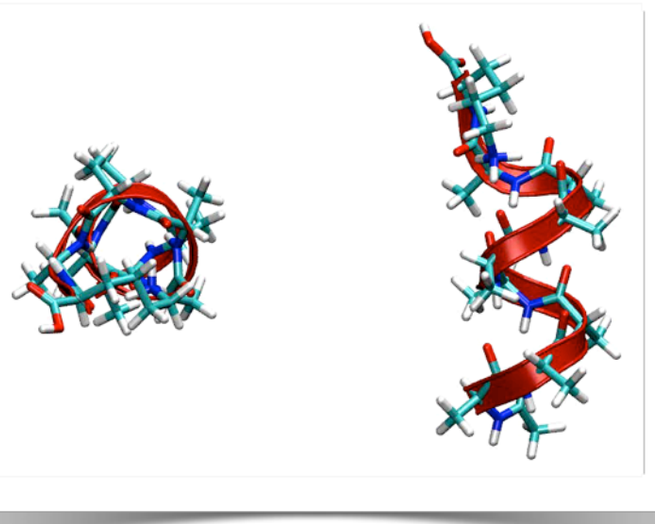

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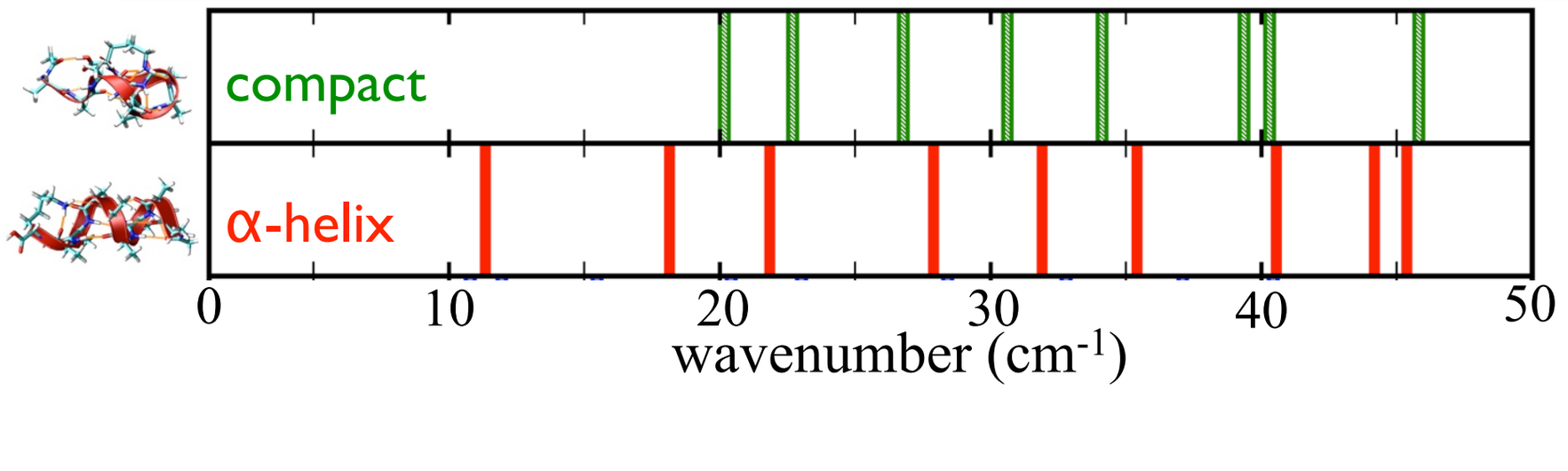

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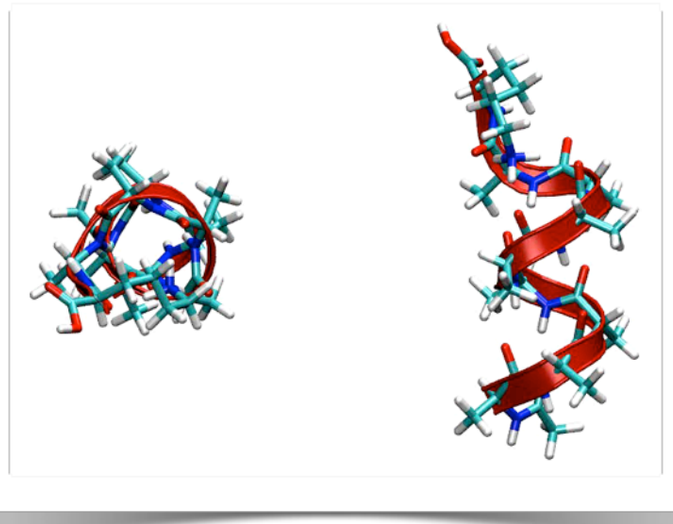

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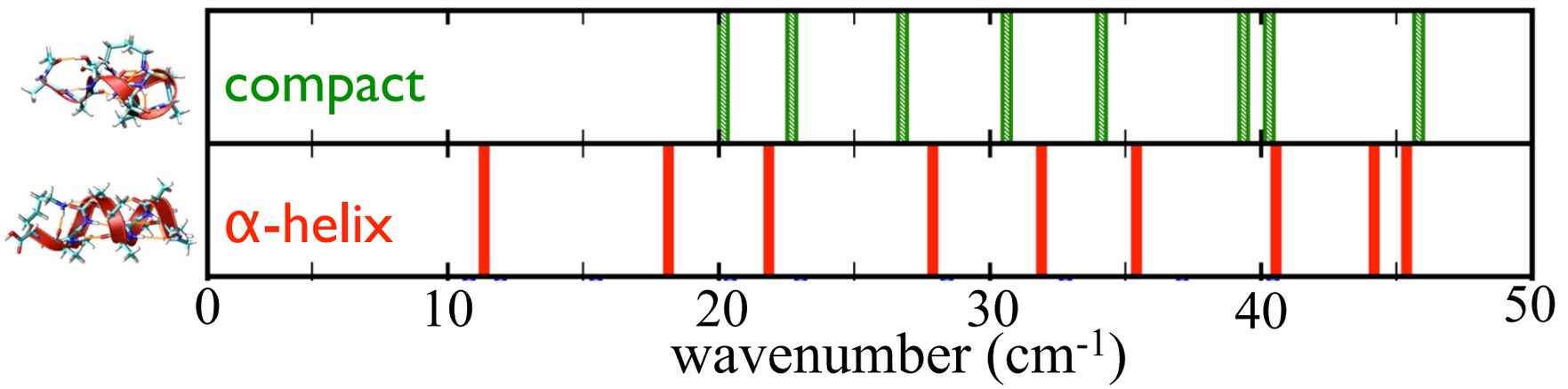

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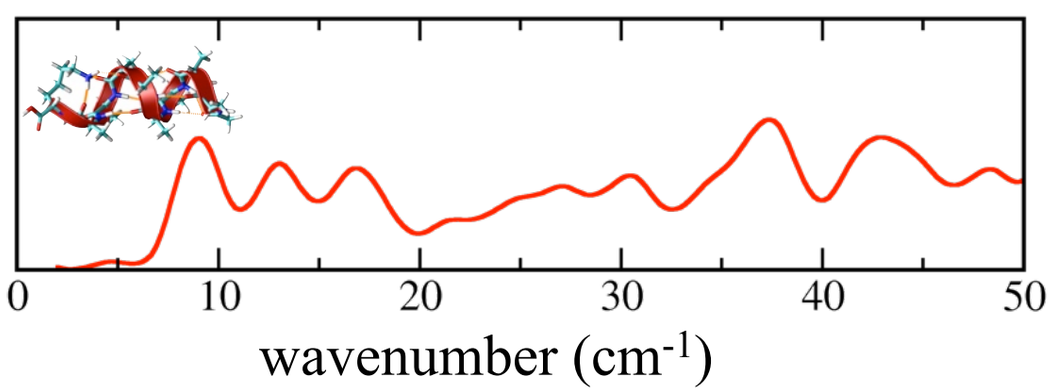
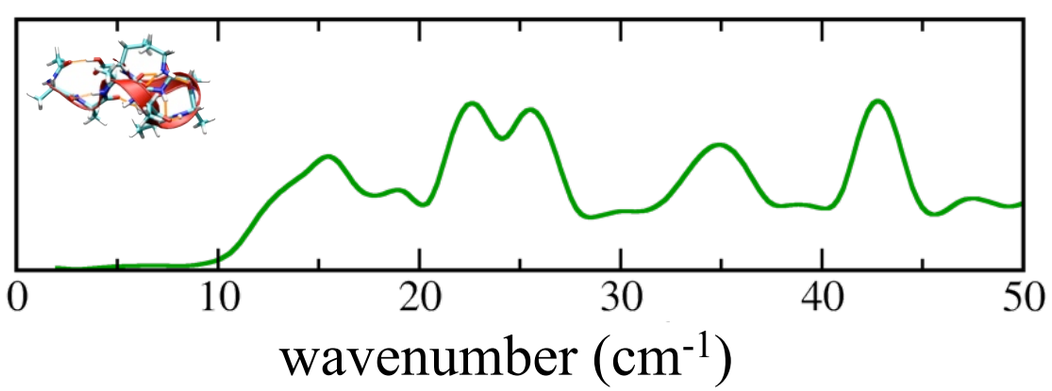
- 21ps of *ab initio* molecular dynamics (PBE+vdW), microcanonical ensemble

"anharmonic"
300K

$$\mathrm{VDOS}(\omega) \propto \int_0^\infty \langle \mathbf{v}(t)\mathbf{v}(0)\rangle \, e^{i\omega t}$$





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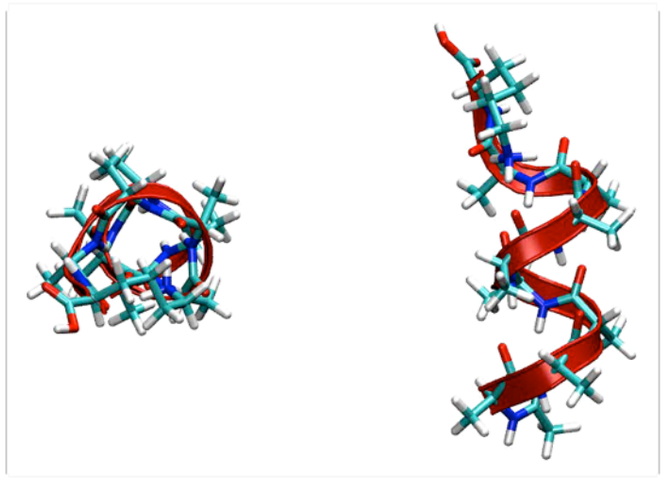

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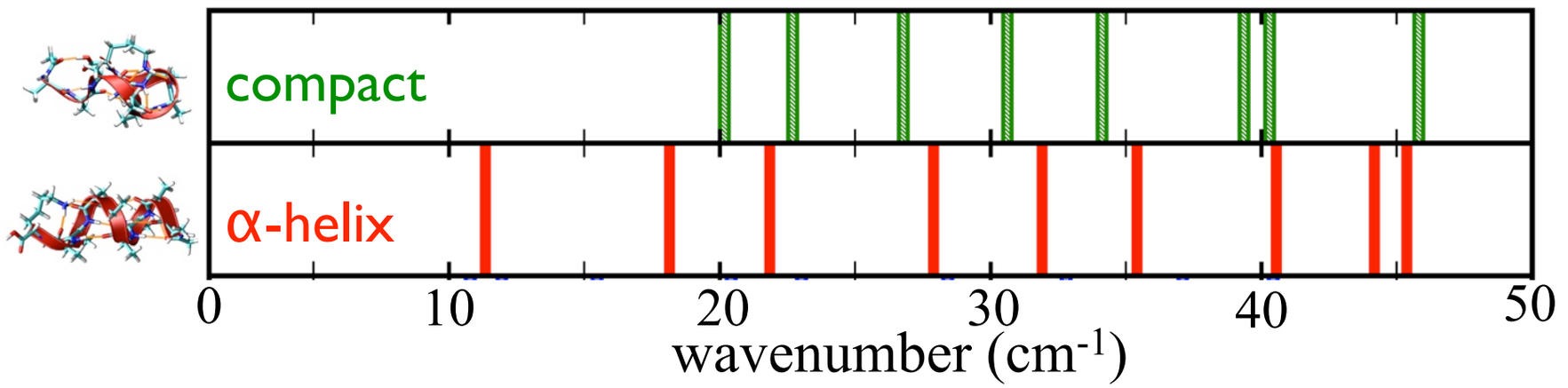

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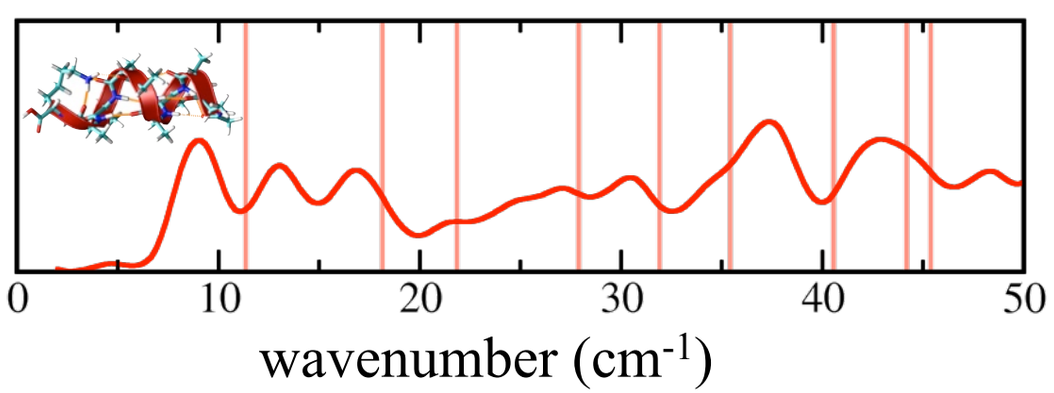
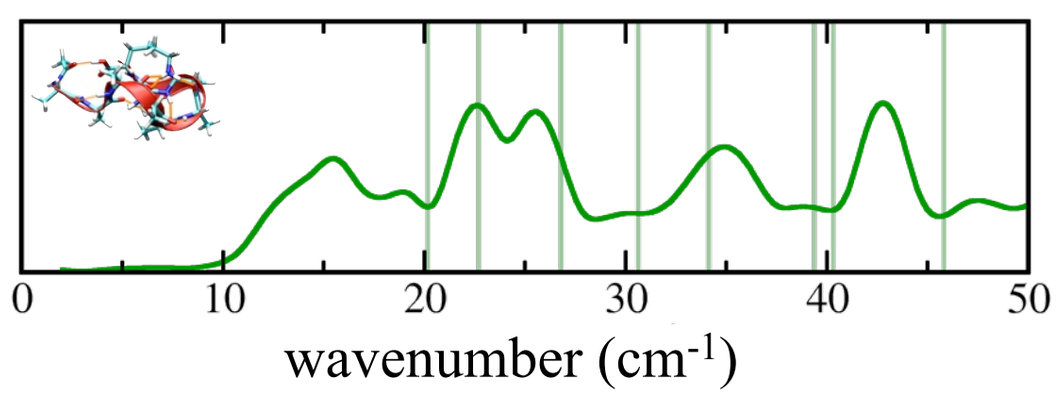
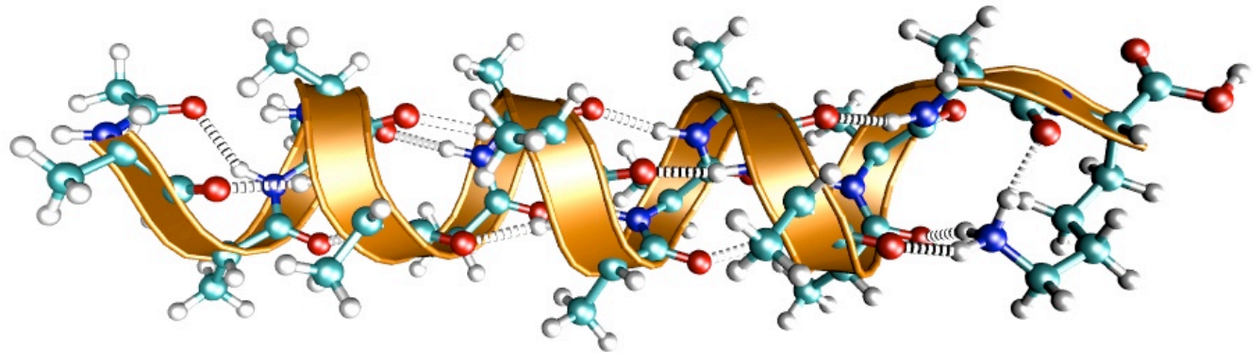
harmonic





What stabilizes helices in Polyalanine?



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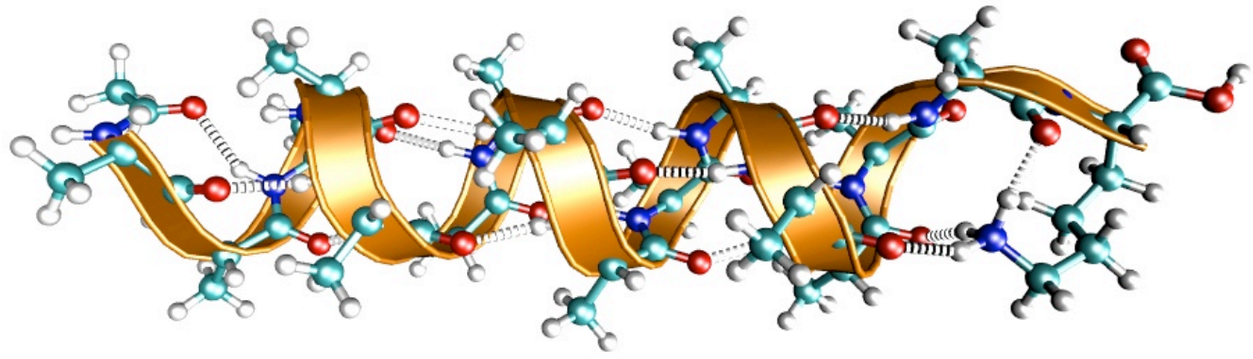


Conspiracy of:

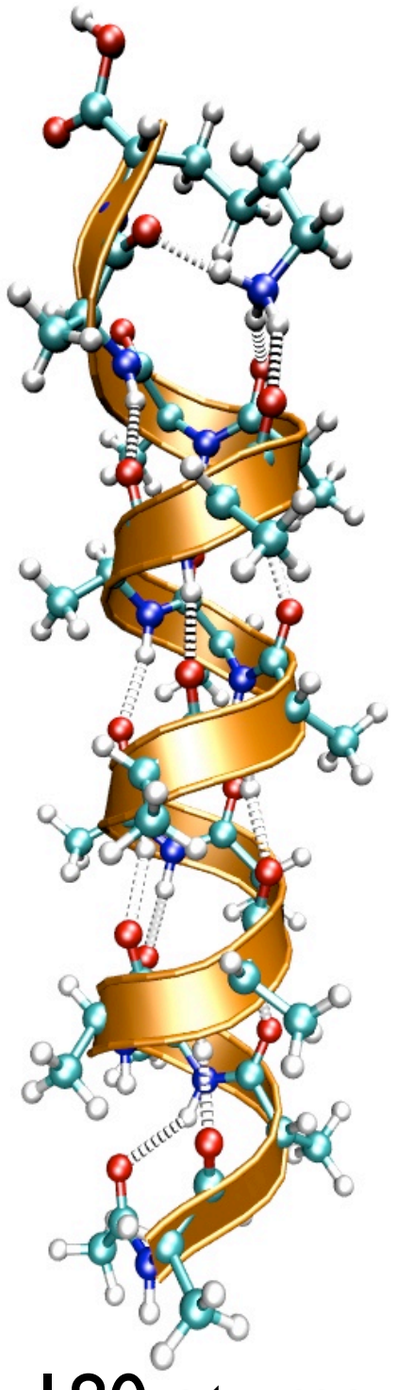
Hydrogen bonds & cooperativity
(need sufficient chain length)

van der Waals
(favors compact structures)

Entropy: Low-frequency vibrations
(disfavors compact structures with increasing *T*)

Vibrational spectroscopy: Ac-Ala$_{15}$-LysH$^+$

α-helical Ac-Ala$_{15}$-LysH$^+$

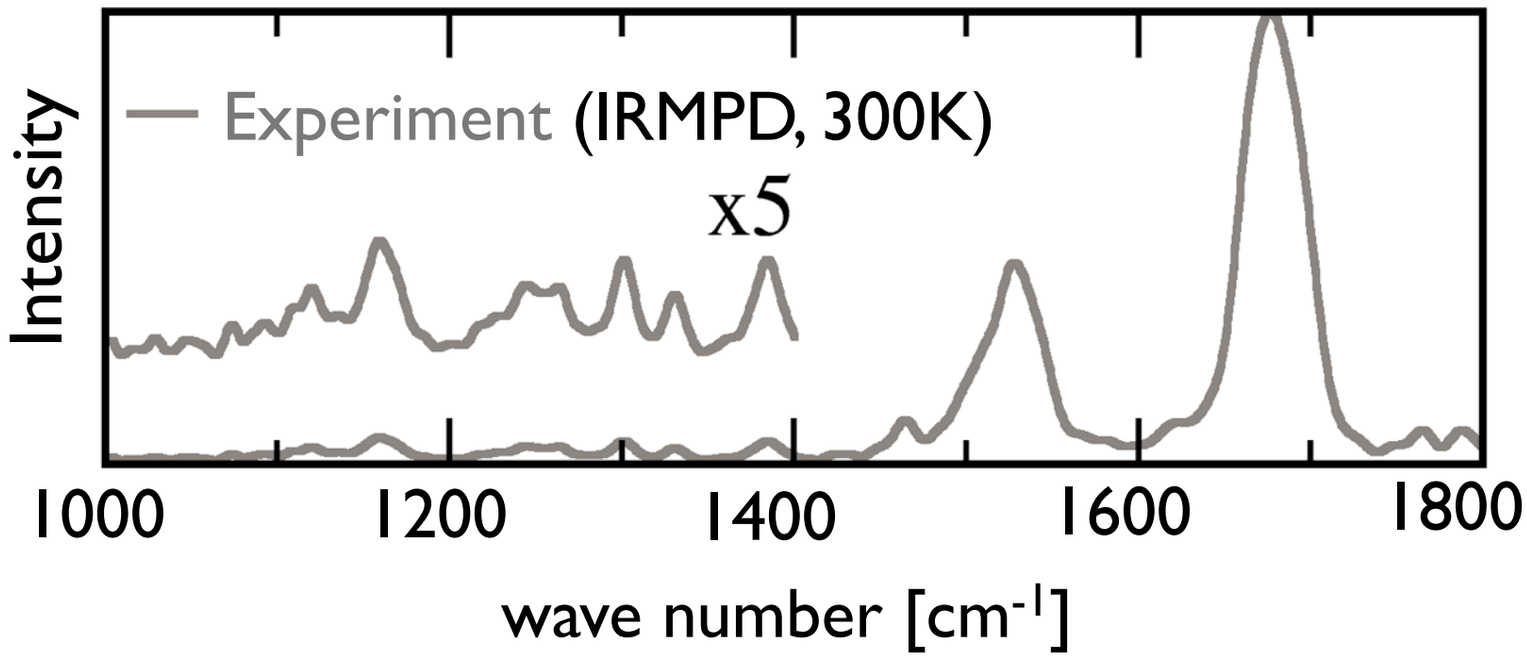


180 atoms

<u>Experiment</u>:
von Helden, Kupser, Bierau, Meijer, Molecular Physics, FHI Berlin

Infrared multiphoton dissociation spectroscopy, FELIX free electron laser

Room temperature



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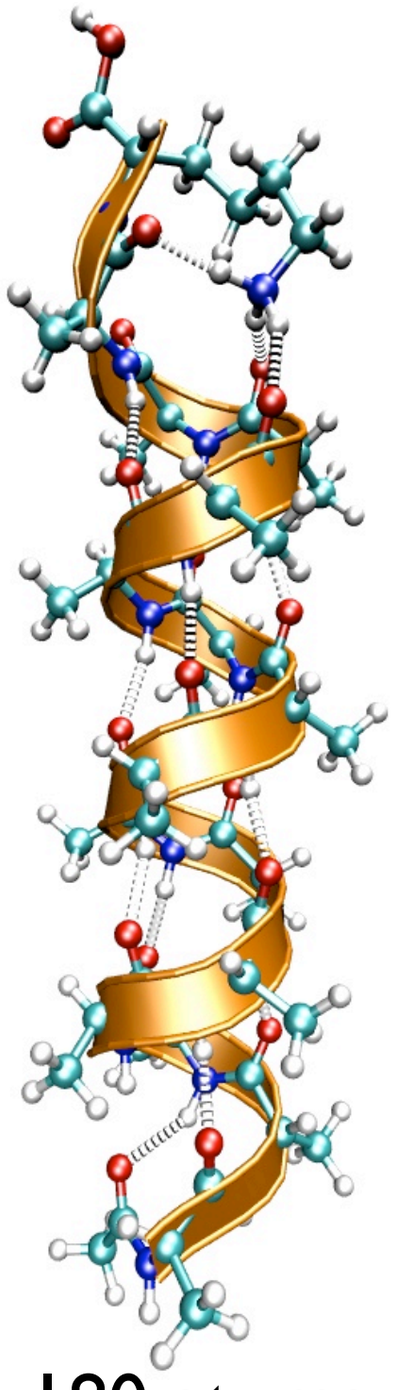

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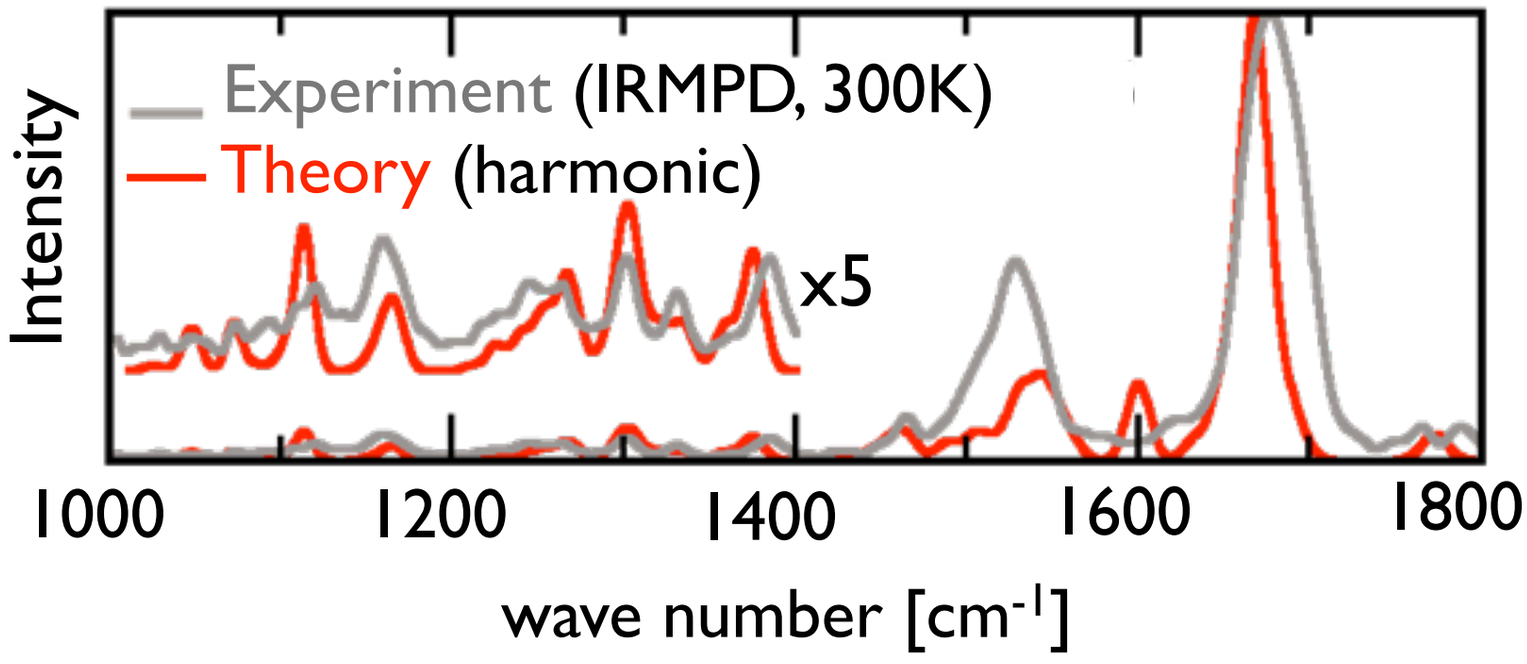

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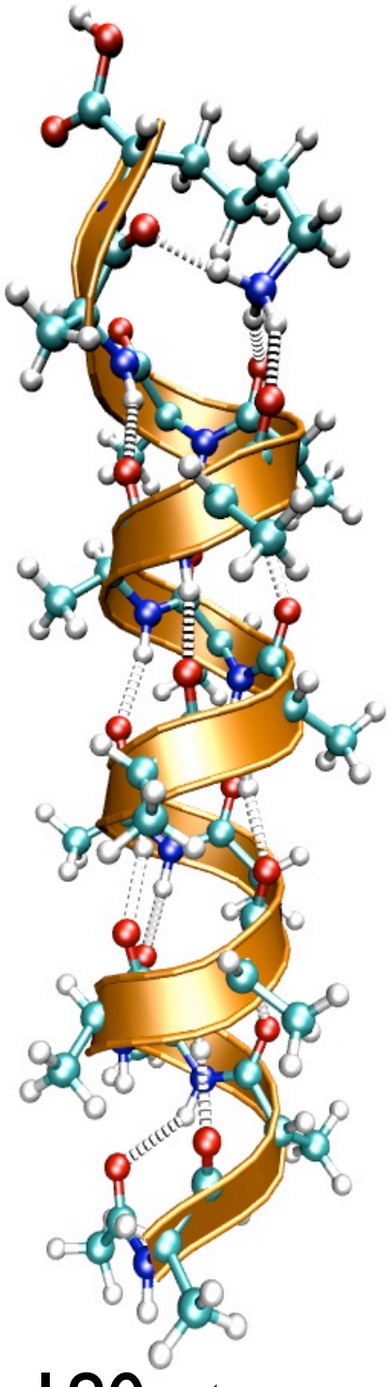

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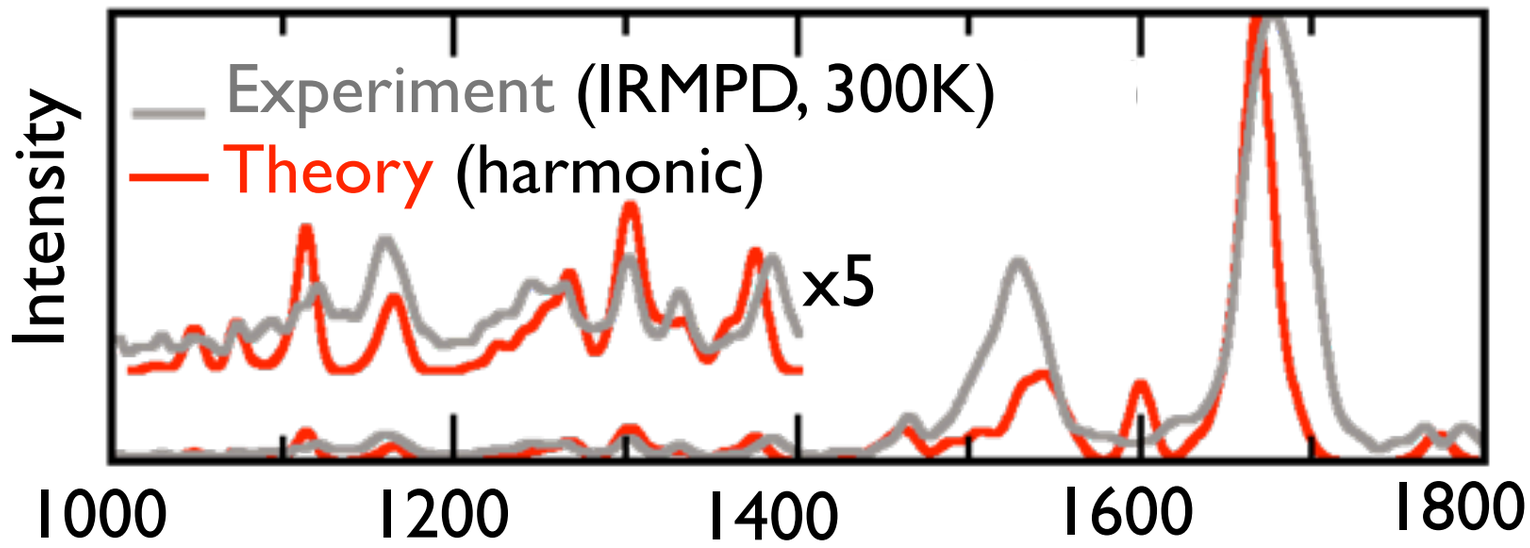
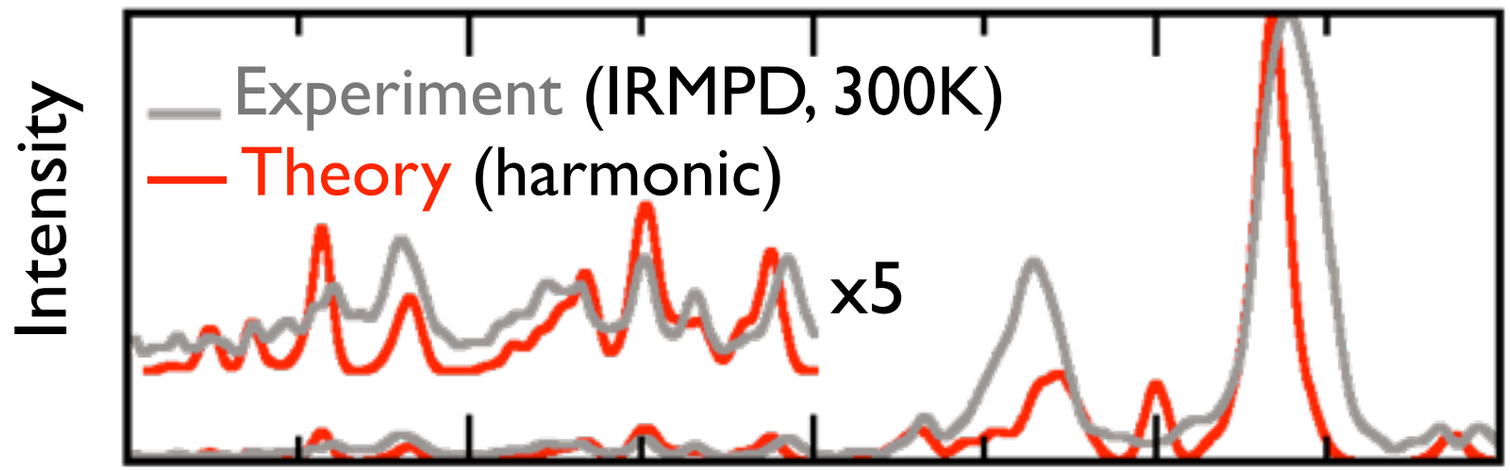


Vibrational spectroscopy: Ac-Ala$_{15}$-LysH$^+$

25 ps Born-Oppenheimer molecular dynamics, DFT-PBE+vdW

*M. Rossi, V. Blum, P. Kupser, G. von Helden, F. Bierau, K. Pagel, G. Meijer, and M. Scheffler, J. Phys. Chem. Lett. **1**, 3465 (2010)*

Theory: PBE+vdW, shifted, not scaled



$$I(\omega) \propto \omega^2 \int_{\infty}^{\infty} dt \, \underbrace{\langle \vec{M}(t) \cdot \vec{M}(0) \rangle}_{} \, e^{iwt}$$

dipole-dipole time correlation function

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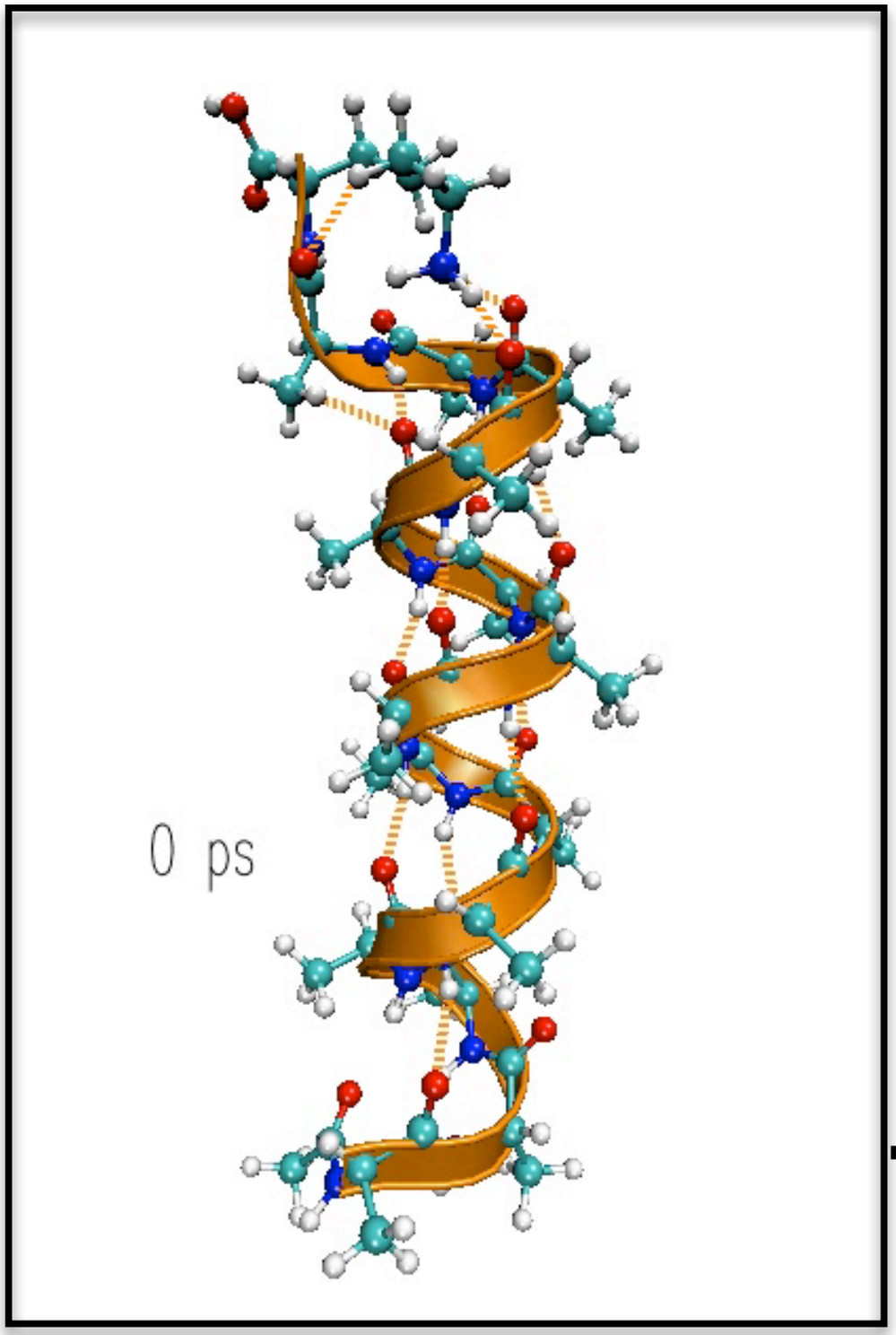

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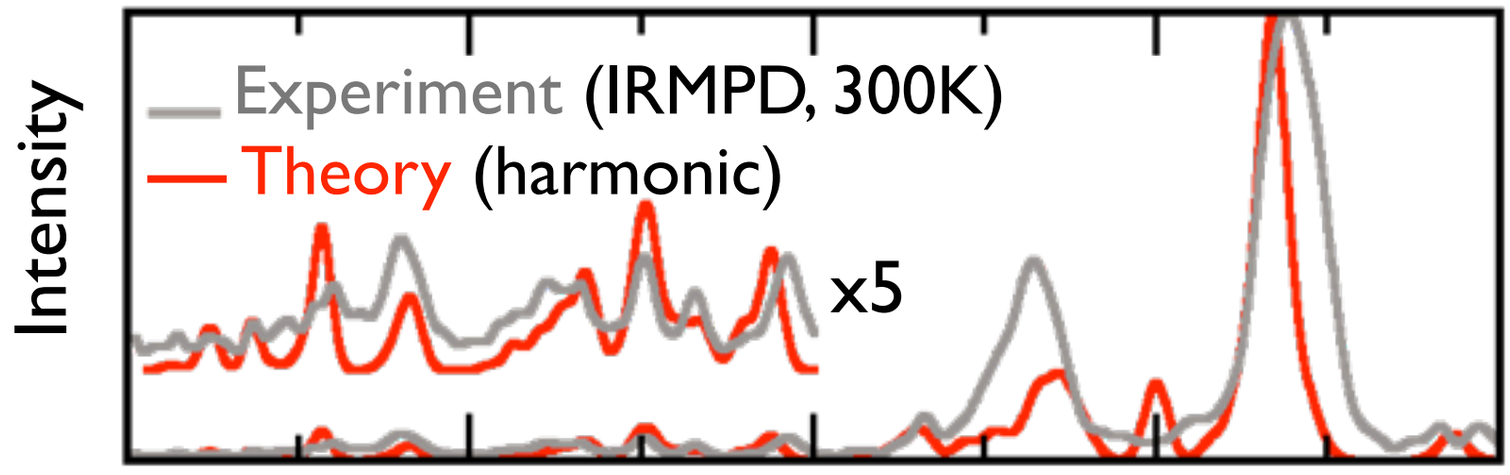

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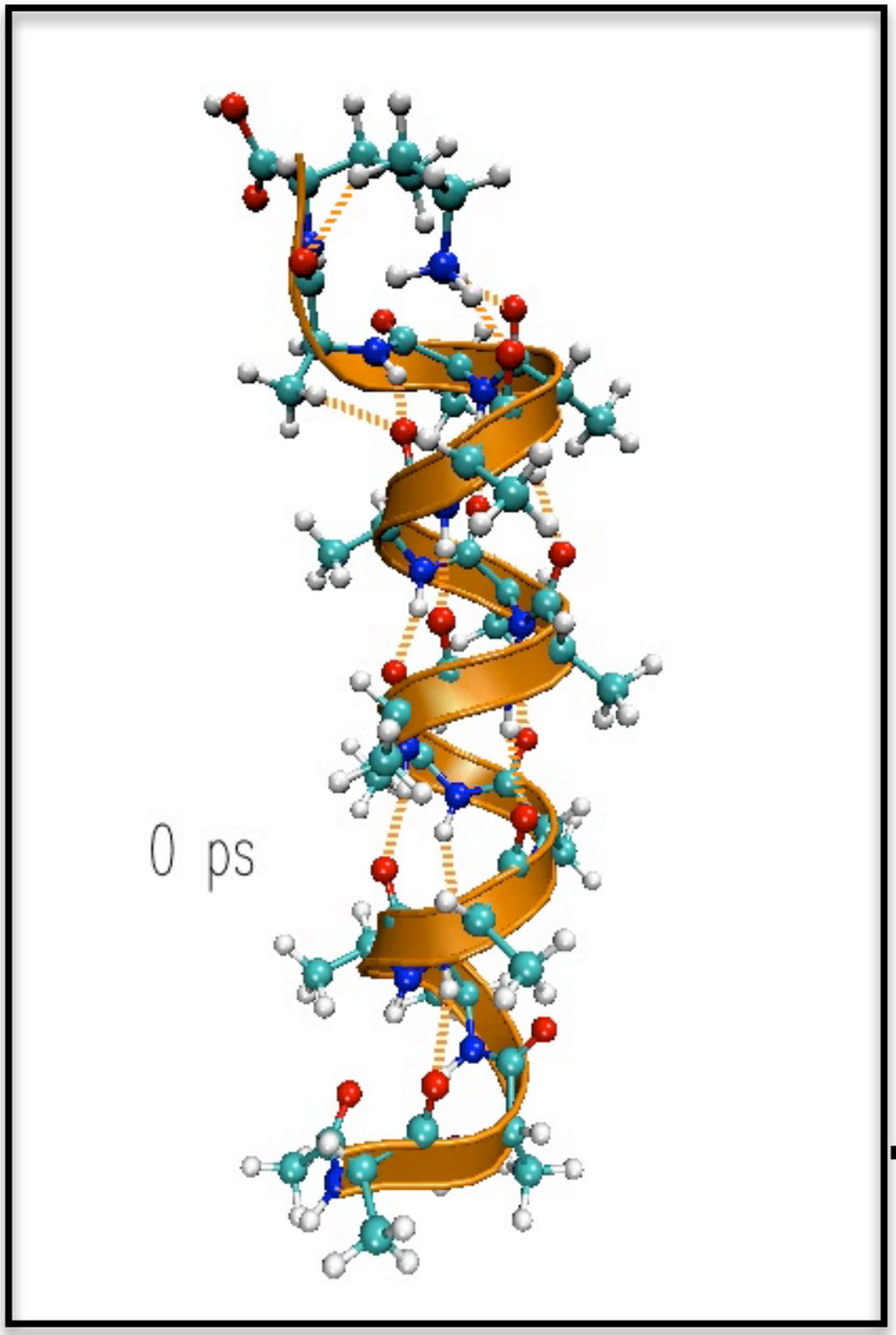

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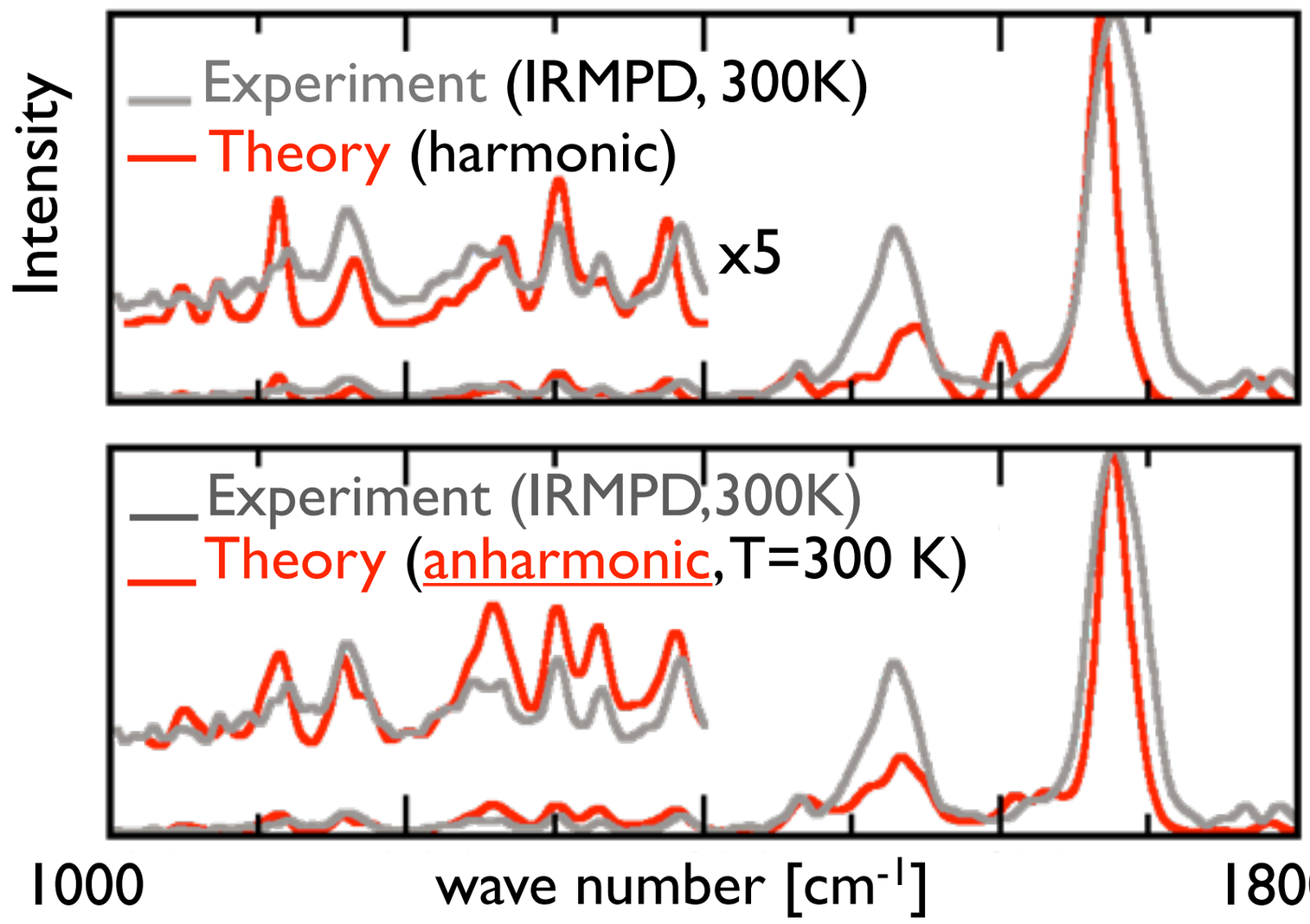

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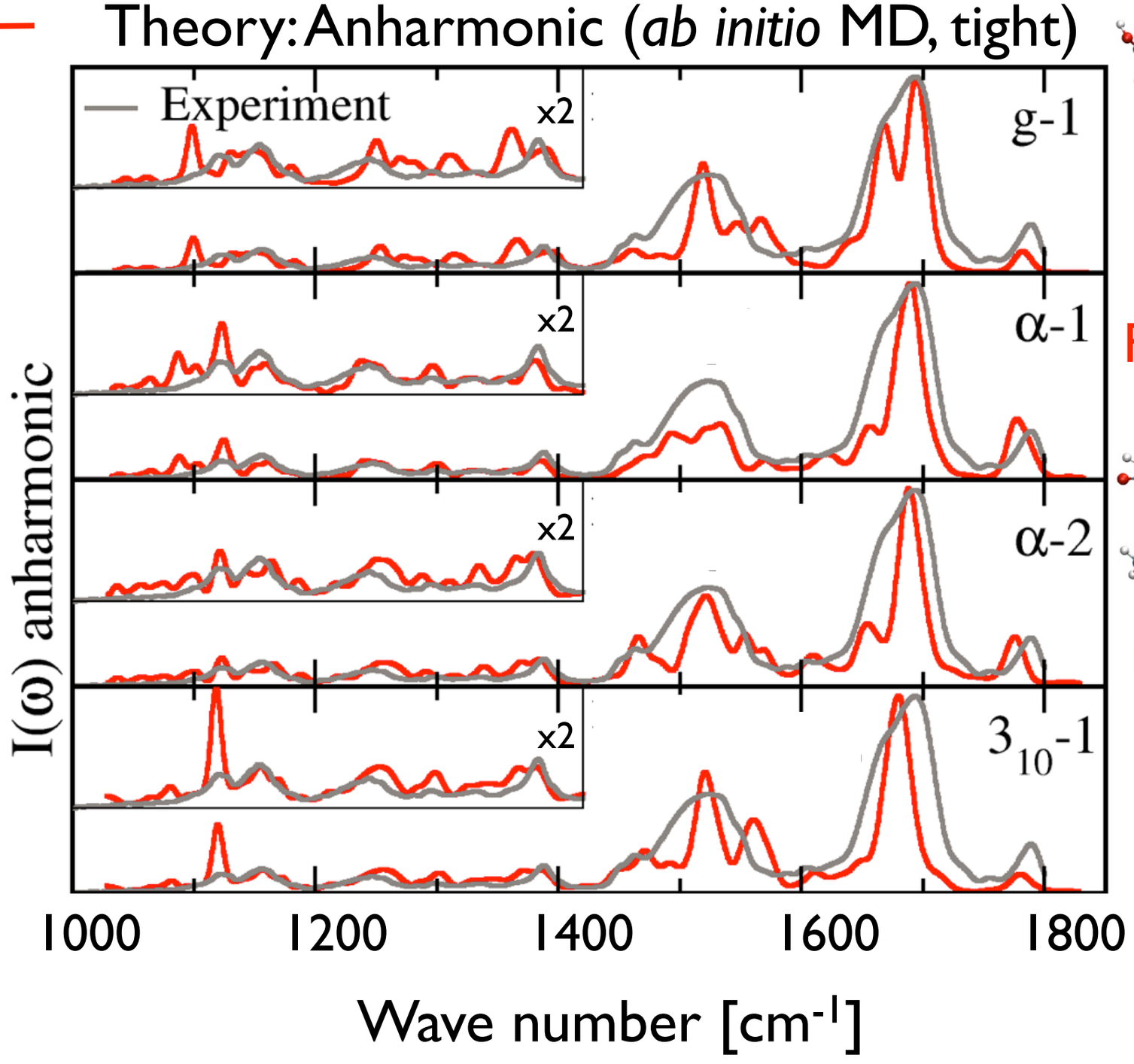
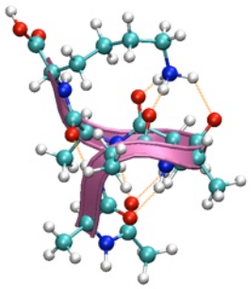
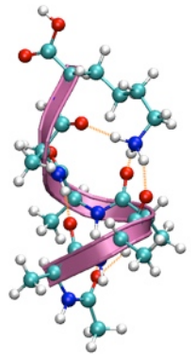
dipole-dipole time correlation function

Ac-Ala$_5$-LysH$^+$: Anharmonic theory vs experiment

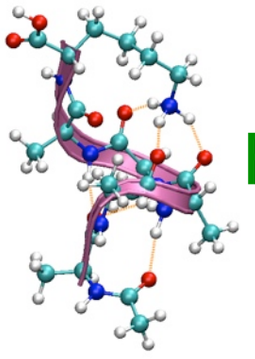




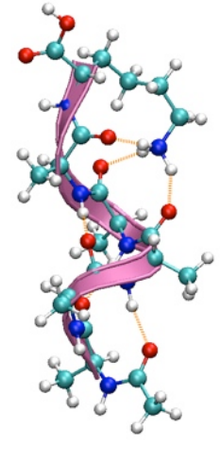
Fam. 1 :g-1



Fam. 2: α-1

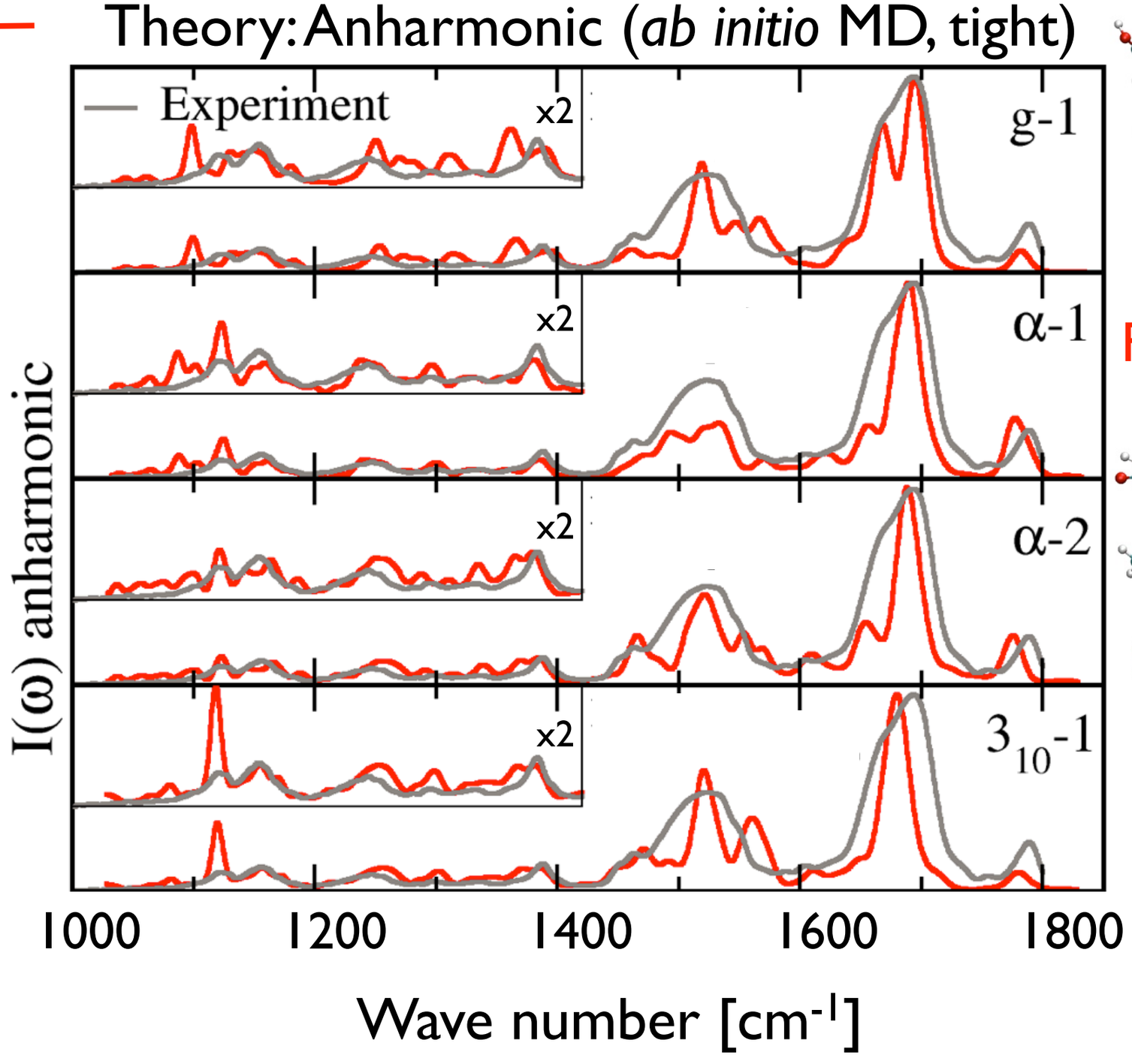


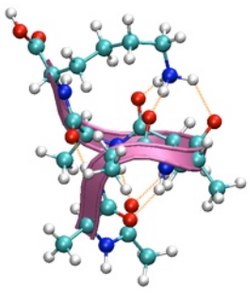
Fam. 3: α-2



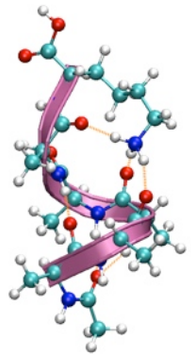
3$_{10}$-1

Ac-Ala$_5$-LysH$^+$: Anharmonic theory vs experiment

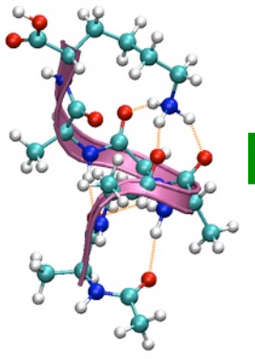




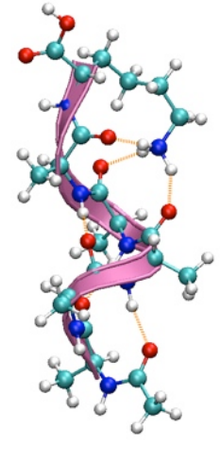
Fam.1 :g-1



Fam. 2: α-1



Fam. 3: α-2

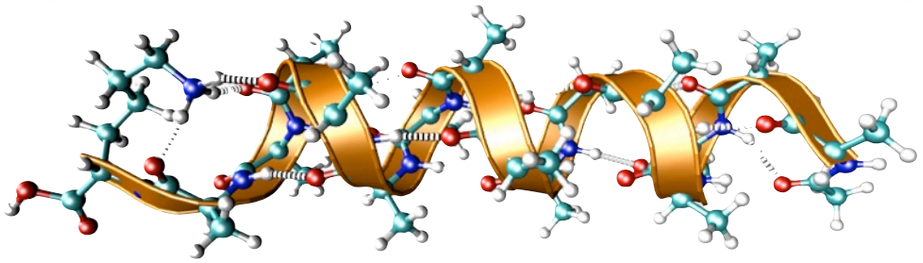


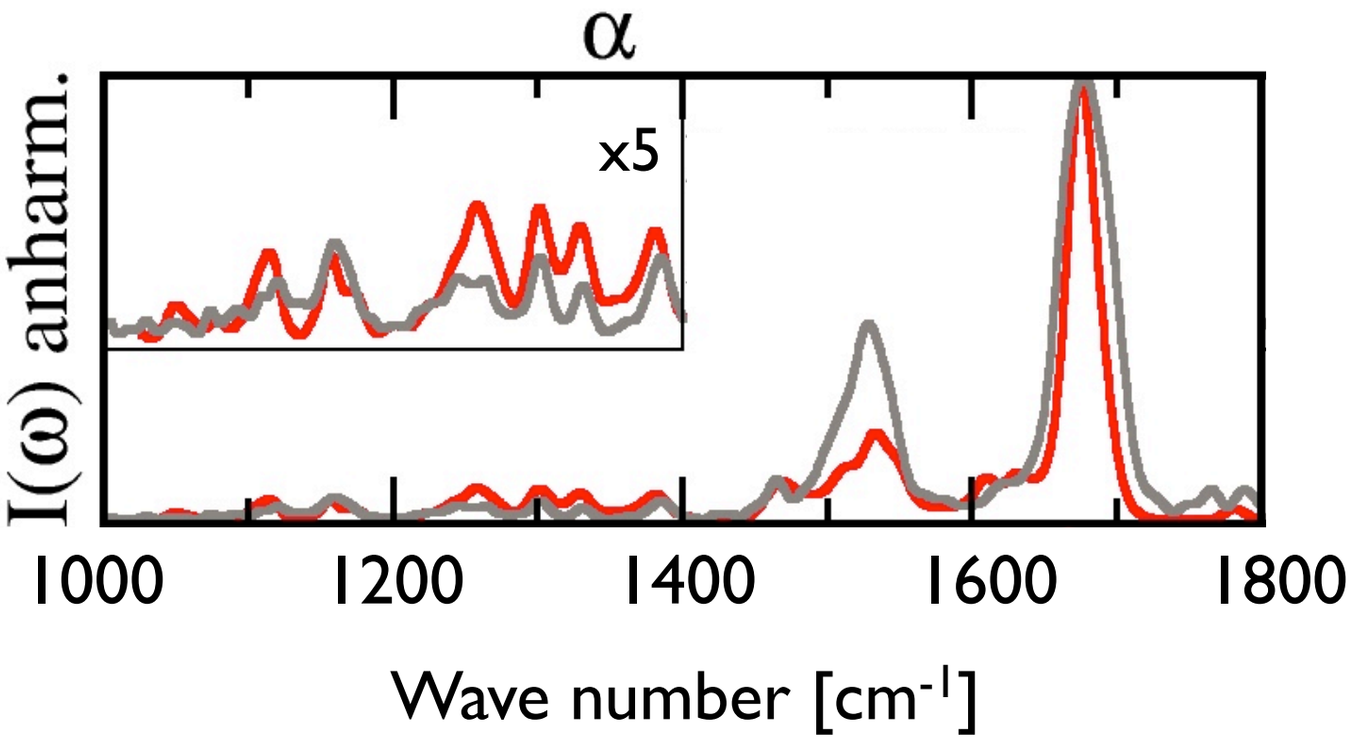
3_{10}-1

Eye inspection does not really help...

Quantifying continuous spectra: The Pendry R-factor

Example: α helical Ac-Ala$_{15}$-LysH$^+$





Experiment-theory comparison:

- continuous spectra (300 K)
- peak positions matter, not so much absolute intensities

Quantifying continuous spectra: The Pendry R-factor

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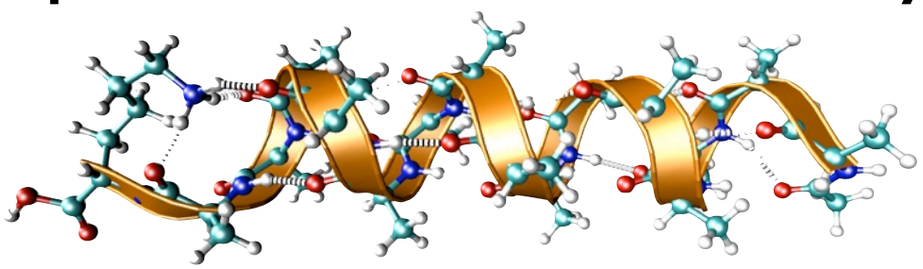

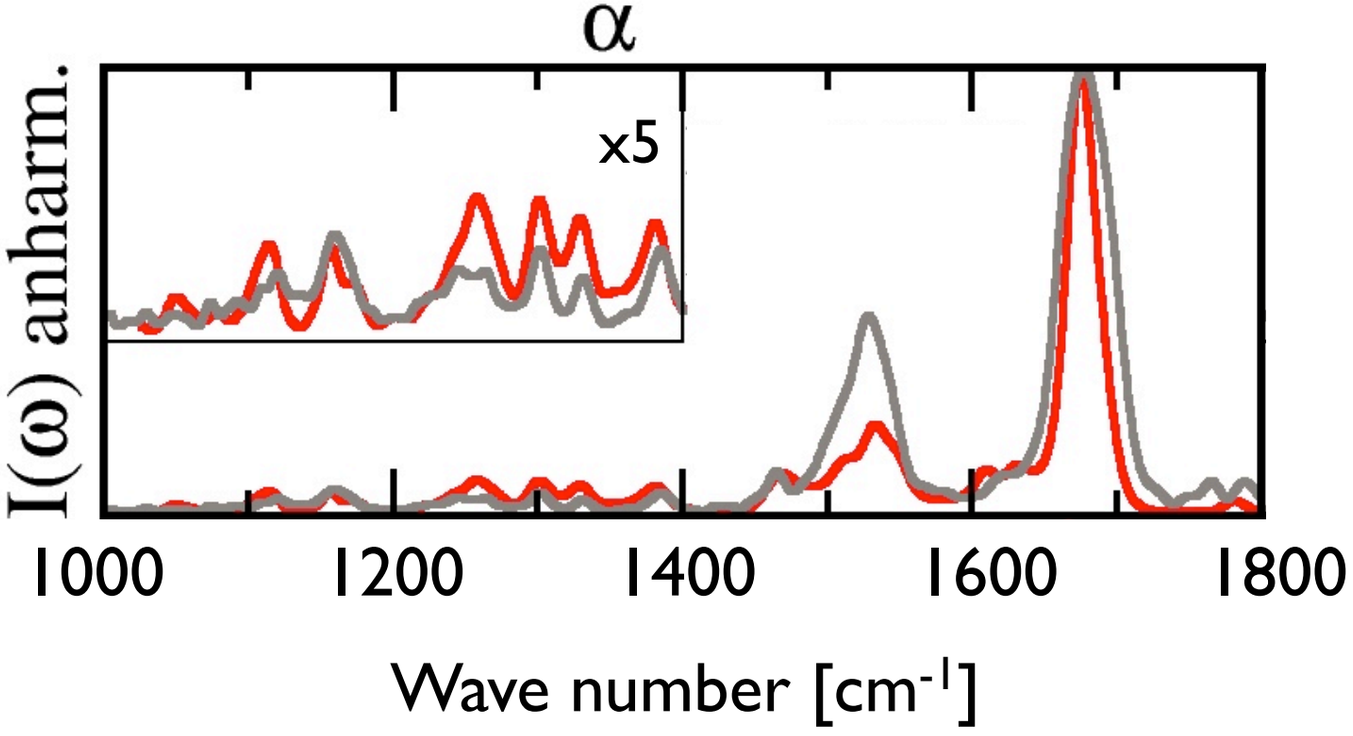

Experiment-theory comparison:

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→ Solved problem

(Low energy electron diffraction): "Pendry R-factor"

J.B. Pendry, J. Phys. C 3, 937 (1980)

Compare rescaled logarithmic derivative of intensity:

$$R_P = \frac{\int dk [Y_{\rm th}(k) - Y_{\rm exp}(k)]^2}{\int dk [Y_{\rm th}(k) + Y_{\rm exp}(k)]^2}$$

$$Y(k) = \frac{I(k)/I'(k)}{[I(k)/I'(k)]^2 + w^2}$$

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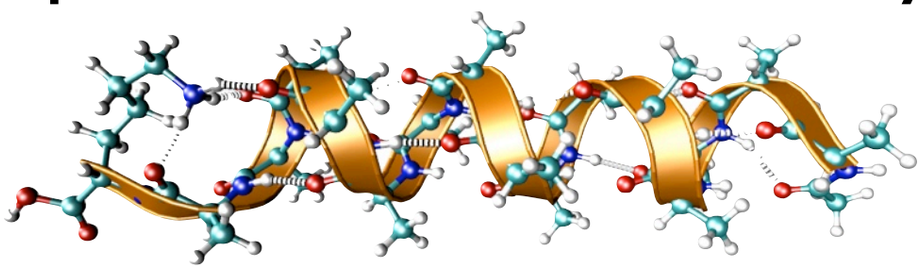

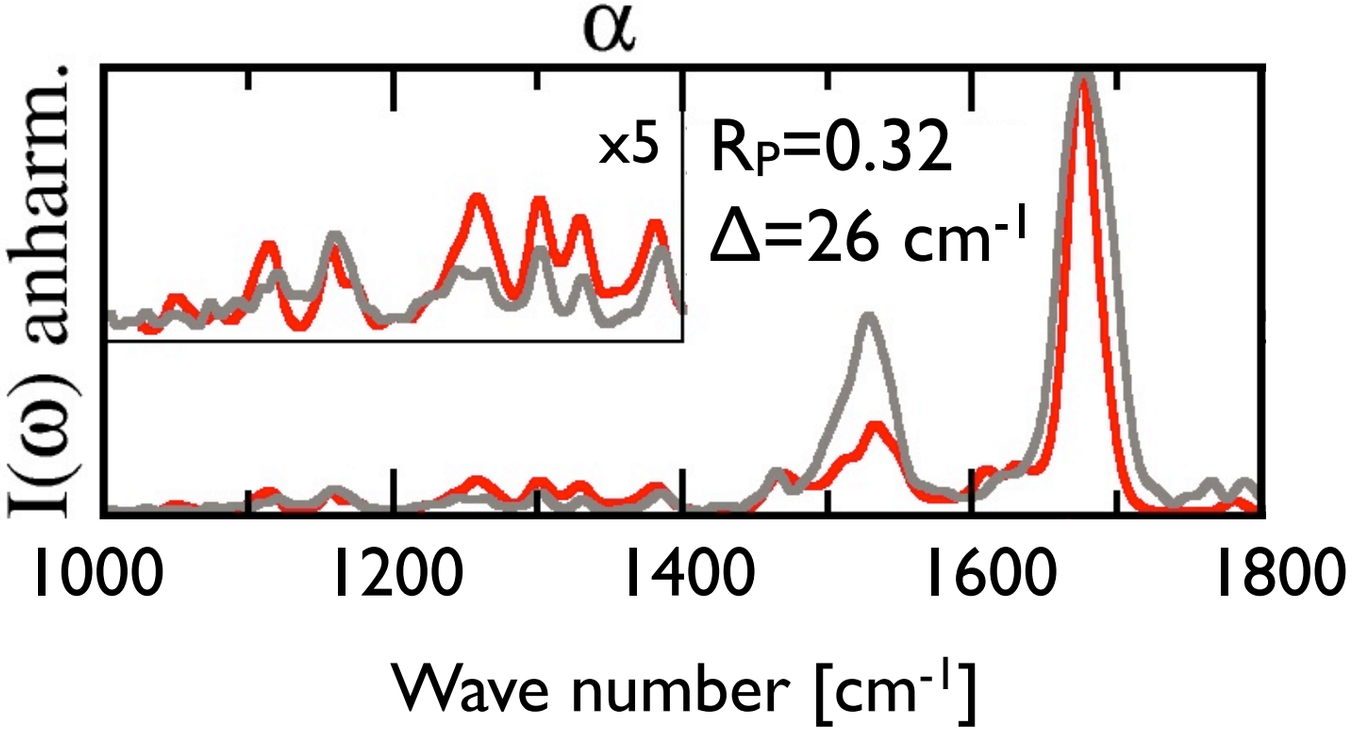

— Theory (anharmonic, T=300 K)

— Experiment (IRMPD, 300K)

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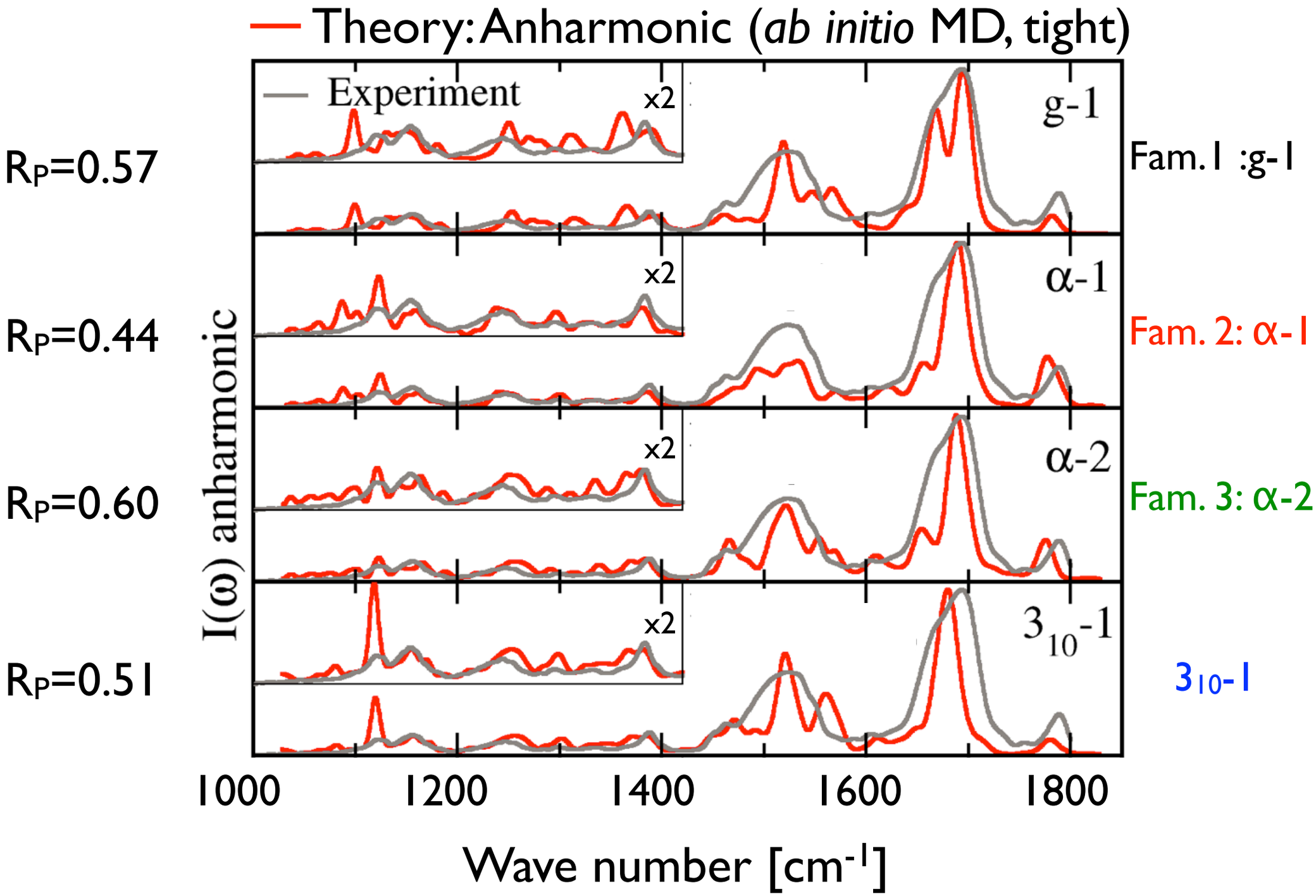
Ac-Ala$_5$-LysH$^+$: Anharmonic theory vs experiment



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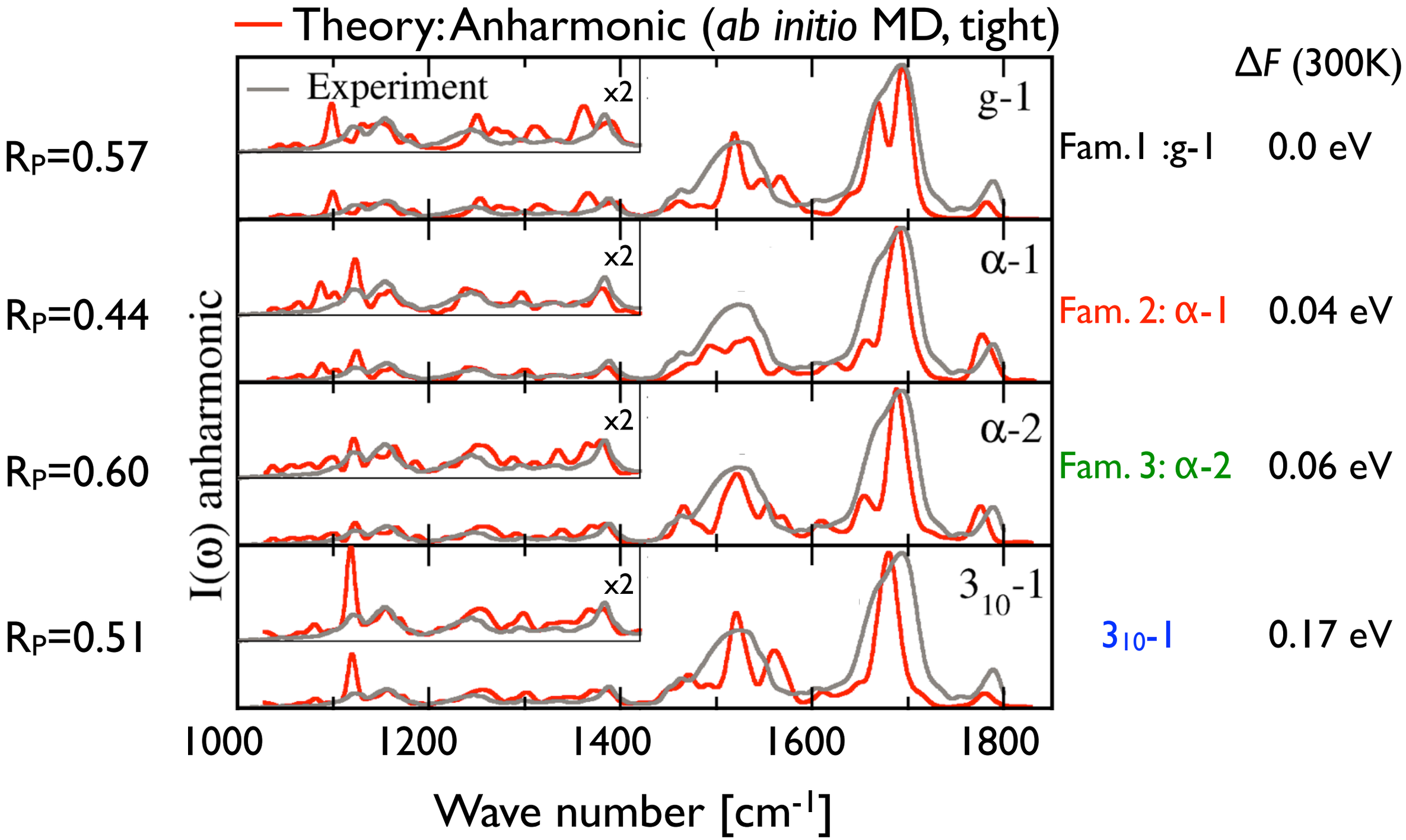
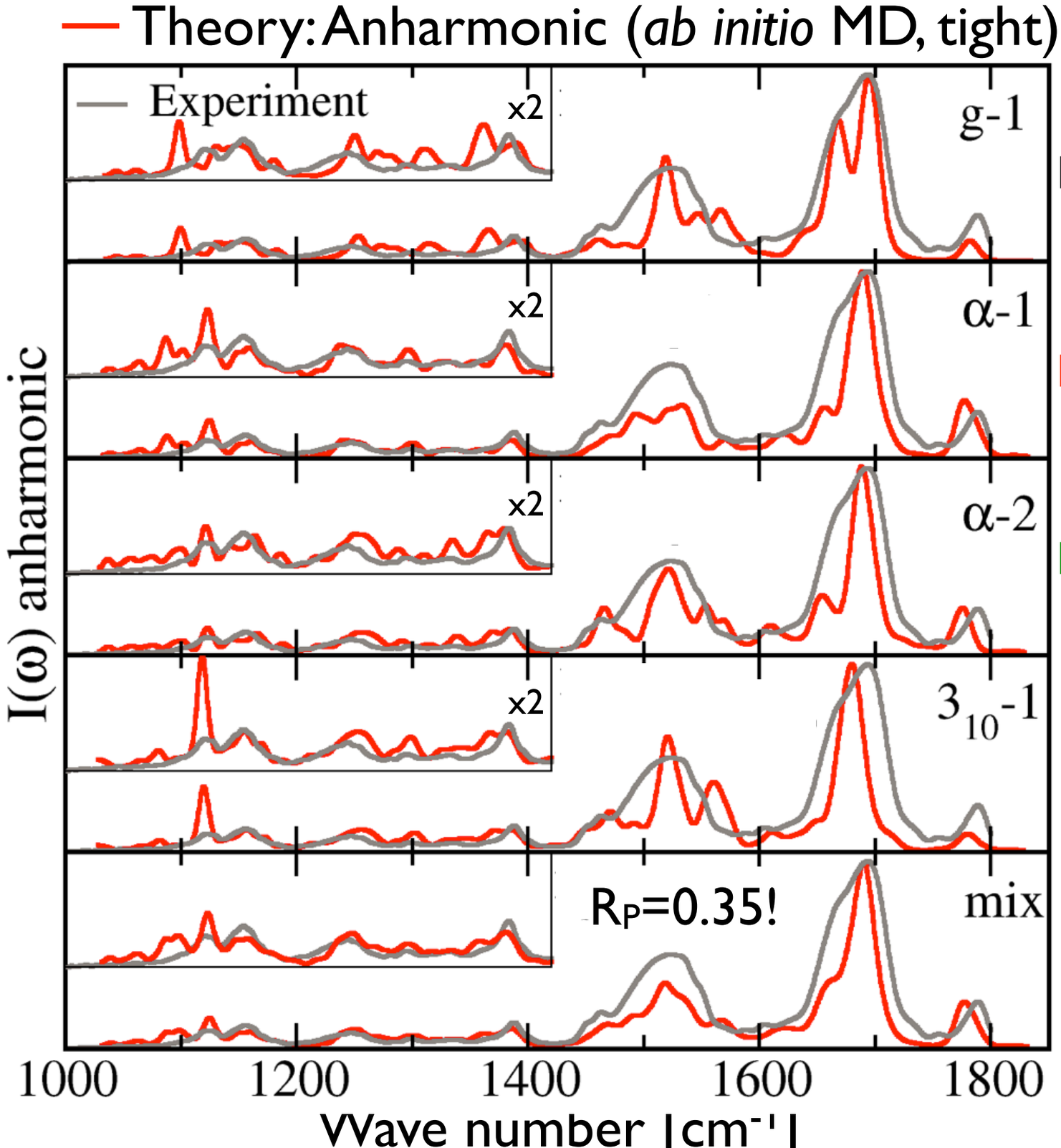


		ΔF (300K)
R_P=0.57	Fam.1 :g-1	0.0 eV
R_P=0.44	Fam. 2: α-1	0.04 eV
R_P=0.60	Fam. 3: α-2	0.06 eV
R_P=0.51	3_{10}-1	0.17 eV

Ac-Ala$_5$-LysH$^+$: Anharmonic theory vs experiment



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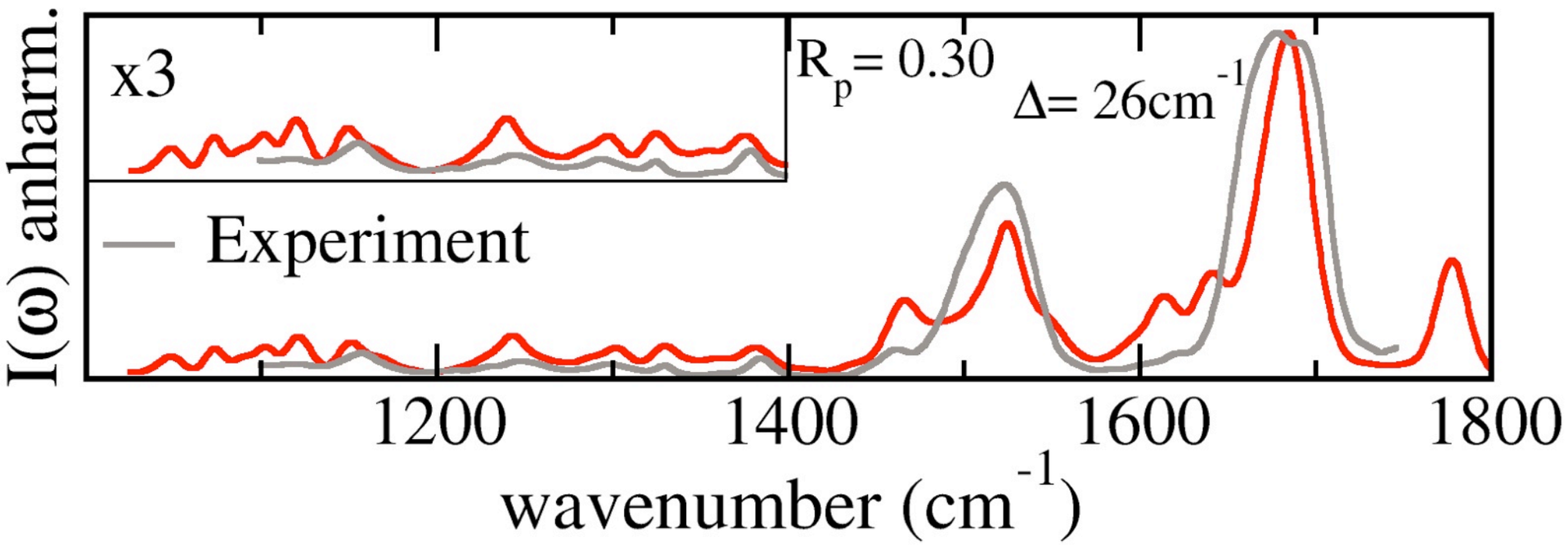
R_P=0.60	Fam. 3: α-2	0.06 eV
R_P=0.51	3$_{10}$-1	0.17 eV

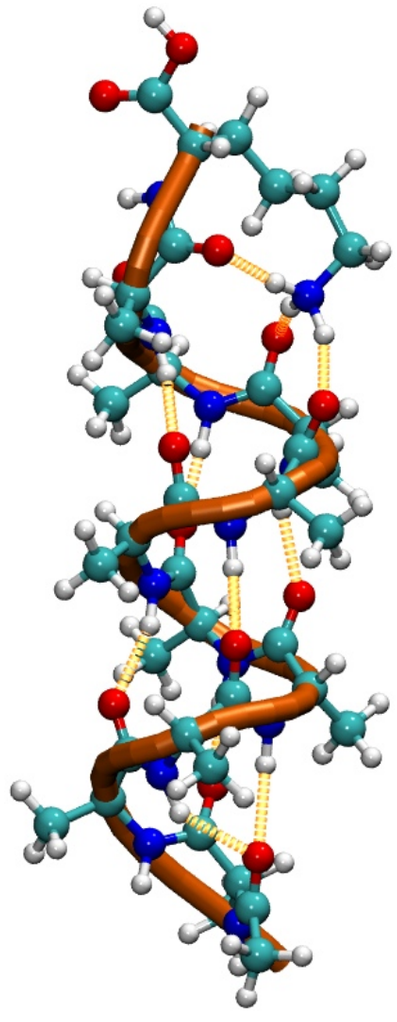
Fit by minimizing R-factor only!

20% g-1
60% α-1
20% α-2
0% 3$_{10}$-1 (!)

AIMD derived IR spectra: importance of vdW

Ac-Ala$_{10}$-LysH$^+$, <*T*>=300K





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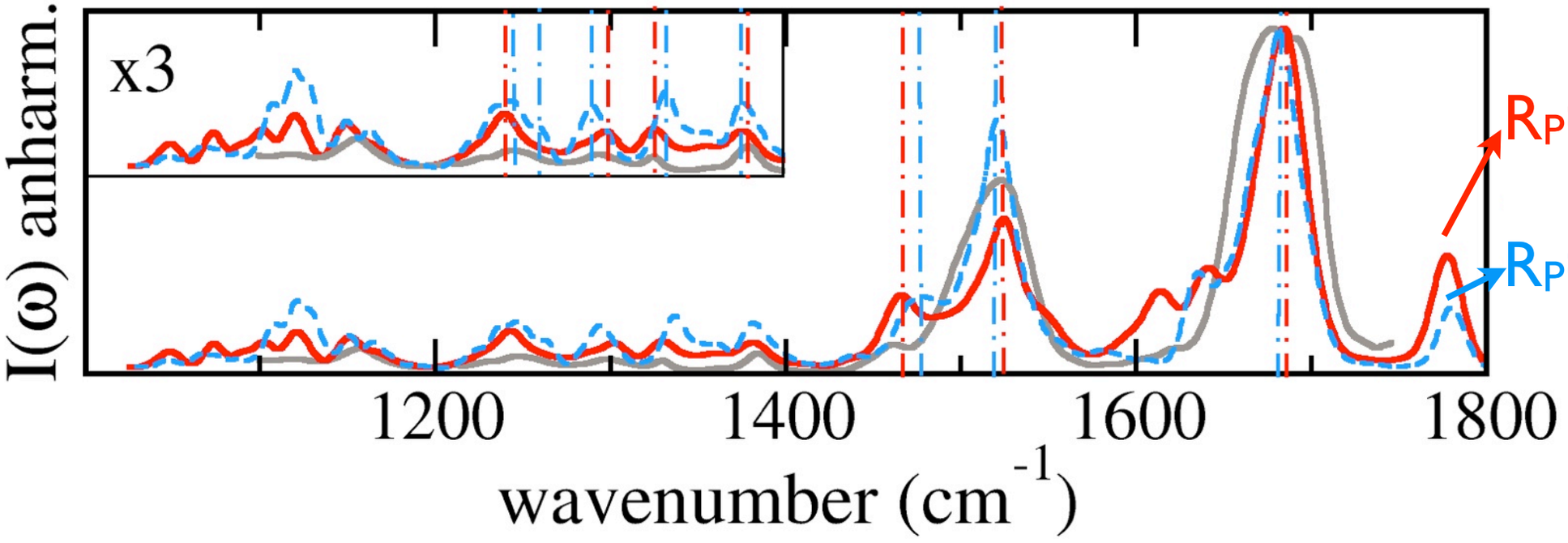

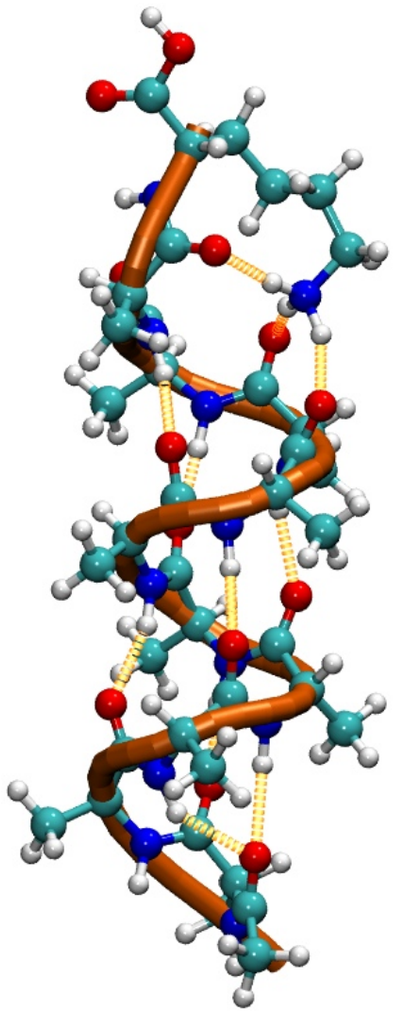

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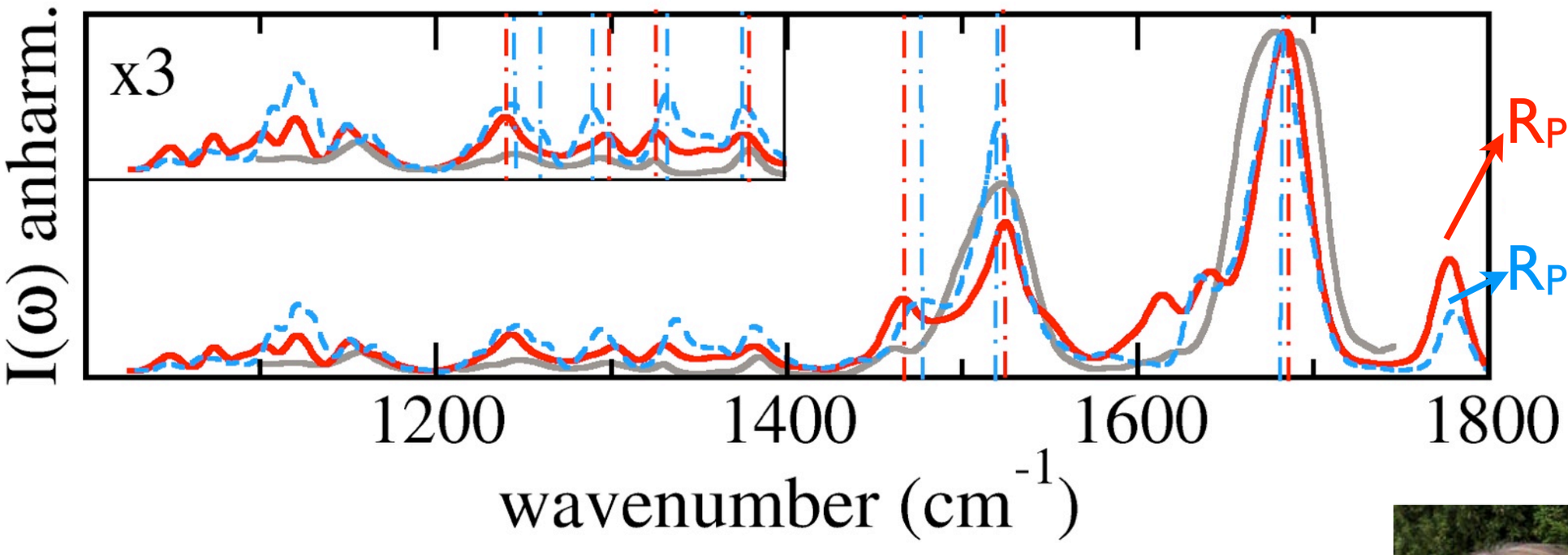
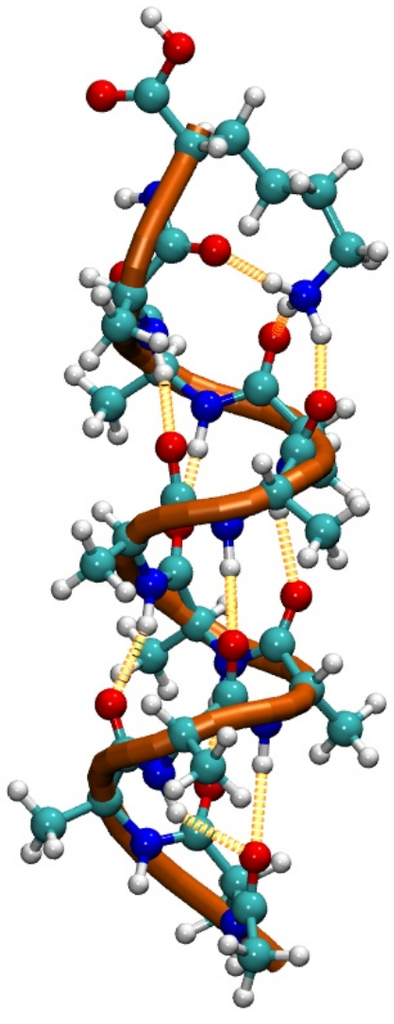
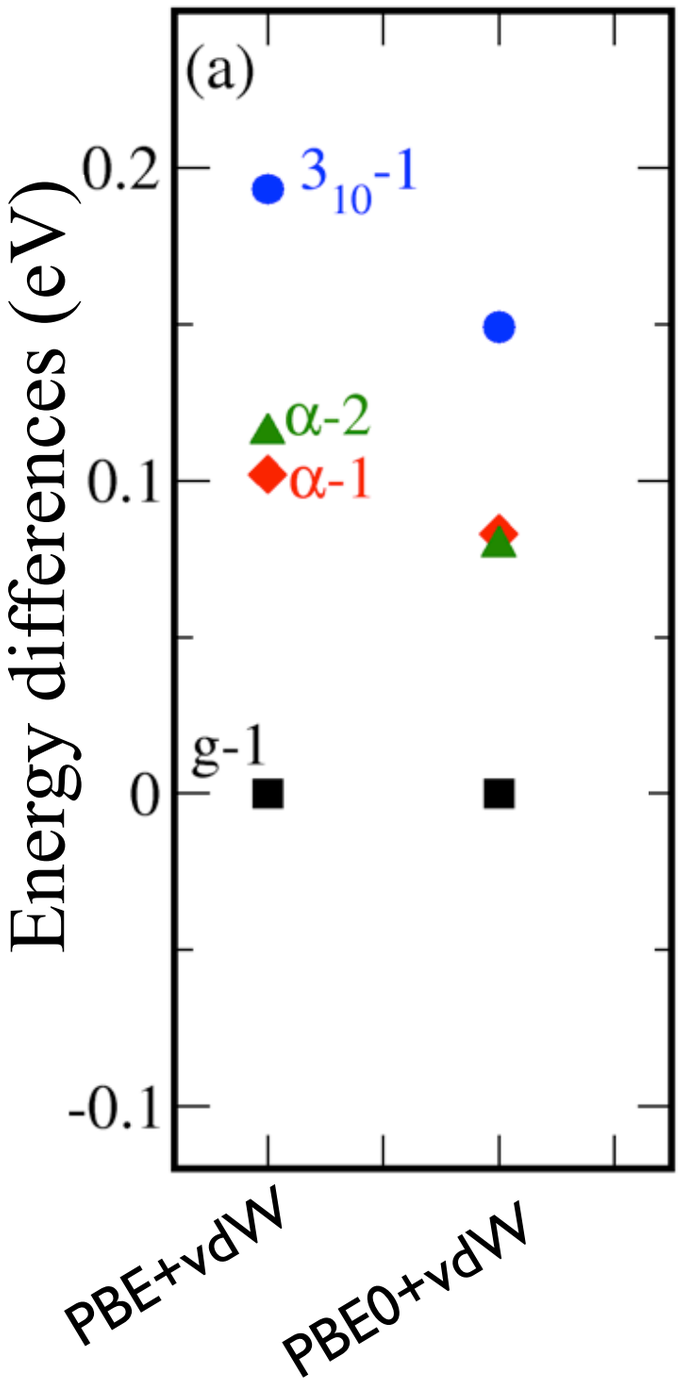
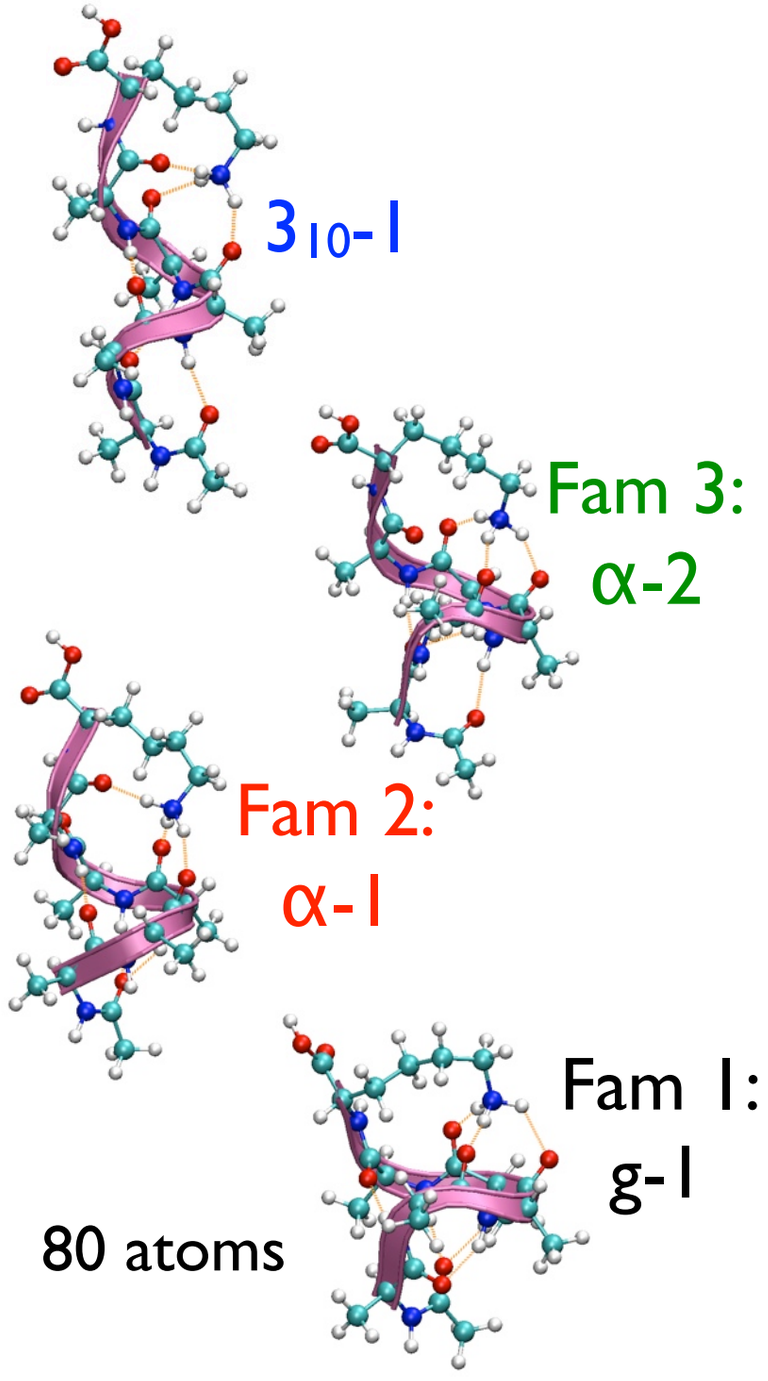




Even larger polypeptides: Franziska Schubert, P 10

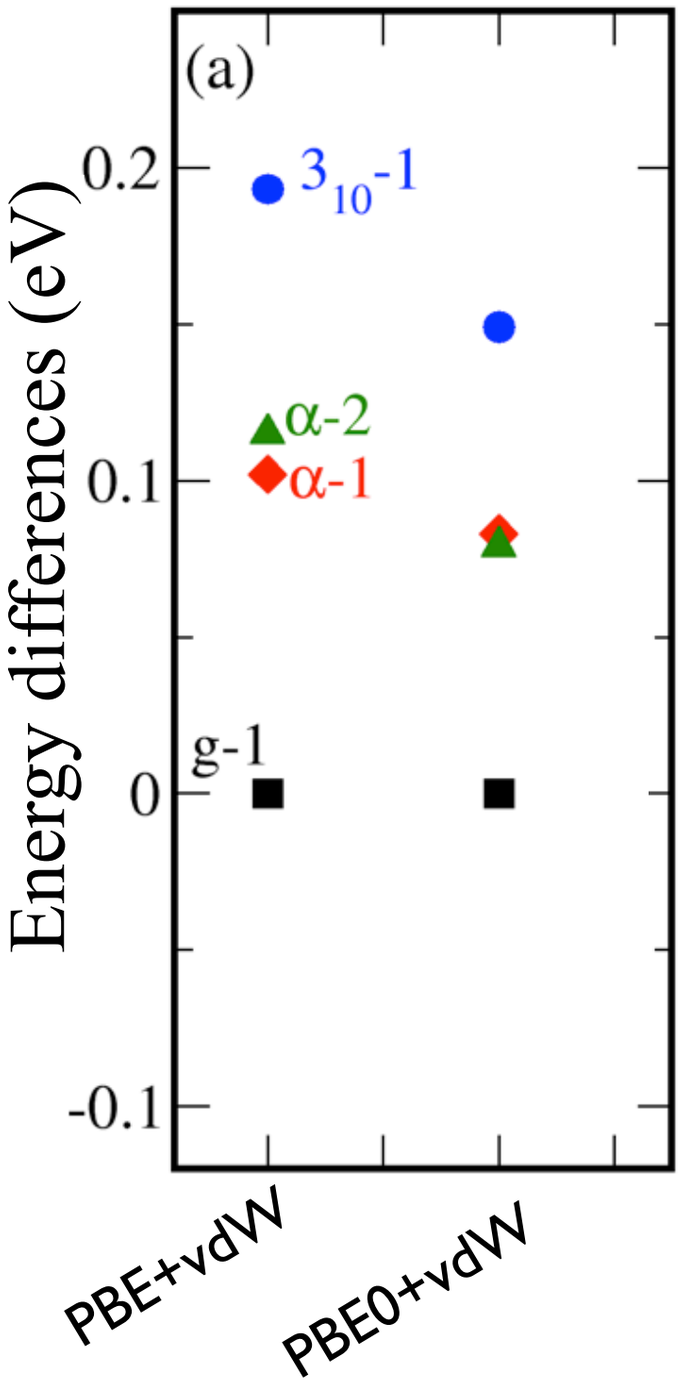
Is DFT(+vdW) accurate enough?

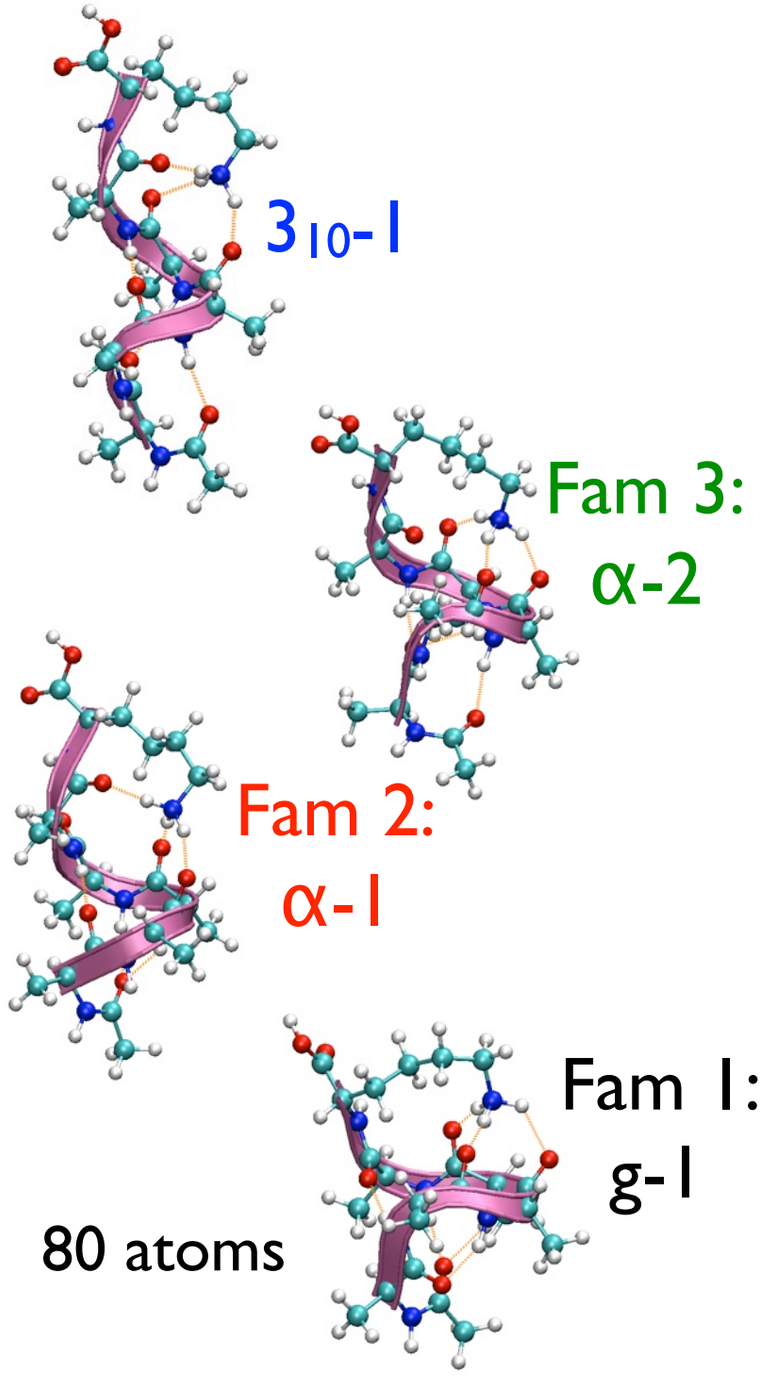


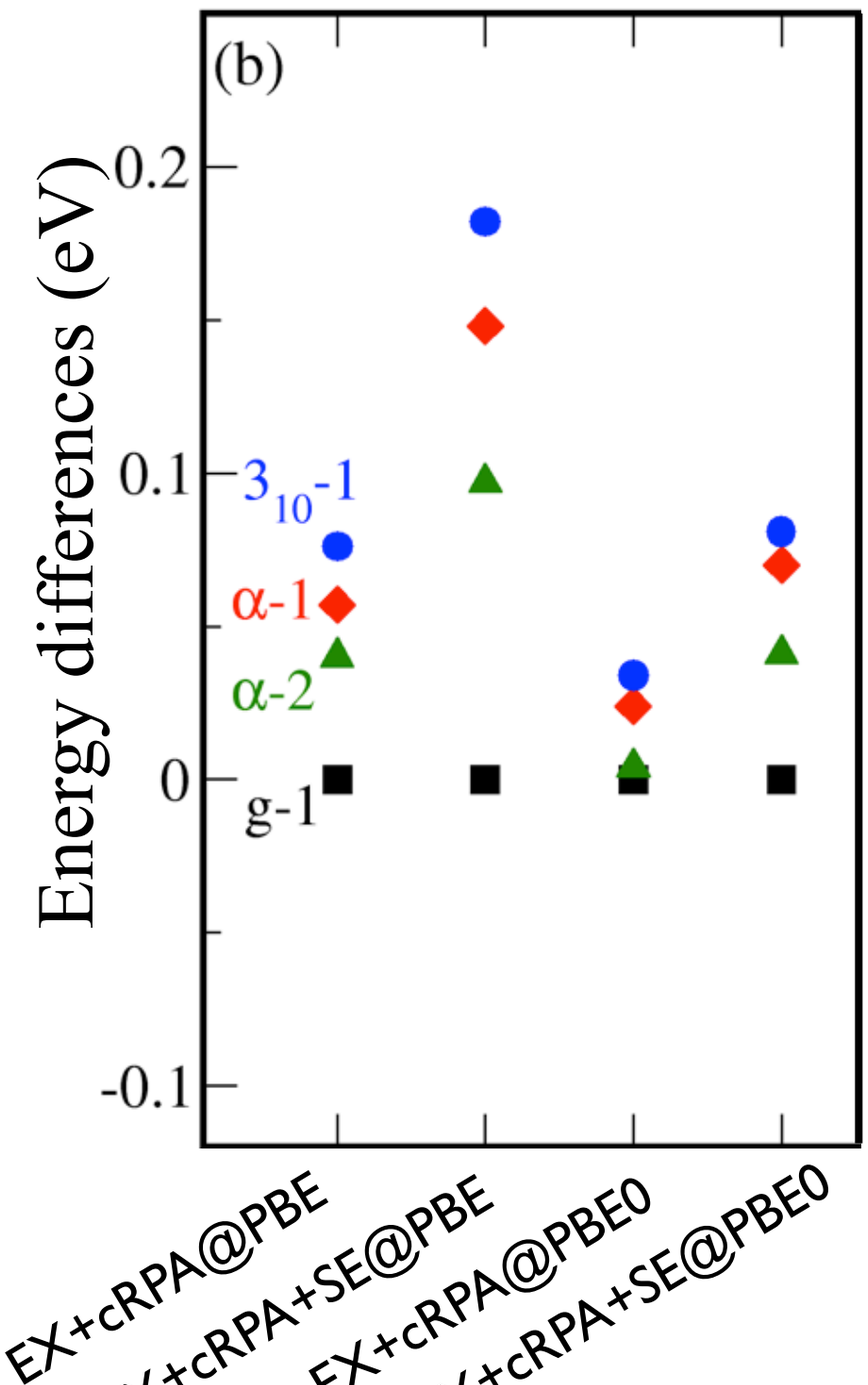


Is DFT(+vdW) accurate enough?

- Even *with optimized basis functions* (capturing most of the core correlation), feasible "higher level" methods are perturbative







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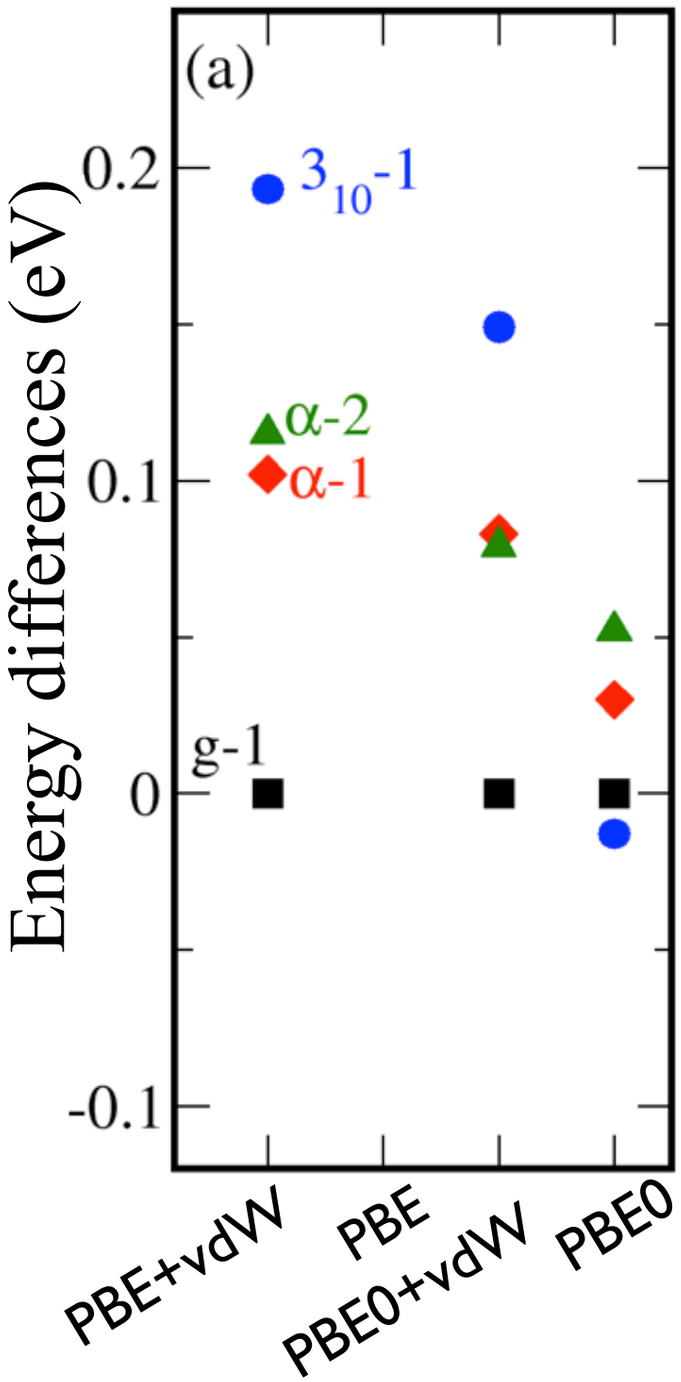
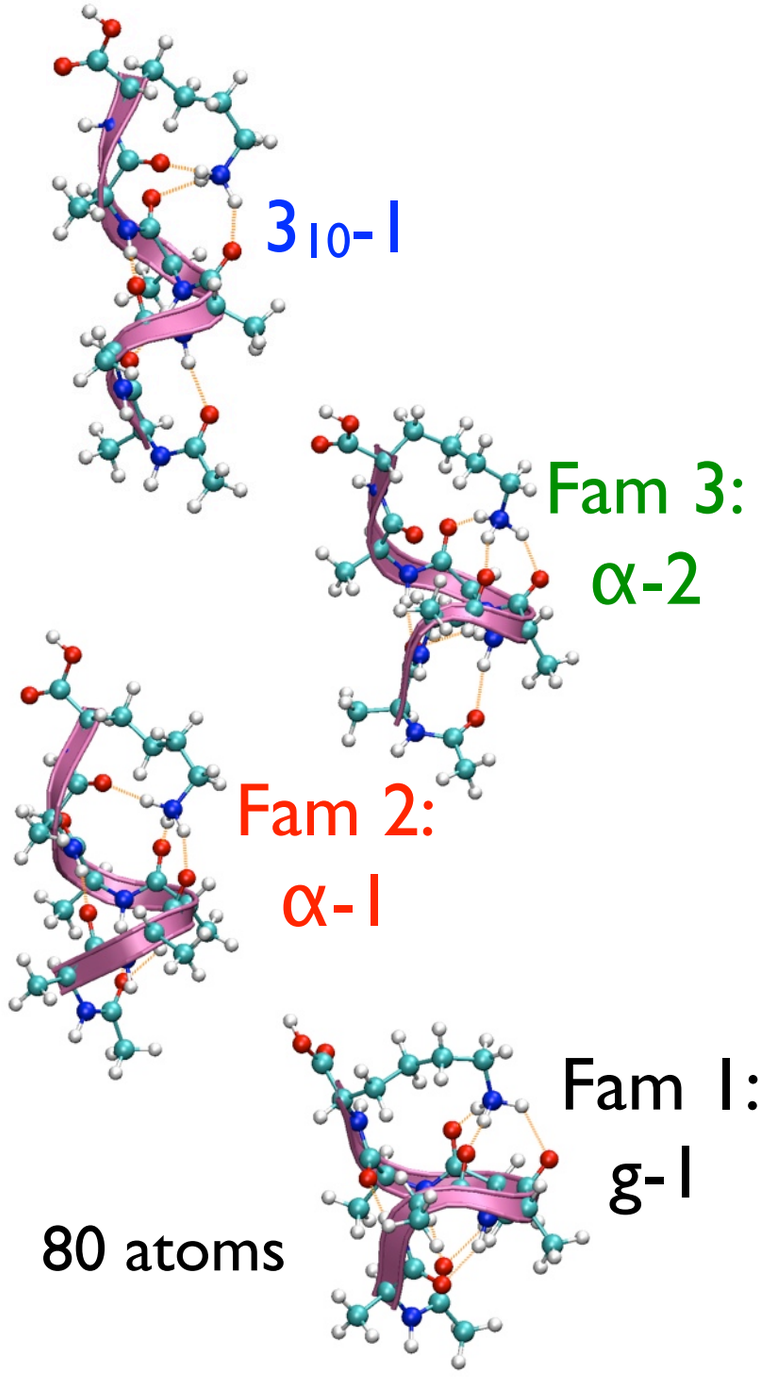
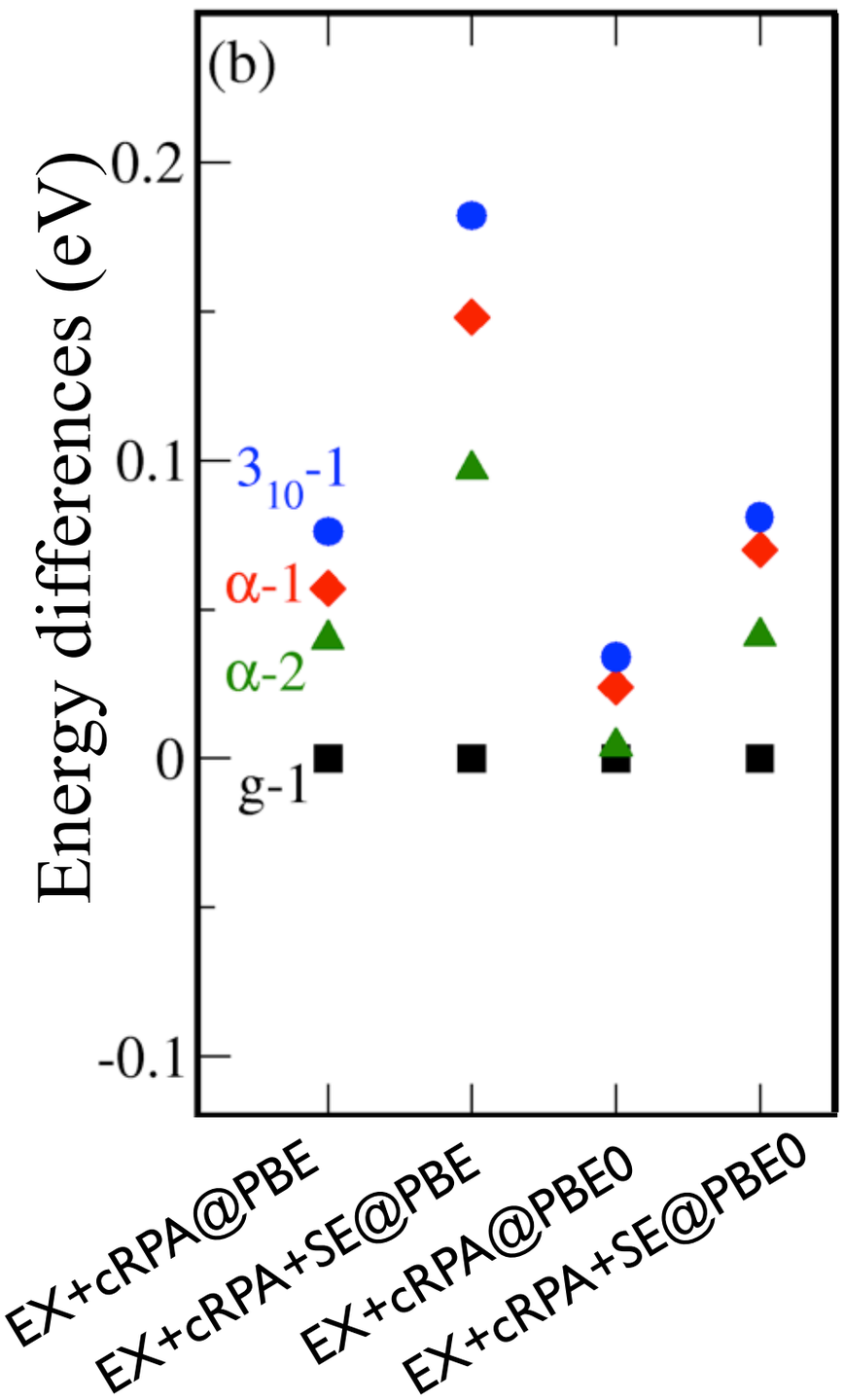






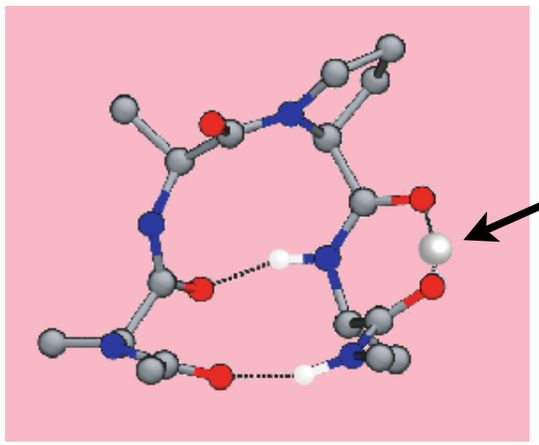
Is the classical treatment of the nuclei accurate enough?

- In many cases, it seems so...
- ... but quantum nuclear effects do play a role in many systems

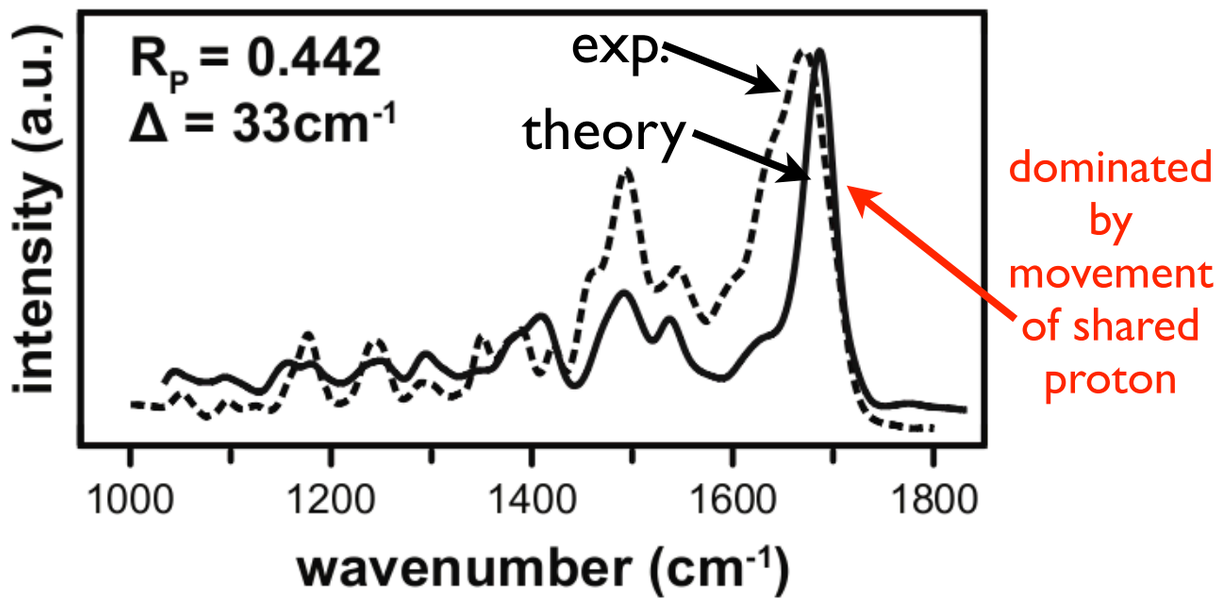
- Example:

C. Baldauf

Ac-Ala$_2$ProAla-NMe + H$^+$



AIMD, PBE+vdW, average over several conf.



- No good match to experiment in this case - quantum effects?

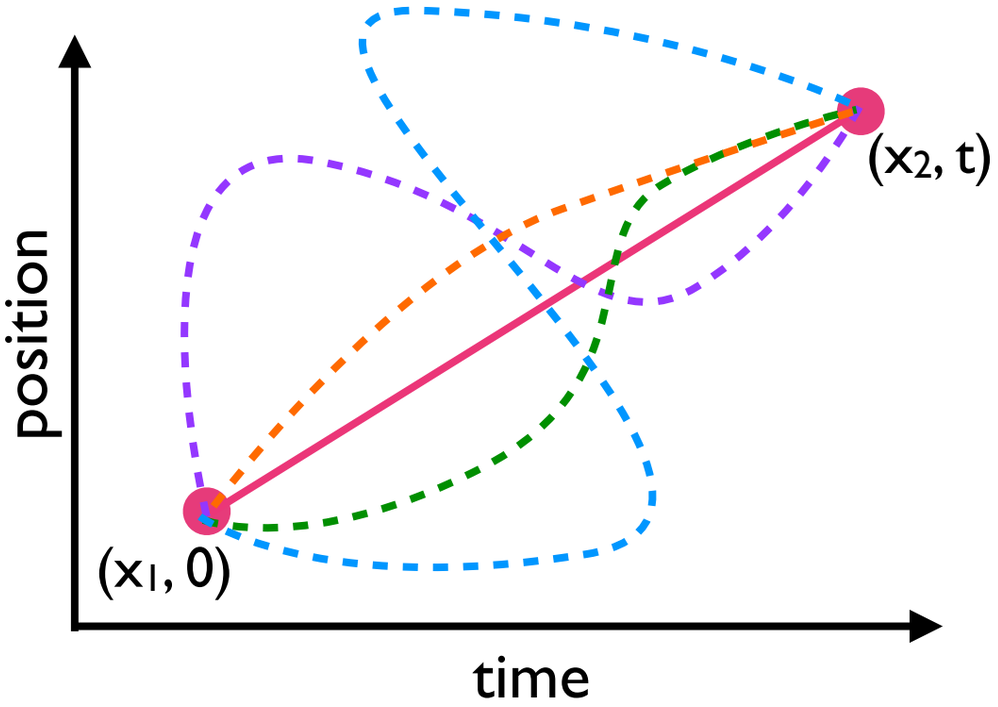
Nuclear quantum effects: path integral molecular dynamics

Time dependent Schrödinger equation

$$i\hbar\frac{\partial}{\partial t}|\Psi\rangle = \hat{H}|\Psi\rangle$$

$$|\Psi(t)\rangle = \exp(-i\hat{H}t/\hbar)|\Psi(0)\rangle = \hat{U}(t)|\Psi(0)\rangle$$

Time evolution propagator



Probability

$$P(x_1, 0; x_2, t) = |\langle x_1|\hat{U}(t)|x_2\rangle|^2$$

All paths contribute:

$$\langle x_1|\hat{U}(t)|x_2\rangle \propto \sum_{paths} \exp\left(-\frac{i}{\hbar}\int_{path}\mathcal{L}dt\right) = \sum_{paths}\exp\left(-\frac{i}{\hbar}S_{path}\right)$$

action

Nuclear quantum effects: path integral molecular dynamics

- There is a relation between the quantum canonical density matrix and the quantum time evolution propagator:

$$\beta = 1/(k_B T) \qquad |\Psi(t)\rangle = \exp(-i\hat{H}t/\hbar)|\Psi(0)\rangle = \hat{U}(t)|\Psi(0)\rangle$$

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- One can solve everything in imaginary time (canonical density matrix!) and then go back to the real time

Nuclear quantum effects: path integral molecular dynamics

- For evaluating observables (quantum canonical averages), one needs the partition function

$$Z = \mathrm{Tr}(\hat{\rho}) = \langle \mathbf{x} | \exp(\beta \hat{H}) | \mathbf{x} \rangle$$

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$$Z \approx \frac{1}{(2\pi\hbar)^{NP}} \int d\mathbf{p}^{NP} \int d\mathbf{x}^{NP} \exp\left[\frac{-\mathcal{H}_P(\mathbf{x},\mathbf{p})}{P k_B T}\right]$$

← Exact for $P \to \infty$

Hamiltonian of a classical ring polymer →

$$\mathcal{H}_P(\mathbf{x},\mathbf{p}) = \sum_I^N \sum_k^P \left[\frac{[\mathbf{p}_I^{(k)}]^2}{2M_I} + \frac{M_I \omega_P^2}{2}(\mathbf{x}_I^{(k)} - \mathbf{x}_I^{(k+1)})^2\right] + \sum_k^P V(\mathbf{x}^{(k)})$$

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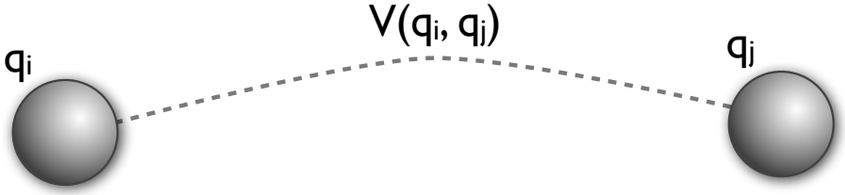
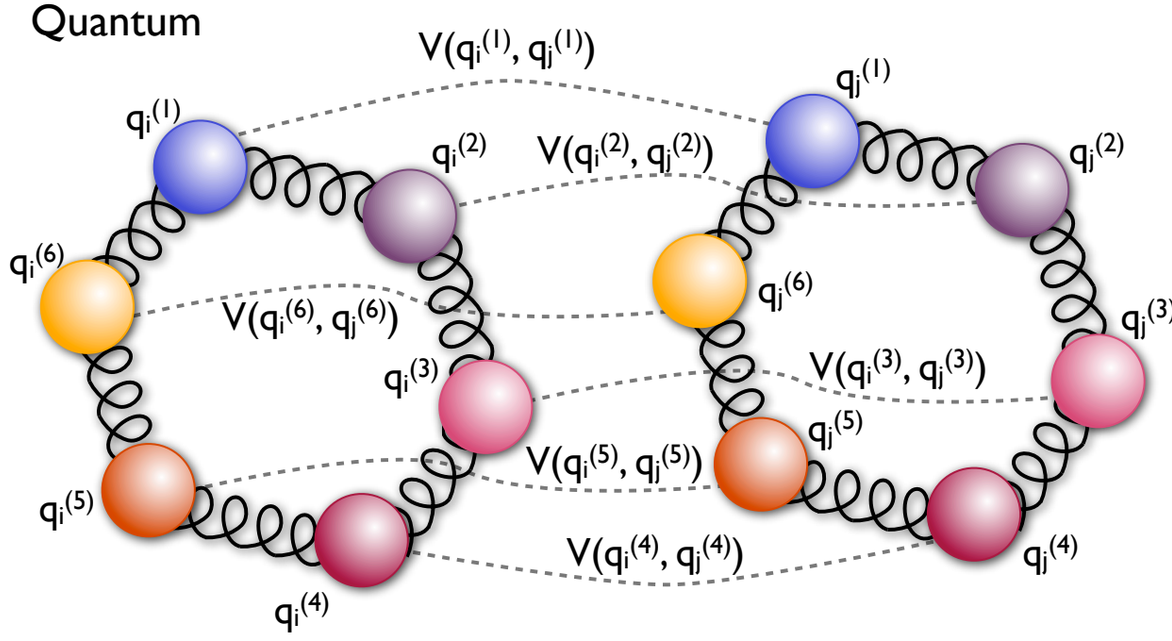


Quantum



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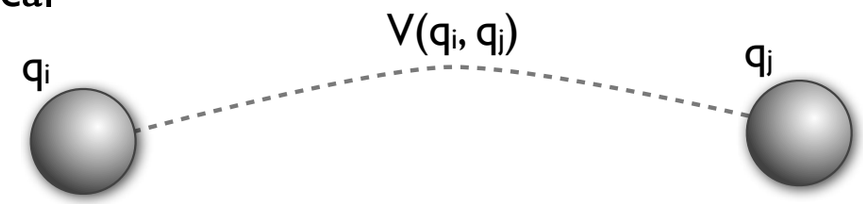
In FHI-aims we now have:

- "In-code" implementation of PIMD, Centroid MD (CMD), and Ring-Polymer MD (RPMD) - Xinzheng Li, P 8
- Interface to external python wrapper "WRAPPI" that works through internet sockets and allows to parallelize even over several machines

Classical



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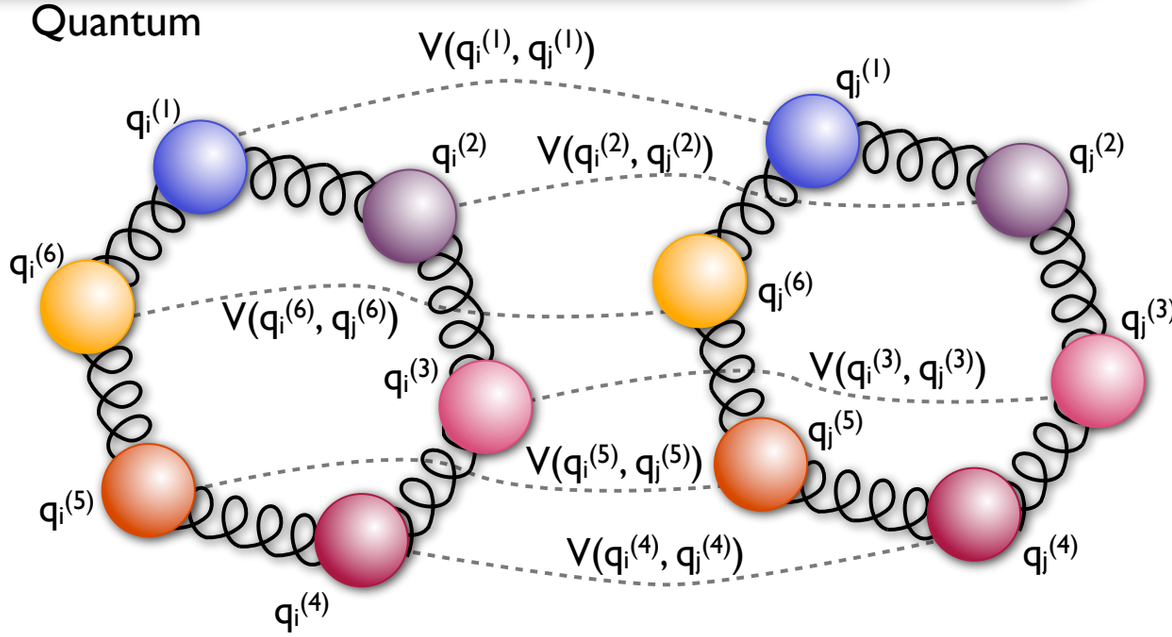

Nuclear quantum effects: colored noise thermostats

M. Ceriotti, G. Bussi, M. Parrinello, *JCTC* **2010**, 6, 1170-1180 (http://gle4md.berlios.de/)

$$\dot{x} = p/m$$

$$\begin{pmatrix} \dot{p} \\ \dot{\mathbf{s}} \end{pmatrix} = \begin{pmatrix} -V'(x) \\ 0 \end{pmatrix} - \begin{pmatrix} a_{pp} & \mathbf{a}_p^T \\ \mathbf{a}_p & \mathbf{A} \end{pmatrix} \begin{pmatrix} p \\ \mathbf{s} \end{pmatrix} + \begin{pmatrix} b_{pp} & \mathbf{b}_p^T \\ \mathbf{b}_p & \mathbf{B} \end{pmatrix} (\xi)$$

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Download input matrices (in FHI-aims input format) from: http://gle4md.berlios.de

What can we do now?

T = 300K

Classical

Quantum thermostat (qt)

WRAPPI: PIMD + qt

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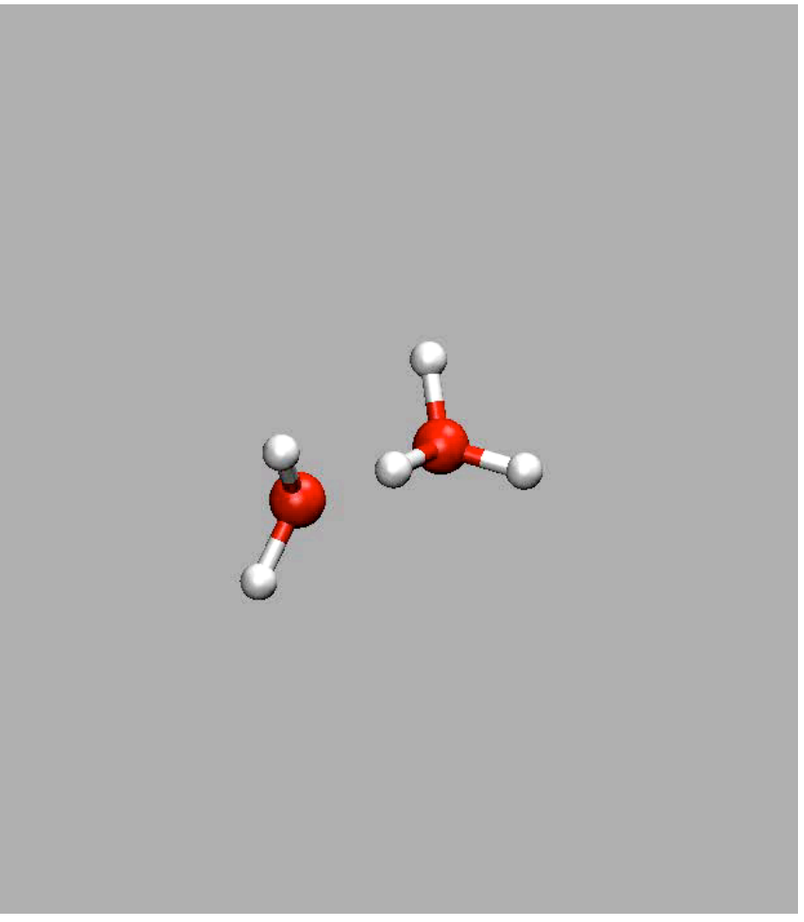

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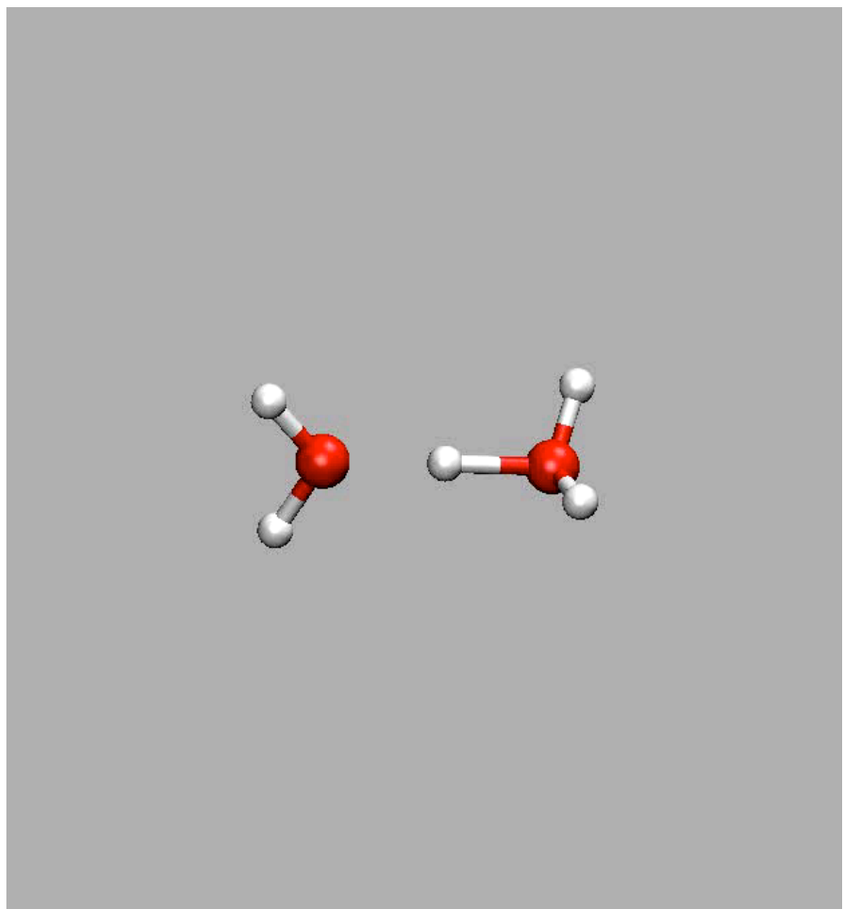

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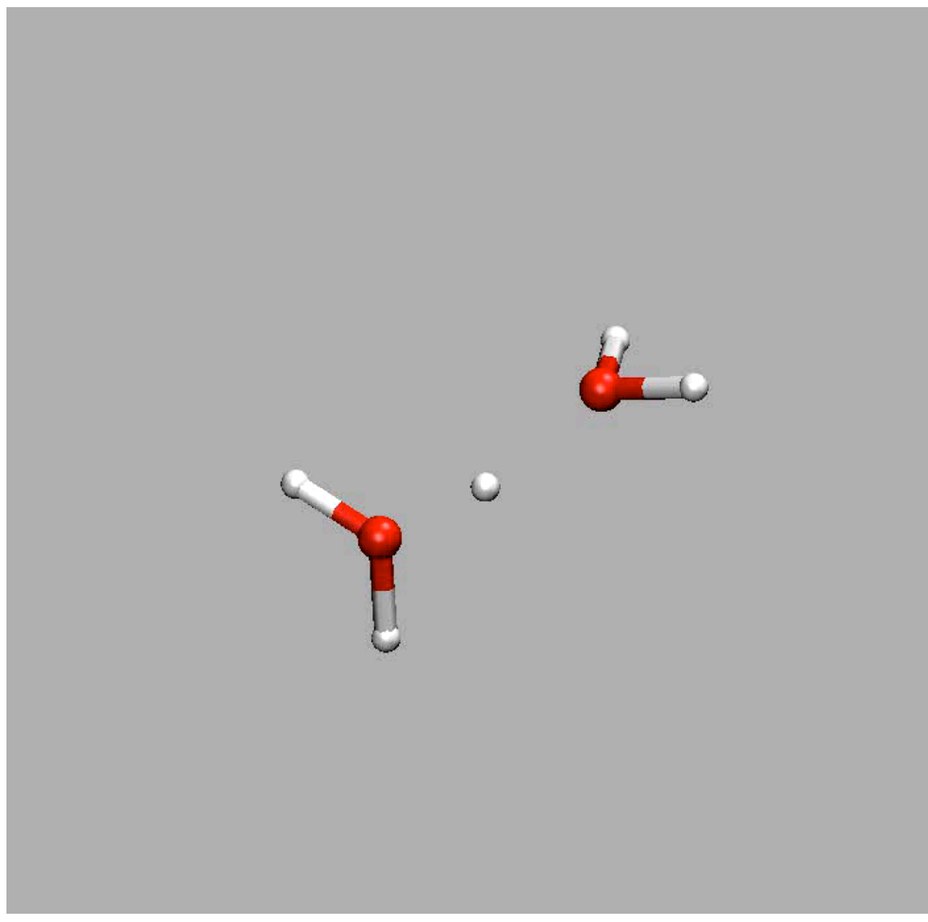

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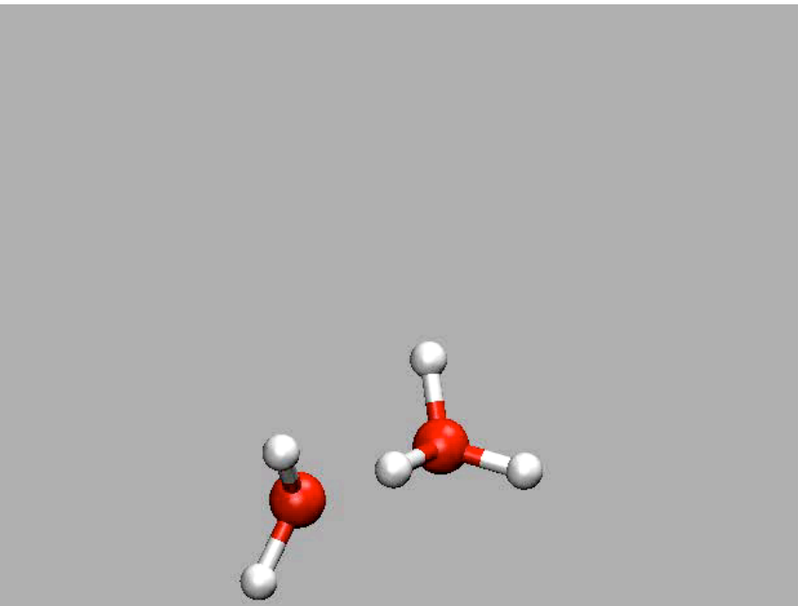

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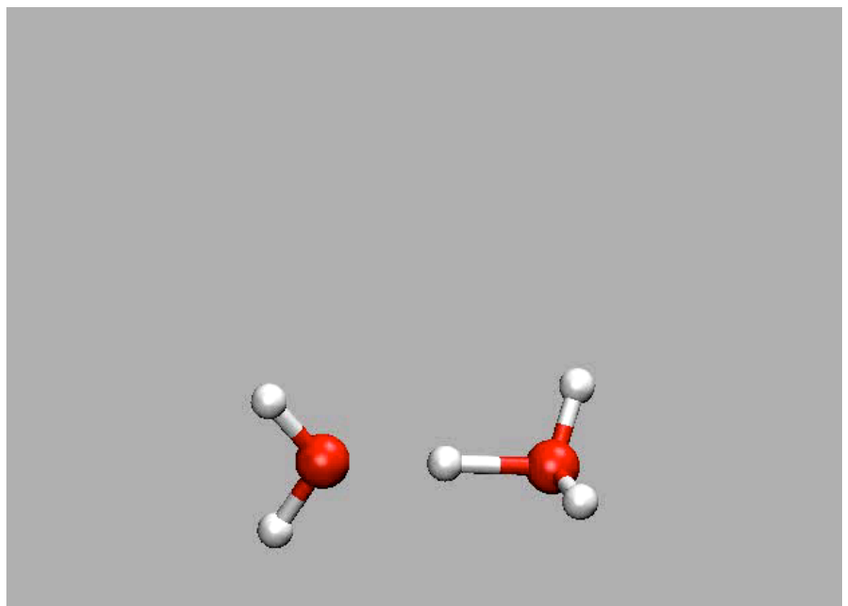

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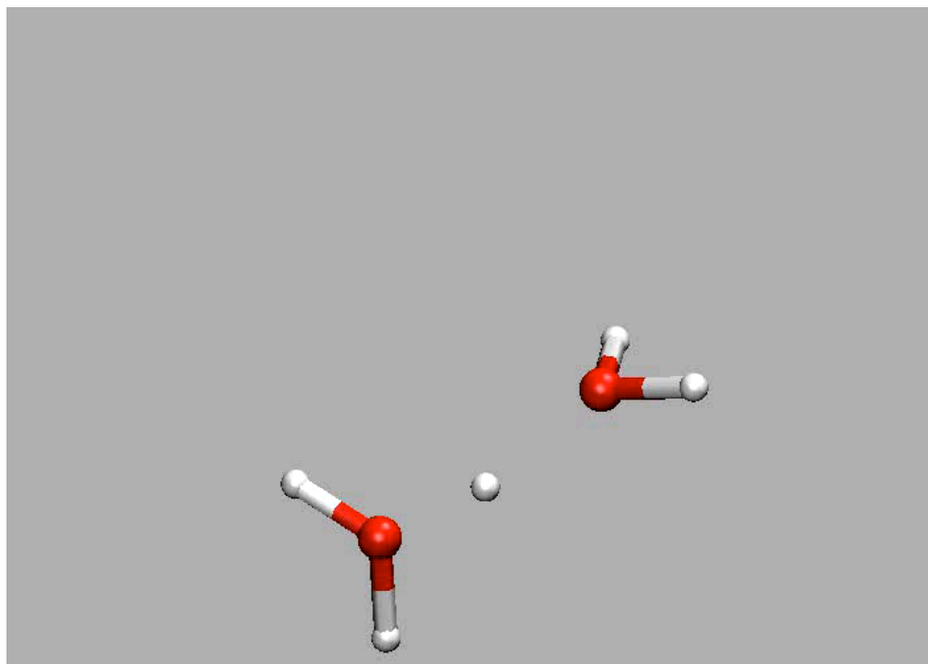
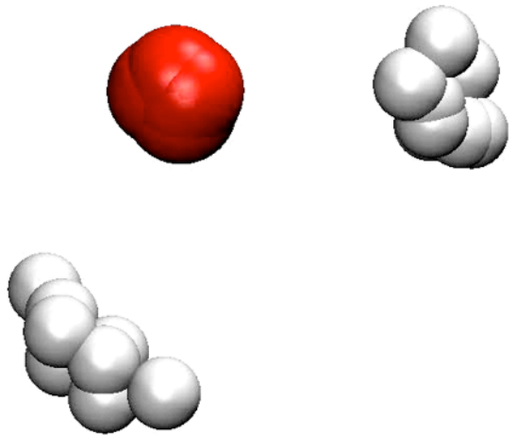
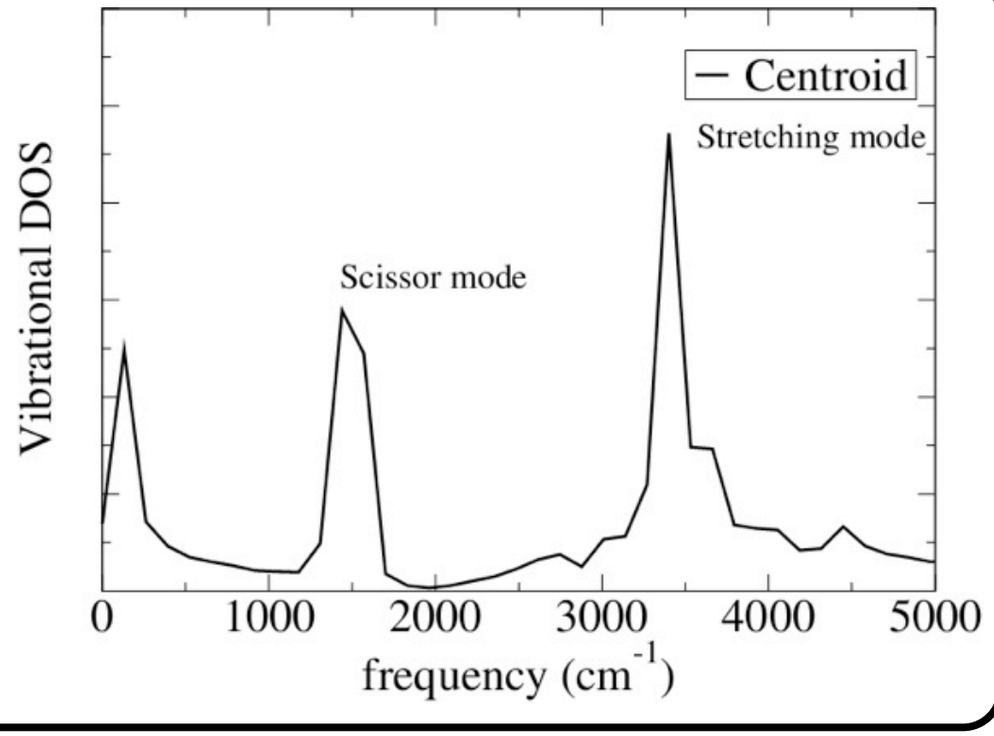


FHI-aims: CMD





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Thank you!