Quickstart Guide to Model Structures and Interactions of Artificial Molecular Muscles with Efficient Computational Methods

Electronic Supplementary Information (ESI)

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List of Abbreviations

AMM	Artificial Molecular Muscle
GFN	Geometries, Frequencies, Non-covalent interactions
FF	Force Field
xTB	extended Tight-Binding
DFT	Density Functional Theory
DFT-D	Dispersion corrected Density Functional Theory
MD	Molecular Dynamics simulation
SQM	Semiempirical Quantum Mechanical method
PMx	Parametric Method Version X
DFTB	Density Functional Tight-Binding
CREST	Conformer Rotamer Ensemble Sampling Tool
ALPB	Analytically generalized Poisson Boltzmann continuum solvation model
SPE	Single Point Energy
ESI	Electronic Supporting Information
NDI	Naphthalene diimide
CR	Contraction Ratio
SIE	Self Interaction Error
mRRHO	modified Rigid Rotor Harmonic Oscillator
COSMO-RS	Conductor-like Screening Model for Real Solvents
TZVP	Triple Zeta Valence Polarization
DFA	Density Functional Approximation
SASA	Solvent Accessible Solvent Area
SCF	Self Consistent Field
MSINDO	Modified Symmetric Orthogonalized Intermediate Neglect of Differential Overlap
OPLSAA	Optimized Potentials for Liquid Simulations for All Atoms
UFF	Universal Force Field
GAFF	Generalized Amber Force Field
CAESAR	Conformer Algorithm based on Energy Screening and Recursive Buildup
OM	Orthogonalization Methods
CPCM	conductor-like polarizable continuum model
GBSA	Generalized Born Surface Area
USPEX	Universal Structure Predictor: Evolutionary Xtallography
ABC	Artificial Bee Colony genetic algorithm

Additional Computational Details

`xtb` was used as driver for `MOPAC2016` Version 19.179L[S1] for the calculation of PMx energies. *Gibbs* free energies in solution were calculated according to $\Delta G_{c-s} = \Delta E_{el} + \Delta G^{T}_{mRRHO}(+\Delta\delta G_{solv})$ whereas ΔE_{el} is the electronic dispersion corrected energy on various theoretical levels, ΔG^{T}_{mRRHO} is the modified rigid-rotor-harmonic-oscillator (mRRHO) contribution calculated on GFN2-xTB[S2] level of theory at 298 K using the biased Hessian approach (`bhess`),[S3] and $\Delta\delta G_{solv}$ is the solvation free energy calculated with the implicit solvation model ALPB and with COSMO-RS[S4] on BP86/def-TZVP level of theory. As the PMx methods are parametrized to yield reaction enthalpies H, only the -T · S contribution of `bhess` was used for the calculation of ΔG. The solvation corrections were throughout calculated in $CHCl_3$, except for AMM **1** which was investigated in DMSO.[S5] The gas phase contraction free energy was calculated according to $\Delta G_c = \Delta E_{el} + \Delta G^{T}_{mRRHO}$ without solvent contributions. In case of a erroneous SCF convergence of DFA single-point energies, orbitals from a converged calculation using a different DFA were used as starting point. This prevents direct comparison of computation timings in the respective cases as well as the parallelization on more than 4 CPUs.

The MD simulation was conducted in a canonical ensemble, the run time was set to 1 ns with a propagation step size of 1 ps, *Berendsen* thermostat was set to 298 K, the hydrogen mass was set to 2 a.u. at the GFN2-xTB and to 4 a.u. at the GFN-FF level, all bonds were constrained from breaking using the `SHAKE` algorithm. During MDs, constraints to the st-sl distances were applied to maintain the disentangled form but still allowing bending and slipping. The CRs were calculated using the probability weighted average st-st distances, whereby all distances with a occurrence smaller than 5% relative to the maximally occurring distance were neglected and the first 20% of trajectory length were cut off to exclude the equilibration phase from statistics.
The proposed workflow may in principle also be executed using other programs than CREST on GFN2-xTB(ALPB) level. Alternatives to xTB are the established PM6 or PM7 method, OM methods[S6], MSINDO[S7] or classical FF like GAFF[S8], OPLSAA[S9] or UFF[S10]. Other implicit solvent models are e.g. COSMO[S4], GBSA[S11] or CPCM[S12]. The conformer search can also be conducted with methods like for example USPEX[S13], ABC[S14], simulated annealing or CAESAR[S15].

Additional Tables and Figures

In the following, supporting tables for applied distance constraints, single-point energy timings, additional relative contraction energies, absolute energies, statistical data of the distance distributions and the distance distributions themselves are displayed.

Table S1: Applied distance constraints during structure generation and MDs using the numbering of the appended structures.

AMM	d(st-st)	d(st-sl)	d(sl-r)
$\mathbf{1}_{long}$	144-329	4-144, 258-329	33-342, 63-271
			89-340, 115-221
$\mathbf{1}_{short}$	144-329	4-144, 258-329	134-345, 152-225
			53-283, 6-223
$\mathbf{2}_{long}$	178-325	2-178, 258-325	231-252, 232-420
			3-276, 130-249
$\mathbf{2}_{short}$	178-325	2-178, 258-325	220-437, 221-299
			130-264, 231-254
$\mathbf{3}_{long}$	12-314	314-430, 12-164	230-489, 410-489
			238-480, 191-480
$\mathbf{3}_{short}$	12-314	314-430, 12-164	315-490, 104-490
			360-489, 235-489
$\mathbf{4}_{long}$	147-285	285-366, 1-147	84-379, 85-330
			5-376, 46-262
$\mathbf{4}_{short}$	147-285	285-366, 1-147	63-290, 2-298
			127-356, 122-309

Table S2: CPU timings in seconds for single point energies at different theoretical levels, conducted in parallel on 4 CPUs of model Intel®Xeon®CPU E3-1270 v5 @ 3.60GHz. [1)]: value not comparable to other data due to different parallelization and starting point.

	$\mathbf{1}_{\text{long}}$	$\mathbf{1}_{\text{short}}$	$\mathbf{2}_{\text{long}}$	$\mathbf{2}_{\text{short}}$	$\mathbf{3}_{\text{long}}$	$\mathbf{3}_{\text{short}}$
r^2SCAN-3c	2823	3219	7033	7715	140953	-[1)]
GFN1-xTB[S16]	12	12	14	14	55	61
GFN2-xTB	10	10	12	13	53	61
GFN-FF[S17]	0.3	0.3	0.6	0.4	0.5	0.6
PM6-D3H4X	6	6	11	12	15	12
PM7	251	205	9	10	29	52

Table S3: Gas phase reaction *Gibbs* free energies (ΔG_c) of several contraction reactions in kcal $\cdot$ mol^{-1} calculated on additional levels of theory. All methods were calculated with the def2-TZVP basis set.

	$\mathbf{1}_{long} \longrightarrow \mathbf{1}_{short}$	$\mathbf{2}_{long} \longrightarrow \mathbf{2}_{short}$	$\mathbf{3}_{long} \longrightarrow \mathbf{3}_{short}$
ωB97X-V[S18]	22.9	-21.6	-241.2
B3LYP-D4[S19]	23.3	-16.1	-231.7
B3LYP-NL[S20]	22.6	-53.5	-248.8

Table S4: Reaction *Gibbs* free energies in solution (ΔG_{c-s}) of several contraction reactions in kcal $\cdot$ mol^{-1} calculated on different levels of theory with $\Delta\delta G_{solv}$ from COSMO-RS.

	$\mathbf{1}_{long} \longrightarrow \mathbf{1}_{short}$	$\mathbf{2}_{long} \longrightarrow \mathbf{2}_{short}$	$\mathbf{3}_{long} \longrightarrow \mathbf{3}_{short}$
ωB97X-D4	-1.6	6.9	-553.1
ωB97X-V	-0.7	0.9	-546.9
B3LYP-D4	-0.3	6.5	-537.4
B3LYP-NL	-1.0	-30.9	-554.5
PBE0-D4	-1.4	7.8	-551.5
PBE-D4	1.6	7.6	-498.0
r^2SCAN-3c	-0.9	9.8	-521.0
PM6-D3H4X	-13.3	-16.7	-542.8
PM7	-38.2	-13.3	-565.5
GFN2-xTB	0.2	10.6	-489.0
GFN1-xTB	-3.0	6.6	-463.8
GFN-FF	-28.2	-6.0	-471.5

Table S5: Reaction *Gibbs* free energies in solution (ΔG_{c-s}) of several contraction reactions in kcal $\cdot$ mol^{-1} calculated on different levels of theory with $\Delta\delta G_{solv}$ from ALPB.

	$\mathbf{1}_{long} \longrightarrow \mathbf{1}_{short}$	$\mathbf{2}_{long} \longrightarrow \mathbf{2}_{short}$	$\mathbf{3}_{long} \longrightarrow \mathbf{3}_{short}$
ωB97X-D4	-14.8	-2.1	-221.2
ωB97X-V	-14.0	-8.1	-215.1
B3LYP-D4	-13.6	-2.5	-205.6
B3LYP-NL	-14.3	-39.9	-222.7
PBE0-D4	-14.7	-1.2	-219.7
PBE-D4	-11.6	-1.3	-166.1
r^2SCAN-3c	-14.1	0.8	-189.2
PM6-D3H4X	-26.5	-25.7	-211.0
PM7	-51.6	-22.2	-233.6
GFN2-xTB	-13.1	1.6	-157.2
GFN1-xTB	-16.3	-2.3	-132.0
GFN-FF	-41.4	-15.0	-139.6

Table S6: Absolute energies in Eh (E_{el}) on different levels of theory using `xtb V6.4.1` (as driver for `MOPAC`).

	E_{el} / Eh				
AMM	PM6-D3H4X	PM7	GFN1-xTB	GFN2-xTB	GFN-FF
1_{long}	-1.112160025951	-2.112870739555	-601.179958	-570.669568	-57.161583
1_{short}	-1.093055288427	-2.133595551742	-601.144725	-570.62923	-57.166361
2_{long}	-3.650569691603	-3.904188305381	-801.974302	-753.844935	-76.120179
2_{short}	-3.723050292875	-3.971161034436	-802.010582	-753.874858	-76.176602
3_{long}	1.562062250334	0.457503580849	-749.834777	-734.593872	-91.351477
3_{short}	1.194897092606	0.054247418063	-750.10231	-734.901645	-91.631258

Table S7: Absolute energies in Eh (E_{el}) on different levels of theory applying a def2-TZVP basis set wherever possible using `TURBOMOLE V7.5.1`.

AMM	E_{el} / Eh					
	ωB97X	ωB97X-V	B3LYP-D4	PBE0-D4	PBE-D4	r^2SCAN-3c
1_{long}	-8733.227931	-8733.011357	-8731.061426	-8725.809757	-8725.272168	-8730.290759
1_{short}	-8733.189338	-8732.972414	-8731.021866	-8725.771941	-8725.229464	-8730.252063
2_{long}	-11633.412718	-11633.163580	-11630.660760	-11623.655037	-11623.000085	-11629.546169
2_{short}	-11633.428942	-11633.208963	-11630.697259	-11623.689463	-11623.034738	-11629.577358
3_{long}	-14880.060056	-14879.660998	-14877.175900	-14869.943800	-14869.094125	-14876.508548
3_{short}	-14880.454042	-14880.061050	-14877.560811	-14870.351117	-14869.416139	-14876.867233

Table S8: Absolute energies in Eh and kcal $\cdot$ mol^{-1}for different energy contributions. [1)]: DMSO instead of CH_3Cl.

AMM	G^T_{mRRHO} / Eh GFN2-xTB(298K)	G_{solv} / Eh ALPB(CH_3Cl)	G_{solv} / kcal $\cdot$ mol^{-1} COSMO-RS(CH_3Cl)	E_{disp} / Eh D4	$-T \cdot S$ / Eh GFN2-xTB(298 K)
1_{long}	2.818118	-0590187448[1)]	-327.214[1)]	-0.115014	-0.421368
1_{short}	2.815688	-0.648964[1)]	-350.842[1)]	-0.116011	-0.424044
2_{long}	3.539885	-0.356676	-138.438	-0.182651	-0.525197
2_{short}	3.550770	-0.335018	-115.888	-0.202246	-0.515336
3_{long}	3.623274	-0.628557	-76.575	-0.166457	-0.500206
3_{short}	3.638995	-0.587037	-382.347	-0.182260	-0.510782

Table S9: Statistical data of distance distributions derived from MDs under neglect of distance probabilities below 5% of the maximal probability. Average distances, the most probable distances and standard deviations (SD) are given in Å.

	av. dist.	most prob. dist.	SD
$\mathbf{4}_{\text{long}}$ (GFN2-xTB)	64.9	64.9	10.2
$\mathbf{4}_{\text{long}}$ (GFN-FF)	63.4	63.4	20.0
$\mathbf{4}_{\text{short}}$ (GFN2-xTB)	41.9	41.6	10.1
$\mathbf{4}_{\text{short}}$ (GFN-FF)	42.2	43.2	21.5

Table S10: Probabilities in % of stopper-to-stopper distances in pm for the RDF of AMM $\mathbf{4}_{\text{long}}$ at the GFN2-xTB(CH_3Cl) level.

stopper-to-stopper distance / pm	absolute probability / %	stopper-to-stopper distance / pm	absolute probability / %
6269	0.141181957	6659	0.345878421
6275	0.081735176	6665	0.388443074
6281	0	6671	0.091733848
6287	0	6677	0.160589914
6293	0.071629934	6683	0
6299	0.509157710	6689	0.121489634
6305	0.523121075	6695	0.280155931
6311	0.363418067	6701	0.185006336
6317	0.245120333	6707	0.000047580
6323	0.465077163	6713	0.194493686
6329	0.618102452		
6335	0.706939597		
6341	0.753013982		
6347	1.293048867		
6353	1.445103661		
6359	0.946523561		
6365	0.846544863		
6371	0.793239146		
6377	0.513971611		
6383	2.087710871		
6389	2.027127039		
6395	2.790245060		
6401	3.559293066		
6407	3.234311866		
6413	3.200176778		
6419	2.501690702		
6425	2.564043669		
6431	3.274975616		
6437	3.629205812		
6443	4.563754075		
6449	4.102334884		
6455	4.561424340		
6461	5.339871255		
6467	3.826474364		
6473	4.128280896		
6479	5.463818136		
6485	6.195438768		
6491	7.457726765		
6497	6.527786151		
6503	5.489291683		
6509	5.143577326		
6515	4.546541888		
6521	5.253803029		
6527	5.667897013		
6533	4.526353743		
6539	4.619265697		
6545	4.058687467		
6551	4.964871948		
6557	4.012333247		
6563	3.560627868		
6575	2.618322586		
6581	3.338885053		
6587	1.909097085		
6593	2.118800612		
6599	1.380492313		
6605	1.060558610		
6611	0.903800286		
6617	1.243222419		
6623	1.202927044		
6629	1.708209507		
6635	0.620698306		
6641	0.575171507		
6647	0.290611235		
6653	0.106044581		

Table S11: Probabilities in % of stopper-to-stopper distances in pm for the RDF of AMM $\mathbf{4}_{\text{short}}$ at the GFN2-xTB(CH_3Cl) level.

stopper-to-stopper distance / pm	absolute probability / %	stopper-to-stopper distance / pm	absolute probability / %
4012.5	0.007363829	4332.5	0.8655608721
4017.5	0.264690794	4337.5	0.3280508855
4022.5	0.039498314	4342.5	0.6081145590
4027.5	0.231286786	4347.5	0.7992080066
4032.5	0.005089173	4352.5	0.4491715447
4037.5	0.387542682	4357.5	0.3702331665
4042.5	0.556937918	4362.5	0.09203645302
4047.5	1.117878339	4367.5	0.1685684209
4052.5	0.445043418	4372.5	0.2996525791
4057.5	0.421509626	4377.5	0.2206293563
4062.5	0.803091431	4382.5	0
4067.5	1.105784709	4387.5	0.1699085048
4072.5	1.361139074	4392.5	0.2856181944
4077.5	2.465984834	4397.5	0
4082.5	2.178458030	4402.5	0
4087.5	1.277409261	4407.5	0
4092.5	3.742417523	4412.5	0
4097.5	2.739753117	4417.5	0.2099941339
4102.5	3.039154834	4422.5	0.0149735133
4107.5	3.496847762	4427.5	0
4112.5	3.298837371	4432.5	0
4117.5	3.900250099	4437.5	0.0154168348
4122.5	3.259313125	4442.5	0.2070941612
4127.5	4.141494899		
4132.5	3.230301113		
4137.5	5.616679354		
4142.5	6.309210759		
4147.5	4.401443311		
4152.5	5.455943751		
4157.5	6.678266509		
4162.5	4.463100935		
4167.5	4.870342716		
4172.5	4.484095443		
4177.5	4.176905908		
4182.5	4.725709930		
4187.5	6.555778054		
4192.5	5.779577647		
4197.5	5.101869647		
4202.5	3.237572638		
4207.5	4.844254477		
4212.5	3.985228739		
4217.5	5.269154280		
4222.5	5.143098873		
4227.5	3.560501807		
4232.5	5.152023407		
4237.5	3.925855301		
4242.5	4.152382555		
4247.5	4.189623108		
4252.5	3.493840965		
4257.5	3.868501303		
4262.5	2.787429740		
4267.5	2.912068866		
4272.5	2.331008181		
4277.5	2.598950644		
4282.5	3.700020511		
4287.5	3.245622680		
4292.5	2.630060268		
4297.5	2.685027894		
4302.5	2.080557169		
4307.5	1.678294936		
4312.5	1.148202633		
4317.5	1.154469706		
4322.5	1.199787316		
4327.5	1.786228787		

Table S12: Probabilities in % of stopper-to-stopper distances in pm for the RDF of AMM $\mathbf{4}_{\text{long}}$ at the GFN-FF(CH_3Cl) level.

stopper-to-stopper distance / pm	absolute probability / %	stopper-to-stopper distance / pm	absolute probability / %
5804.5	0	6389.5	2.728671111
5813.5	0	6398.5	2.505481995
5822.5	0	6407.5	3.541265215
5831.5	0	6416.5	3.878673176
5840.5	0	6425.5	3.706049651
5849.5	0.259527301	6434.5	3.579230904
5858.5	0.263383032	6443.5	3.561350093
5867.5	0.128383426	6452.5	3.413568341
5876.5	0	6461.5	2.513499930
5885.5	0	6470.5	3.213266140
5894.5	0	6479.5	2.988358030
5903.5	0.158547583	6488.5	2.243063875
5912.5	0.235503035	6497.5	1.617028998
5921.5	0.317451642	6506.5	1.545014406
5930.5	0.086307310	6515.5	1.103298303
5939.5	0.123013584	6524.5	1.144587159
5948.5	0.151901961	6533.5	0.903832891
5957.5	0.333202692	6542.5	0.541516647
5966.5	0.179338868	6551.5	0.513726553
5975.5	0.023412747	6560.5	0.320892201
5984.5	0.153887116	6569.5	0.203574160
5993.5	0.159414193	6578.5	0.241421135
6002.5	0.198958670	6587.5	0.390186381
6011.5	0.085715988	6596.5	0.084083194
6020.5	0.207660136	6605.5	0.090479227
6029.5	0.276409833	6614.5	0.215668991
6038.5	0.191457998	6623.5	0
6047.5	0.372762938	6632.5	0
6056.5	0.730574137	6641.5	0
6065.5	0.207028155	6650.5	0
6074.5	0.195354109	6659.5	0
6083.5	0.186949434	6668.5	0
6092.5	0.185915882	6677.5	0
6101.5	0.327199633	6686.5	0
6110.5	0.475254698	6695.5	0
6119.5	0.624266634		
6128.5	0.400109347		
6137.5	0.231462962		
6146.5	0.593473944		
6155.5	1.142679273		
6164.5	0.927877777		
6173.5	0.484661322		
6182.5	1.155217981		
6191.5	0.567426070		
6200.5	1.028433753		
6209.5	1.603756749		
6218.5	1.529693573		
6227.5	1.283015474		
6236.5	1.639230031		
6245.5	1.828649387		
6254.5	1.478634455		
6263.5	2.858851549		
6272.5	2.175913567		
6281.5	2.538904275		
6290.5	3.300588567		
6299.5	2.560661511		
6308.5	2.520195036		
6317.5	2.512100904		
6326.5	2.896517860		
6335.5	4.046456488		
6344.5	3.634390111		
6353.5	2.665897822		
6362.5	2.892477926		
6371.5	3.726352100		
6380.5	3.260909836		

Table S13: Probabilities in % of stopper-to-stopper distances in pm for the RDF of AMM $\mathbf{4}_{\text{short}}$ at the GFN-FF(CH_3Cl) level.

stopper-to-stopper distance / pm	absolute probability / %	stopper-to-stopper distance / pm	absolute probability / %
3803.5	0	4258.5	2.134888780
3810.5	0	4265.5	2.636668651
3817.5	0	4272.5	2.384521874
3824.5	0	4279.5	2.047609157
3831.5	0	4286.5	2.653515540
3838.5	0	4293.5	2.722544306
3845.5	0	4300.5	3.475889831
3852.5	0.043033074	4307.5	4.245537497
3859.5	0.170741076	4314.5	4.130707082
3866.5	0.161148446	4321.5	4.678503527
3873.5	0.051510288	4328.5	3.251742389
3880.5	0.205733302	4335.5	3.512054349
3887.5	0.005559009	4342.5	3.968556939
3894.5	0.000000000	4349.5	3.202819578
3901.5	0.020531078	4356.5	4.390374877
3908.5	0.605802241	4363.5	4.053949006
3915.5	0.572243342	4370.5	3.230099135
3922.5	0.558719632	4377.5	2.053522158
3929.5	0.522339415	4384.5	2.235297453
3936.5	0.493397483	4391.5	2.026558218
3943.5	0.471501372	4398.5	1.898296577
3950.5	0.536591147	4405.5	0.909189776
3957.5	0.277699924	4412.5	1.156103077
3964.5	0.760404908	4419.5	1.079612684
3971.5	0.705877590	4426.5	0.579356812
3978.5	0.368392026	4433.5	0.320755219
3985.5	0.775552918	4440.5	0.317909908
3992.5	1.009825371	4447.5	0.105445895
3999.5	0.919201592	4454.5	0.064509606
4006.5	0.802171770	4461.5	0.159301995
4013.5	0.418730960	4468.5	0.000555800
4020.5	1.141820848	4475.5	0
4027.5	1.537218727	4482.5	0
4034.5	1.508264407	4489.5	0
4041.5	1.236530147	4496.5	0
4048.5	1.822981889		
4055.5	1.792240662		
4062.5	1.756529218		
4069.5	1.749104387		
4076.5	1.917520341		
4083.5	1.310038231		
4090.5	2.249495983		
4097.5	2.001072202		
4104.5	1.944556347		
4111.5	2.335247714		
4118.5	2.053552068		
4125.5	1.862942336		
4132.5	1.544368000		
4139.5	2.259113230		
4146.5	2.600280674		
4153.5	1.435486592		
4160.5	1.709119191		
4167.5	2.025201281		
4174.5	1.892854801		
4181.5	1.878474501		
4188.5	1.912459281		
4195.5	1.009936438		
4202.5	1.779716524		
4209.5	2.321300018		
4216.5	2.063798400		
4223.5	2.556651611		
4230.5	2.557883782		
4237.5	2.299958262		
4244.5	1.225740995		
4251.5	1.482578094		

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