Perform pure salt simulation (NH_4Cl)

1. Parameterisation methods
2. Measurements

Research on NH4 conduction in ion channel

[a] Detailed Mechanism for AmtB Conducting NH4 /NH3: Molecular Dynamics Simulations

- Optimised charges by restrained ESP-fit method using ChelpG approach
    - N: -0.824; H: +0.456

[b] Ammonium Recruitment and Ammonia Transport by E. coli Ammonia Channel AmtB

- NH4+ partial charges using OPLS charges
- NH4+ bond and bond angle using CHARMM27 parameters, same as NH3 moiety of Lysine

[c] Molecular Dynamics Simulations on the Escherichia coli Ammonia Channel Protein AmtB: Mechanism of Ammonia/ Ammonium Transport

- Apply Mulliken charges at the HF/6-31G(d)
- LJ parameters same as amide groups

[d] Ammonium Transporters Achieve Charge Transfer by Fragmenting Their Substrate

- NH4+ and surrounding water molecules and protein side chains are described by a polarizable force field based on the classical Drude oscillator, (62-65) and parametrized to reproduce both the free energy of hydration and the ion–protein interactions
- Pair-specific LJ parameters between the ions and atoms of the ligands are adjusted to reproduce the ab initio interaction energies
- Full geometry optimizations of the complexes between these ligands and the three cations Na+, K+, and NH4+ are performed at the MP2(FC)/6-311++G(d,p) level using Gaussian 09 program

Research on NH4 conduction in ion channel

	Method	Force field, water	Charges
Default	N from primary NH3+, phosphatidylethanolamine H from polar H+	CHARMM36, TIP3P	N: -0.33 H: +0.33
[a]	NH4 charges by restrained ESP-fit method using ChelpG approach	GROMOS87, SPC	N: -0.824 H: +0.456
[b]	NH4+ partial charges using OPLS charges, as OPLS and CHARMM partial charges of NH3+ in Lysine are nearly identical	CHARMM27, H atoms were added to crystal waters using PSFGEN in NAMD	N: -0.40 H: +0.35
[c]	N, H charges using Mulliken charges at the HF/6-31G(d)	CHARMM, TIP3P	Not specified
[d]	- NH4+ and surrounding water molecules and protein side chains are described by a polarizable force field based on the classical Drude oscillator, and parametrised to reproduce both the free energy of hydration and the ion–protein interactions. - Pair-specific LJ parameters between the ions and atoms of the ligands are adjusted to reproduce the ab initio interaction energies. - Full geometry optimizations of the complexes between these ligands and the three cations Na+, K+, and NH4+ are performed at the MP2(FC)/6-311++G(d,p) level using Gaussian 09 program.	CHARMM27, TIP3P	/

Other NH4 parameterisation

	Method	Force field, water	Charges
Default	N from primary NH3+, phosphatidylethanolamine H from polar H+	CHARMM36, TIP3P	N: -0.33 H: +0.33
Madrid [5]	N, H charges using OPLS-based model, scaled by 0.85	Madrid-2019, TIP4P/2005	N: −0.3400 H: +0.2975

RDF data (Na-O)

	No. of OH2 in first hydration shell	First peak	First minimum
Simulation [1]	5.702	2.36	3.18
Literature [2]	4.0-8.0	2.36	
MC in TIP4P [3]	6.2	2.50	
Madrid [6]	5.4	2.33	

RDF data (N-O)

	No. of OH2 in first hydration shell	First peak	First minimum
Simulation [1]	6.581	2.82	3.66
Literature [2]	8.1-10.0	2.6-3.05	
MC in TIP4P [3]	7.3	2.90	
MC in TIP3P [4]	7.0-7.1	2.63-2.70	
Madrid [5]	5.5	2.66	

RDF data (Cl-O)

	No. of OH2 in first hydration shell	First peak	First minimum
Simulation, NaCl [1]	7.911	3.16	3.84
Simulation, NH4Cl [1]	7.227	3.16	3.80
Literature [2]	5.9-8.5	3.1-3.3	
MC in TIP4P [3]	7.6	3.25	
Madrid [6]	5.9	3.05	

Free energy calculations

	Absolute hydration energy of NH4	Absolute hydration energy of Na	Relative hydration energies between NH4+ and Na+
Experiment [7]	-78.6		-21.7 kcal/mol
Free energy perturbation [4]	-79.55 (+ Born) -98.85		-28.87 kcal/mol
Empirical model [8]	-68.1	-87.2	-19.1 kcal/mol
MC simulation [3]	-73.1	-92.3	-19 kcal/mol

Osmotic coefficient at 1M

	NH4Cl	NaCl
Isopiestic vapour pressure method [9]	0.897	
MC simulations [10]		0.91-0.92
Experiment [11]		0.94
MD simulations [12]		0.93

References

[1] https://github.com/Heiley-W/project/blob/main/RDF-analysis.ipynb
[2] Ionic radii in aqueous solutions https://doi.org/10.1021/cr00090a003
[3] Halide, Ammonium, and Alkali Metal Ion Parameters for Modeling Aqueous Solutions https://doi/10.1021/ct600252r
[4] Free Energy Calculations Involving NH4+in Water https://doi.org/10.1002/jcc.540120106
[5] Further extension of the Madrid-2019 force field: Parametrization of nitrate and ammonium ion https://doi.org/10.1063/5.0177363
[6] A force field of Li+, Na+, K+, Mg2+, Ca2+,Cl−, and in aqueous solution based on the TIP4P/2005 water model and scaled charges for the ions https://doi.org/10.1063/1.5121392
[7] Ref 33 and 22 of [4] respectively
[8] A simple empirical model describing the thermodynamics of hydration of ions of widely varying charges, sizes, and shapes https://doi.org/10.1016/0301-4622(94)00051-4
[9] The osmotic and activity coefficients of aqueous solutions of ammonium chloride and ammonium nitrate at 25° https://doi.org/10.1039/TF9534900027
[10] Osmotic and activity coefficients from effective potentials for hydrated ions https://doi.org/10.1103/PhysRevE.55.5689
[11] Ref 20 of [10]
[12] Osmotic coefficients of atomistic NaCl (aq) force fields https://doi.org/10.1063/1.2185105
[a] Detailed Mechanism for AmtB Conducting NH4+/NH3: Molecular Dynamics Simulations https://doi.org/10.1529/biophysj.106.090191
[b] Ammonium Recruitment and Ammonia Transport by E. coli Ammonia Channel AmtB https://doi.org/10.1529/biophysj.106.089714
[c] Molecular Dynamics Simulations on the Escherichiacoli Ammonia Channel Protein AmtB: Mechanism of Ammonia/Ammonium Transport https://doi.org/10.1021/ja0631549
[d] Ammonium Transporters Achieve Charge Transfer by Fragmenting Their Substrate https://doi.org/10.1021/ja300129x