# Protein force field meeting

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Open Force Field Initiative

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# Assessing OpenFF force fields on tetrapeptide torsion profiles

- Dave Cerutti's TorsionDrive datasets on Ace-X-Y-Z-Nme
  - Central residues Y are Ala, Arg, Ash, Asn, Asp, Cys, Glh, Gln, Glu, Gly, Hid, & Hie
  - Flanking residues X & Z are Ala, Gly, Ser, & Val
  - Dihedrals scanned are phi, psi, chi1, chi2, & omega
- Test GAFF 2.11 and OpenFF 1.2.0, 1.3.1, & 2.0.0 with AM1-BCC charges
- Output is RMSE (magnitude) and normalized RMSE (shape), adapted from Simon Boothroyd

# Computing MM torsion profiles

- Reference profiles are QM energies offset to the minimum QM energy

$$x_{\text{min}} = \underset{x}{\text{argmin}}\, U_{\text{QM}}(x)$$

$$E_{\text{QM}}(x) = U_{\text{QM}}(x) - U_{\text{QM}}(x_{\text{min}})$$

- MM energies are evaluated after local minimization $F(x)$ with torsion atoms frozen and are offset to the MM energy of the coordinates with the minimum QM energy

$$E_{\text{MM}}(x) = U_{\text{MM}}\left(F(x)\right) - U_{\text{MM}}\left(F(x_{\text{min}})\right)$$

# Comparing MM torsion profiles to QM reference

- MM energies are shifted to optimally superimpose the MM and QM profiles

$$E_{\mathrm{MM}} = E_{\mathrm{MM}} + \langle E_{\mathrm{QM}} - E_{\mathrm{MM}} \rangle$$

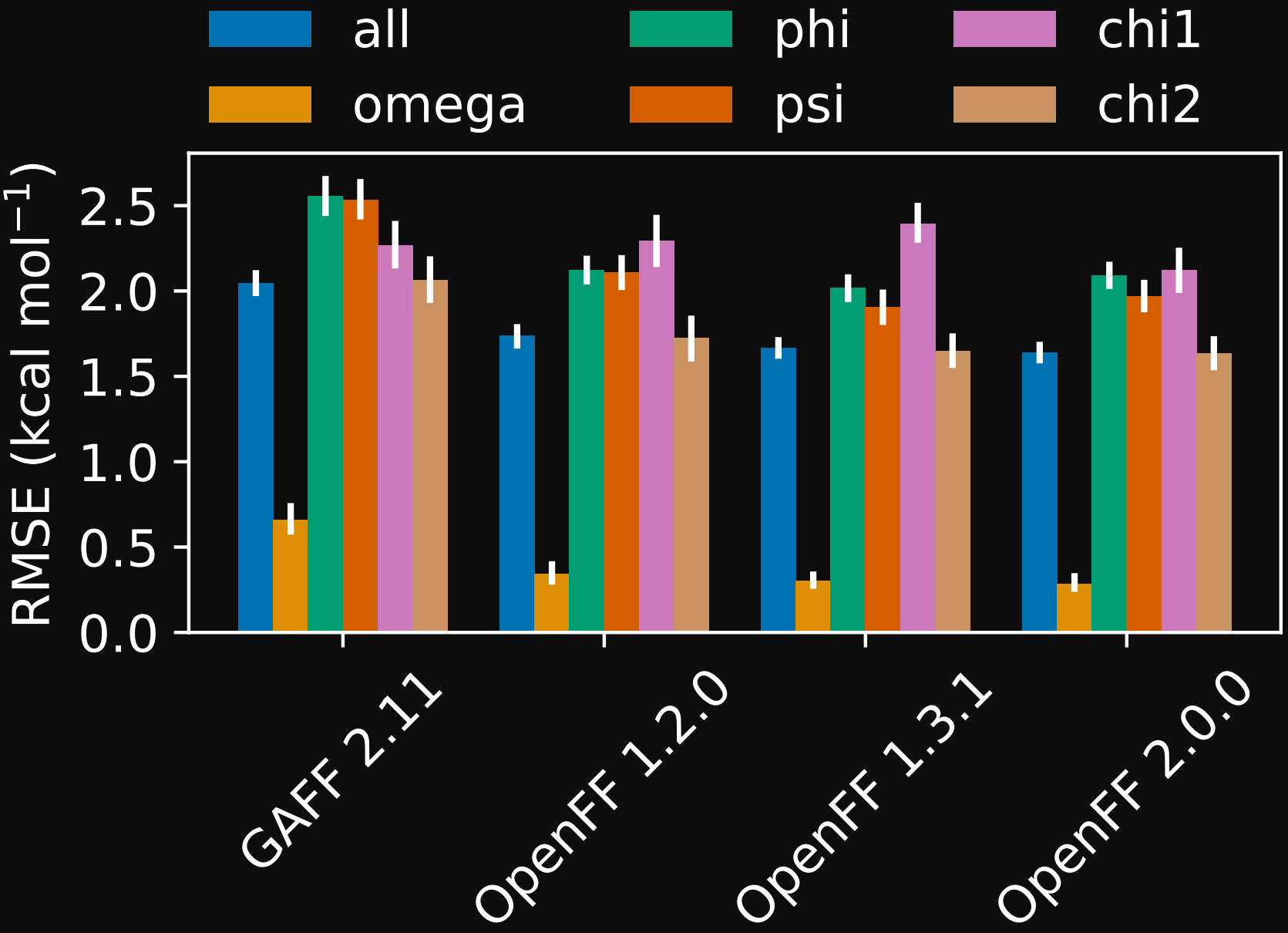
- Magnitude is represented by RMSE

$$\mathrm{RMSE} = \sqrt{\frac{1}{N} \sum \left( E_{\mathrm{QM}} - E_{\mathrm{MM}} \right)^2}$$

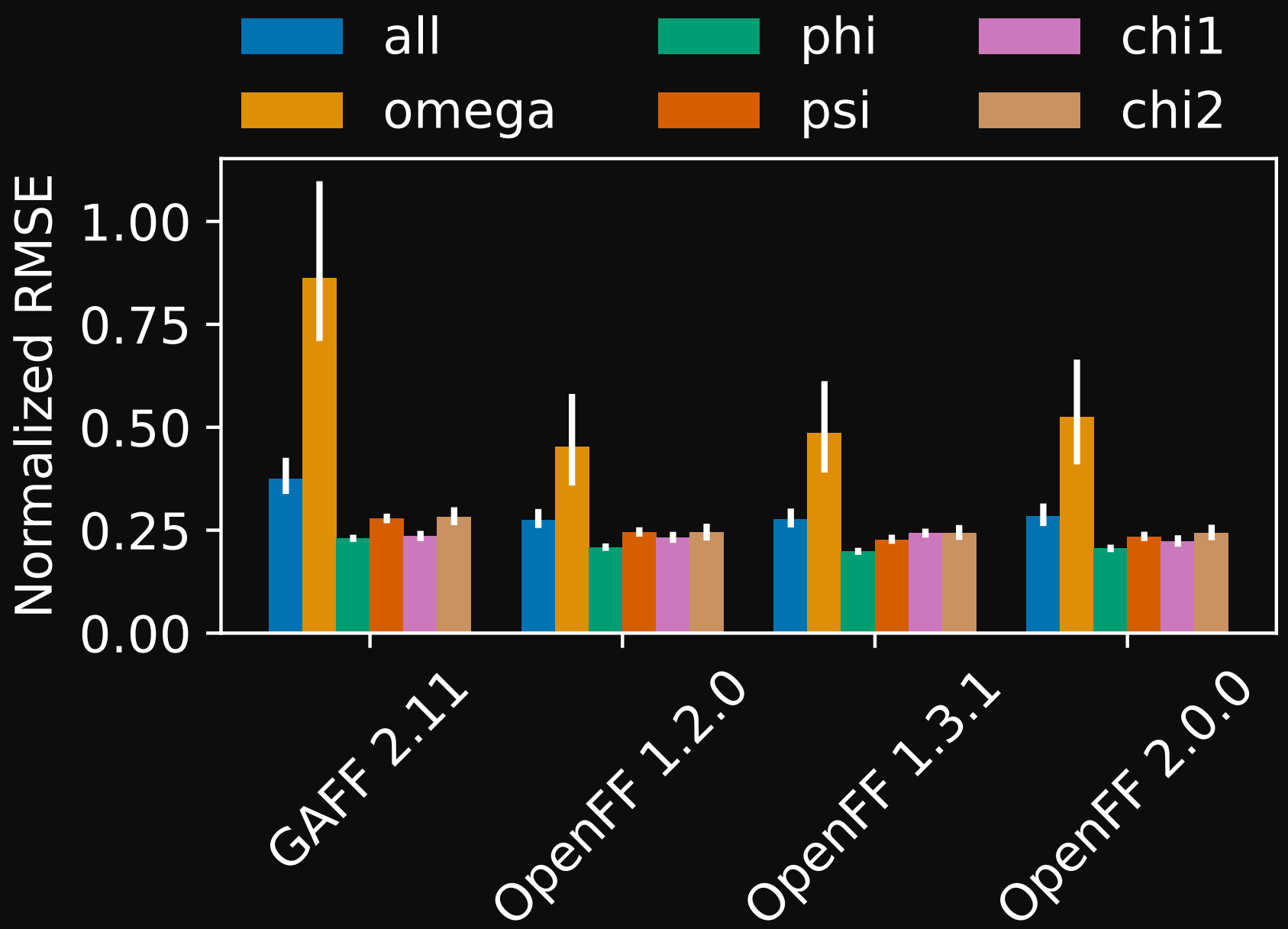
- Shape is represented by normalized RMSE

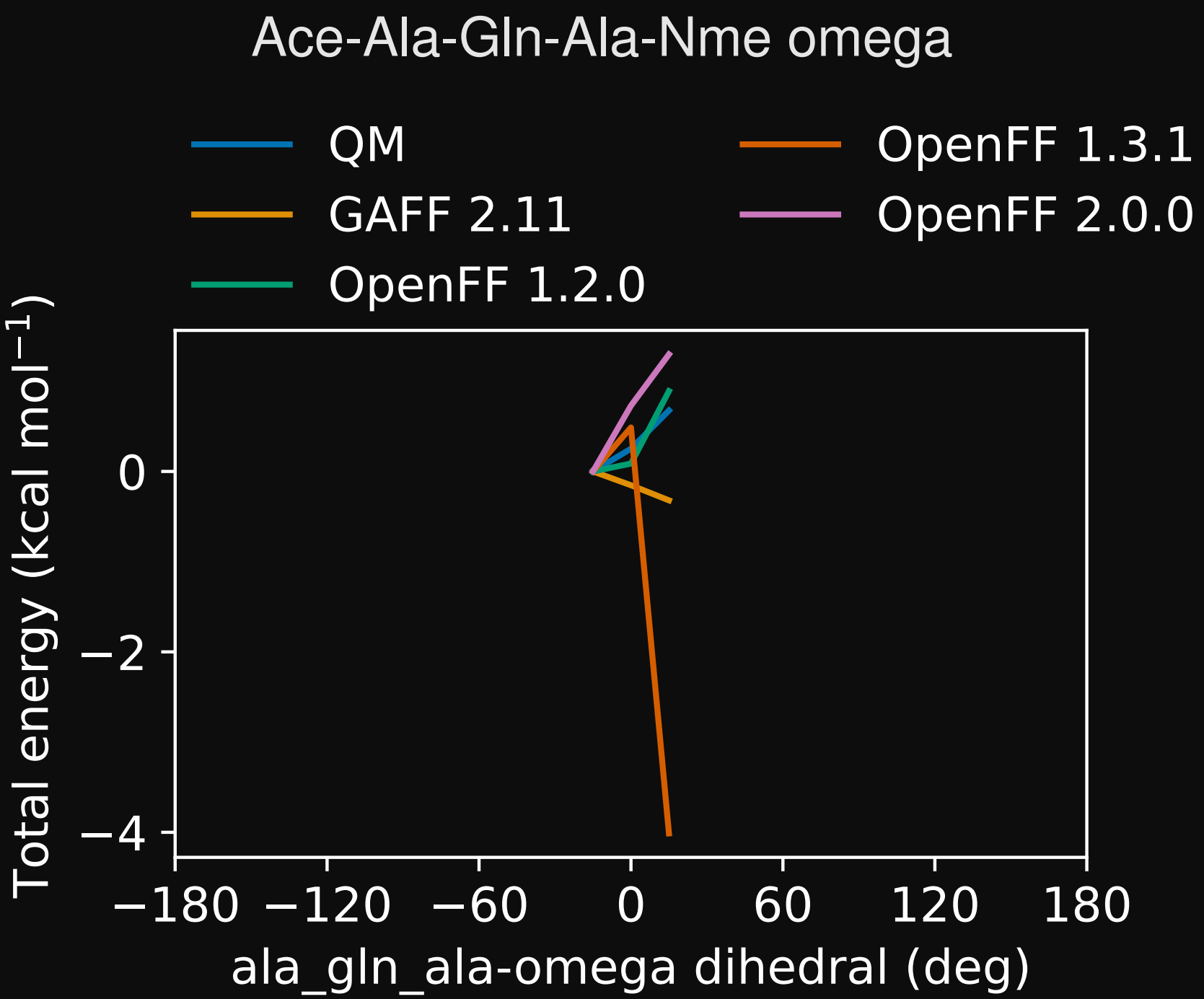
$$\mathrm{NRMSE} = \sqrt{\frac{1}{N} \sum \left( \frac{E_{\mathrm{QM}}}{\max(E_{\mathrm{QM}}) - \min(E_{\mathrm{QM}})} - \frac{E_{\mathrm{MM}}}{\max(E_{\mathrm{MM}}) - \min(E_{\mathrm{MM}})} \right)^2}$$

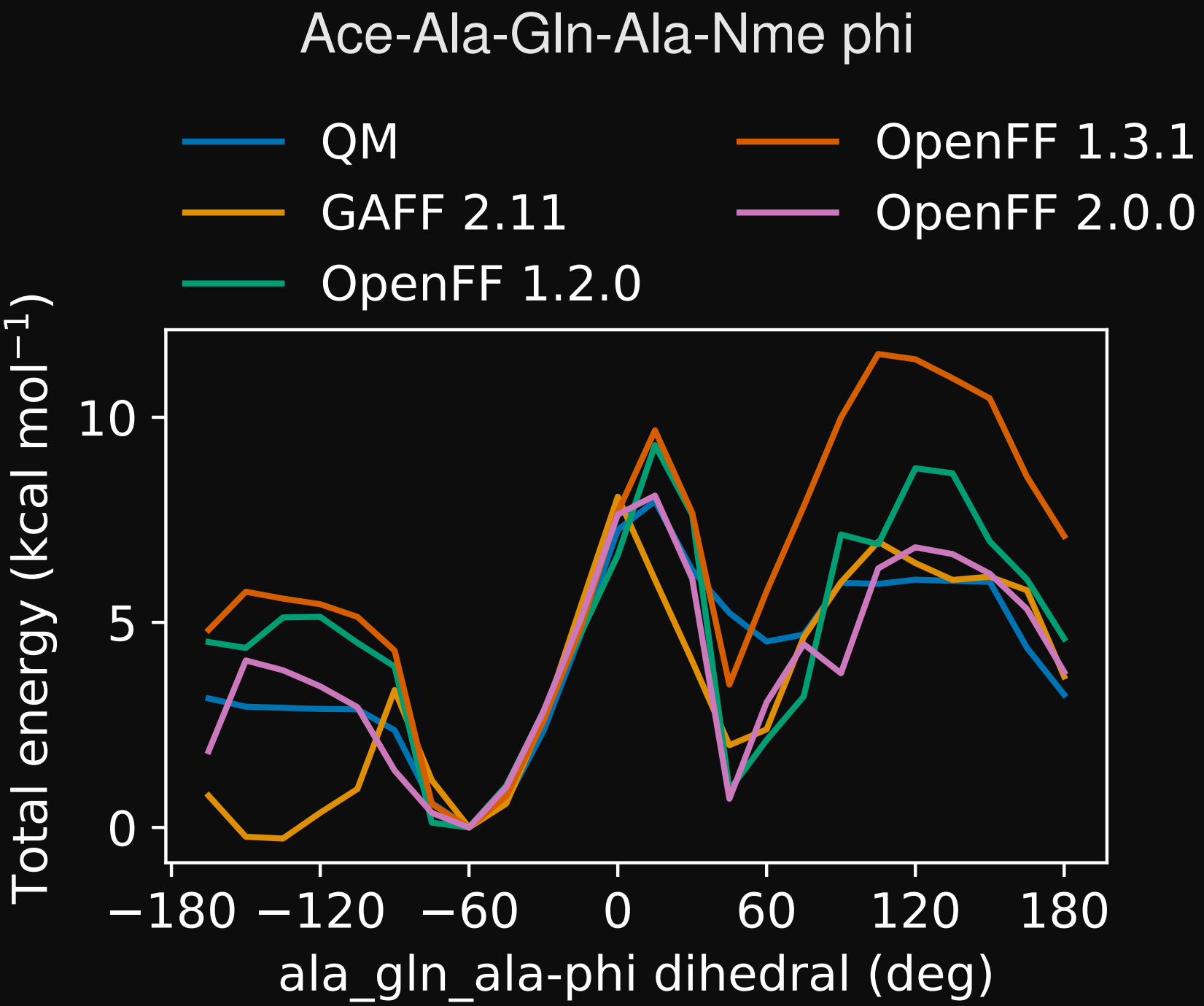
# OpenFF force fields have lower RMSE than GAFF for dihedrals except chi1

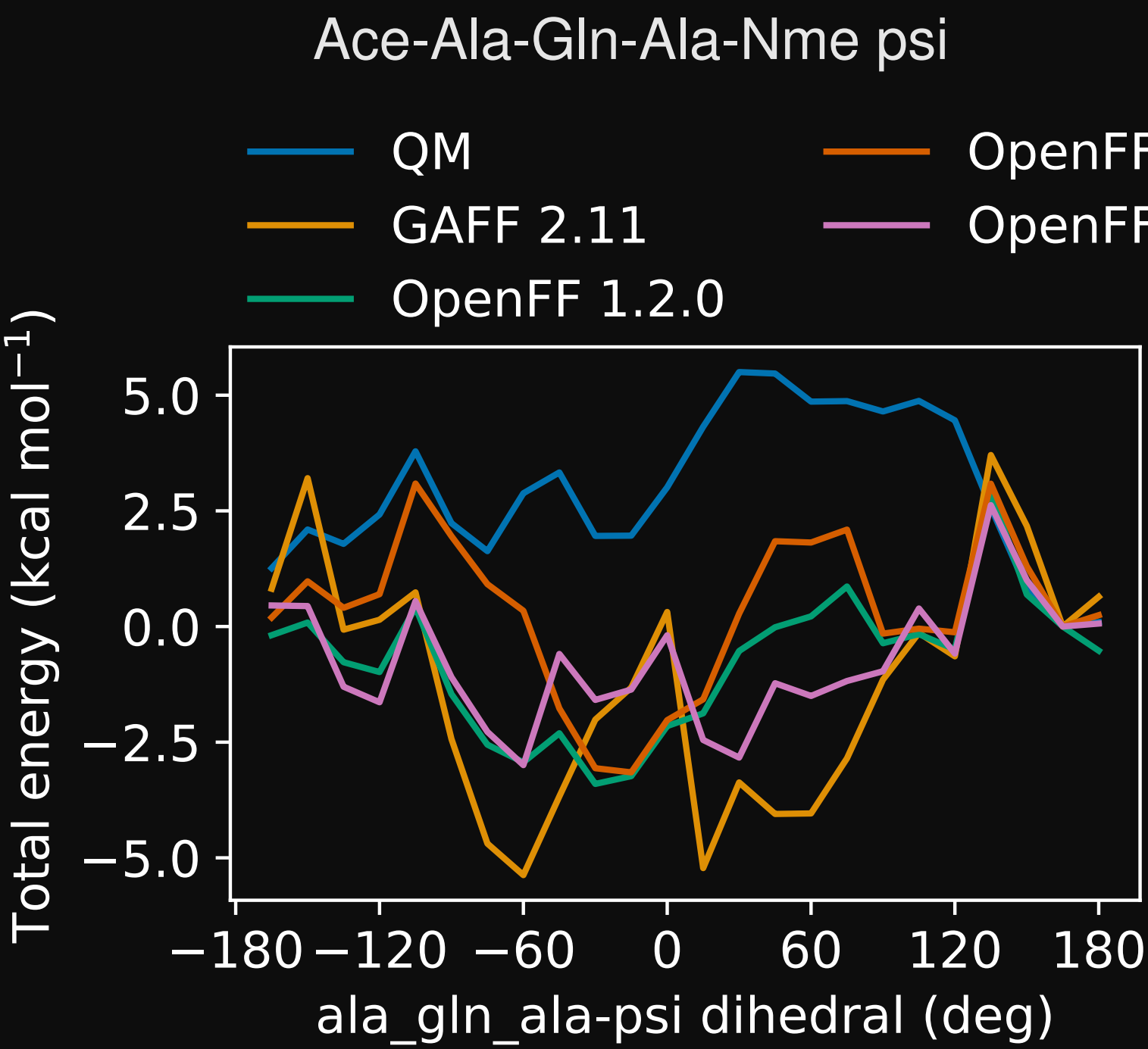


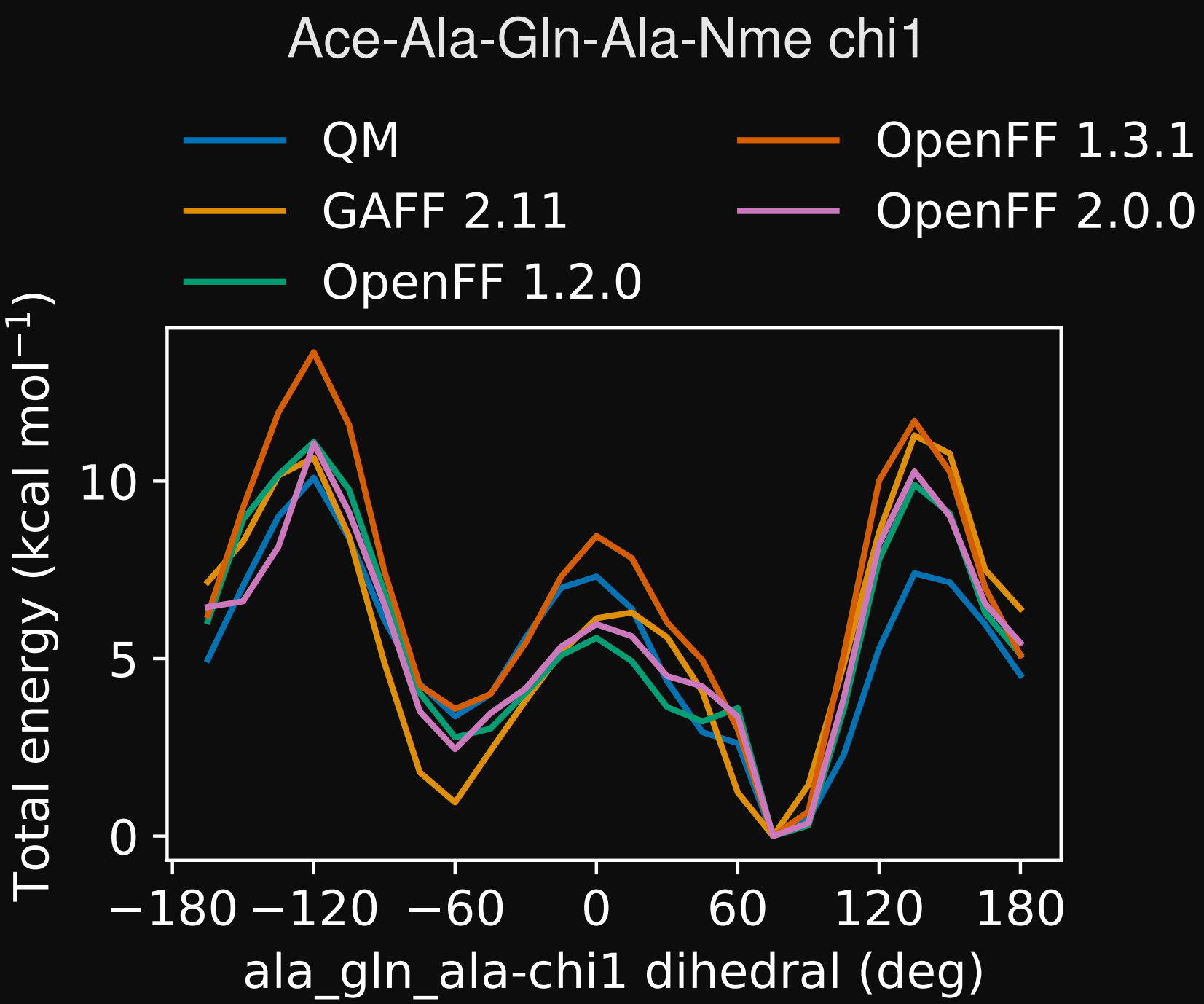
# All FFs fail to describe shape of omega profile

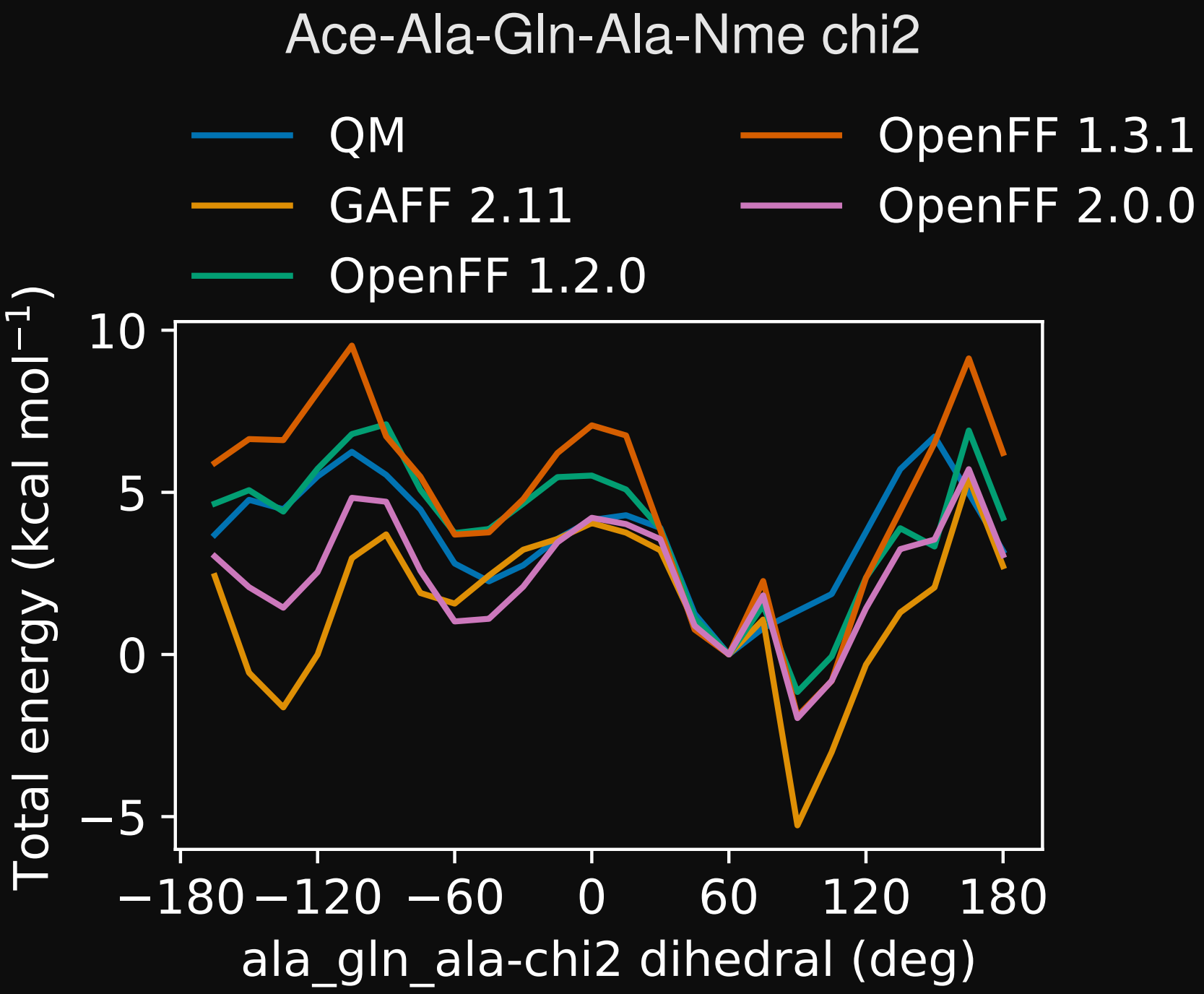



Ace-Ala-Gln-Ala-Nme omega
QM
GAFF 2.11
OpenFF 1.2.0
OpenFF 1.3.1
OpenFF 2.0.0
Total energy (kcal mol$^{-1}$)
0
−2
−4
−180
−120
−60
0
60
120
180
ala_gln_ala-omega dihedral (deg)


Ace-Ala-Gln-Ala-Nme phi
QM
GAFF 2.11
OpenFF 1.2.0
OpenFF 1.3.1
OpenFF 2.0.0
Total energy (kcal mol$^{-1}$)
10
5
0
−180
−120
−60
0
60
120
180
ala_gln_ala-phi dihedral (deg)


Ace-Ala-Gln-Ala-Nme psi
QM
GAFF 2.11
OpenFF 1.2.0
OpenFF 1.3.
OpenFF 2.0.
Total energy (kcal mol$^{-1}$)
5.0
2.5
0.0
−2.5
−5.0
−180
−120
−60
0
60
120
180
ala_gln_ala-psi dihedral (deg)


Ace-Ala-Gln-Ala-Nme chi1
QM
GAFF 2.11
OpenFF 1.2.0
OpenFF 1.3.1
OpenFF 2.0.0
Total energy (kcal mol$^{-1}$)
0
5
10
−180
−120
−60
0
60
120
180
ala_gln_ala-chi1 dihedral (deg)


Ace-Ala-Gln-Ala-Nme chi2
QM
GAFF 2.11
OpenFF 1.2.0
OpenFF 1.3.1
OpenFF 2.0.0
Total energy (kcal mol$^{-1}$)
10
5
0
−5
−180
−120
−60
0
60
120
180
ala_gln_ala-chi2 dihedral (deg)