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1 MDverse: Shedding Light on the Dark 2 Matter of Molecular Dynamics 3 Simulations

4 Johanna K. S. Tiemann^{1*,†}, Magdalena Szczuka², Lisa Bouarroudj³, Mohamed
5 Oussaren³, Steven Garcia⁴, Rebecca J. Howard⁵, Lucie Delemotte⁶, Erik Lindahl^{5,6},
6 Marc Baaden⁷, Kresten Lindorff-Larsen¹, Matthieu Chavent^{2*}, Pierre Poulain^{3*}

***For correspondence:**

johanna.tiemann@gmail.com (JKST);
Matthieu.Chavent@ipbs.fr (MC);
pierre.poulain@u-paris.fr (PP)

Present address: [†]Novozymes
A/S, 2800 Kgs. Lyngby, Denmark

7 ¹Linderstrøm-Lang Centre for Protein Science, Department of Biology, University of
8 Copenhagen, DK-2200 Copenhagen N, Denmark; ²Institut de Pharmacologie et Biologie
9 Structurale, CNRS, Université de Toulouse, 205 route de Narbonne, 31400, Toulouse,
10 France; ³Université Paris Cité, CNRS, Institut Jacques Monod, F-75013 Paris, France;
11 ⁴Independent researcher, Amsterdam, Netherlands; ⁵Department of Biochemistry and
12 Biophysics, Science for Life Laboratory, Stockholm University, Stockholm, Sweden;
13 ⁶Department of Applied Physics, Science for Life Laboratory, KTH Royal Institute of
14 Technology, Stockholm, Sweden; ⁷Laboratoire de Biochimie Théorique, CNRS,
15 Université Paris Cité, 13 rue Pierre et Marie Curie, F-75005 Paris, France

17 Abstract

18 The rise of open science and the absence of a global dedicated data repository for molecular
19 dynamics (MD) simulations has led to the accumulation of MD files in generalist data repositories,
20 constituting the *dark matter of MD* - data that is technically accessible, but neither indexed,
21 curated, or easily searchable. Leveraging an original search strategy, we found and indexed about
22 250,000 files and 2,000 datasets from Zenodo, Figshare and Open Science Framework. With a
23 focus on files produced by the Gromacs MD software, we illustrate the potential offered by the
24 mining of publicly available MD data. We identified systems with specific molecular composition
25 and were able to characterize essential parameters of MD simulation, such as temperature and
26 simulation length, and identify model resolution, such as all-atom and coarse-grain. Based on
27 this analysis, we inferred metadata to propose a search engine prototype to explore collected MD
28 data. To continue in this direction, we call on the community to pursue the effort of sharing MD
29 data, and increase populating and standardizing metadata to reuse this valuable matter.

31 Introduction

32 The volume of data available in biology has increased tremendously (*Marx, 2013; Stephens et al.,*
33 *2015*), through the emergence of high-throughput experimental technologies, often referred to as -
34 omics, and the development of efficient computational techniques, associated with high-performance
35 computing resources. The Open Access (OA) movement to make research results free and avail-
36 able to anyone (including e.g. the Budapest Open Access Initiative and the Berlin declaration on
37 Open Access to Knowledge) has led to an explosive growth of research data made available by
38 scientists (*Wilson et al., 2021*). The FAIR (Findable, Accessible, Interoperable and Reusable) princi-
39 ples (*Wilkinson et al., 2016*) have emerged to structure the sharing of these data with the goals
40 of reusing research data and to contribute to the scientific reproducibility. This leads to a world

41 where research data has become widely available and exploitable, and consequently new applica-
42 tions based on artificial intelligence (AI) emerged. One example is AlphaFold (*Jumper et al., 2021*),
43 which enables the construction of a structural model of any protein from its sequence. However,
44 it is important to be aware that the development of AlphaFold was only possible because of the
45 existence of extremely well annotated and cleaned open databases of protein structures (wwPDB
46 *Berman et al. (2003)*) and sequences (UniProt *Consortium (2022)*). Similarly, accurate predictions
47 of NMR chemical shifts and chemical-shift-driven structure determination was only made possible
48 via a community-driven collection of NMR data in the Biological Magnetic Resonance Data Bank
49 (*Hoch et al., 2023*). One can easily imagine novel possibilities of AI and deep learning reusing pre-
50 vious research data in other fields, if that data is curated and made available at a large scale (*Fan*
51 *and Shi, 2022; Mahmud et al., 2021*).

52 Molecular Dynamics (MD) is an example of a well-established research field where simulations
53 give valuable insights into dynamic processes, ranging from biological phenomena to material sci-
54 ence (*Perilla et al., 2015; Hollingsworth and Dror, 2018; Yoo et al., 2020; Alessandri et al., 2021;*
55 *Krishna et al., 2021*). By unraveling motions at details and timescales invisible to the eye, this well-
56 established technique complements numerous experimental approaches (*Bottaro and Lindorff-*
57 *Larsen, 2018; Marklund and Benesch, 2019; Fawzi et al., 2021*). Nowadays, large amounts of MD
58 data could be generated when modelling large molecular systems (*Gupta et al., 2022*) or when
59 applying biased sampling methods (*Hénin et al., 2022*). Most of these simulations are performed
60 to decipher specific molecular phenomena, but typically they are only used for a single publication.
61 We have to confess that many of us used to believe that it was not worth the storage to collect
62 all simulations (in particular since all might not have the same quality), but in hindsight this was
63 wrong. Storage is exceptionally cheap compared to the resources used to generate simulations
64 data, and they represent a potential goldmine of information for researchers wanting to reana-
65 lyze them (*Antila et al., 2021*), in particular when modern machine-learning methods are typically
66 limited by the amount of training data. In the era of open and data-driven science, it is critical to
67 render the data generated by MD simulations not only technically available but also practically us-
68 able by the scientific community. In this endeavor, discussions started a few years ago (*Abraham*
69 *et al., 2019; Abriata et al., 2020; Merz et al., 2020*) and the MD data sharing trend has been accel-
70 erated with the effort of the MD community to release simulation results related to the COVID-19
71 pandemic (*Amaro and Mulholland, 2020; Mulholland and Amaro, 2020*) in a centralized database
72 (<https://covid.bioexcel.eu>). Specific databases have also been developed to store sets of simulations
73 related to protein structures (MoDEL: *Meyer et al. (2010)*), membrane proteins in general (Mem-
74 ProtMD: *Stansfeld et al. (2015); Newport et al. (2018)*), G-protein coupled receptors in particular
75 (GPCRmd: *Rodríguez-Espigares et al. (2020)*), or lipids (Lipidbook: *Domański et al. (2010)*), NMRlipids
76 Databank: *Kiirikki et al. (2023)*).

77 Albeit previous attempts in the past (*Tai et al., 2004; Meyer et al., 2010*), there is, as of now,
78 no central data repository that could host all kinds of MD simulation files. This is not only due to
79 the huge volume of data and its heterogeneity, but also because interoperability of the many file
80 formats used adds to the complexity. Thus, faced with the deluge of biosimulation data (*Hospital*
81 *et al., 2020*), researchers often share their simulation files in multiple generalist data repositories.
82 This makes it difficult to search and find available data on, for example, a specific protein or a
83 given set of parameters. We are qualifying this amount of scattered data as *the dark matter of*
84 *MD*, and we believe it is essential to shed light onto this overlooked but high-potential volume of
85 data. When unlocked, publicly available MD files will gain more visibility. This will help people to
86 access and reuse these data more easily and overall, by making MD simulation data more FAIR
87 (*Wilkinson et al., 2016*), it will also improve the reproducibility of MD simulations (*Elofsson et al.,*
88 *2019; Porubsky et al., 2020; consortium, 2019*).

89 In this work, we have employed a search strategy to index scattered MD simulation files de-
90 posited in generalist data repositories. With a focus on the files generated by the Gromacs MD
91 software, we performed a proof-of-concept large-scale analysis of publicly available MD data. We

92 revealed the high value of these data and highlighted the different categories of the simulated
93 molecules, as well as the biophysical conditions applied to these systems. Based on these results
94 and our annotations, we proposed a search engine prototype to easily explore this *dark matter of*
95 *MD*. Finally, building on this experience, we provide simple guidelines for data sharing to gradually
96 improve the FAIRness of MD data.

97 Results

98 With the rise of open science, researchers increasingly share their data and deposit them into gen-
99 eralist data repositories, such as Zenodo (<https://zenodo.org>), Figshare (<https://figshare.com>), Open
100 Science Framework (OSF, <https://osf.io>), and Dryad (<https://datadryad.org/>). In this first attempt to
101 find out how many files related to MD are deposited in data repositories, we focused our explo-
102 ration on three major data repositories: Figshare (~3.3 million files, ~112 TB of data, as of January
103 2023), OSF (~2 million files, as of November 2022)¹, and Zenodo (~9.9 million files, ~1.3 PB of data,
104 as of December 2022; *Panero and Benito (2022)*).

105 One immediate strategy to index MD simulation files available in data repositories is to per-
106 form a text-based Google-like search. For that, one queries these repositories with keywords such
107 as 'molecular dynamics' or 'Gromacs'. Unfortunately, we experienced many false positives with
108 this search strategy. This could be explained by the strong discrepancy we observed in the quan-
109 tity and quality of metadata (title, description) accompanying datasets and queried in text-based
110 search. For instance, a description text could be composed of a couple of words to more than 1,200
111 words. Metadata is provided by the user depositing the data, with no incentive to issue relevant
112 details to support the understanding of the simulation. For the three data repositories studied, no
113 human curation other by that of the providers is performed when submitting data. It is also worth
114 mentioning that title and description are provided as free-text and do not abide to any controlled
115 vocabulary such as a specific MD ontology.

116 To circumvent this issue, we developed an original and specific search strategy that we called
117 *Explore and Expand* (E_x^2) (see Fig. 1-A and Materials and Methods section) and that relies on a com-
118 bination of file types and keywords queries. In the *Explore* phase, we searched for files based on
119 their file types (for instance: .xtc, .gro, etc) with MD-related keywords (for instance: 'molecular dy-
120 namics', 'Gromacs', 'Martini', etc). Each of these hit files belonged to a dataset, which we further
121 screened in the *Expand* phase. There, we indexed all files found in a dataset identified in the previ-
122 ous *Explore* phase with, this time, no restriction to the collected file types (see Fig. 1-A and details
123 on the data scraping procedure in the Materials and Methods section).

124 Globally, we indexed about 250,000 files and 2,000 datasets that represented 14 TB of data de-
125 posited between August 2012 and March 2023 (see Table 1). One major difficulty were the numer-
126 ous files stored in zipped archives, about seven times more than files steadily available in datasets
127 (see Table 1). While this choice is very convenient for depositing the files (as one just needs to pro-
128 vide one big zip file to upload to the data repository server), it hinders the analysis of MD files as
129 data repositories only provide a limited preview of the content of the zip archives and completely
130 inhibits, for example, data streaming for remote analysis and visualization. Files within zip files
131 are not indexed and cannot be searched individually. The use of zip archives also hampers the
132 reusability of MD data, since a specific file cannot be downloaded individually. One has to down-
133 load the entire zip archive (sometimes with a size up to several gigabytes) to extract the one file of
134 interest.

135 The first dataset we found related to MD data that has been deposited in August 2012 in
136 Figshare and corresponds to the work of Fuller et al. (*Fuller et al., 2012*) (see Table 1) but we
137 may consider the start of more substantial deposition of the MD data to be 2016 with more than
138 20,000 files deposited, mainly in Figshare (see Fig. 1-B). While the number of files deposited in Zen-
139 odo was first relatively limited, the last few years (2020-2022) saw a steep increase, passing from

¹Figures provided by Figshare and OSF user support teams

Table 1. Statistics of the MD-related datasets and files found in the data repositories Figshare, OSF, and Zenodo.

Data repository	datasets	first dataset	latest dataset	files	total size (GB)	zip files	files within zip	total files
Zenodo	1,011	19/11/2014	05/03/2023	20,250	12,851	1,780	141,304	161,554
Figshare	913	20/08/2012	03/03/2023	3,336	736	590	74,720	78,056
OSF	55	24/05/2017	05/02/2023	6,146	495	14	0	6,146
Total	1,979	-	-	29,732	14,082	2,384	216,024	245,756

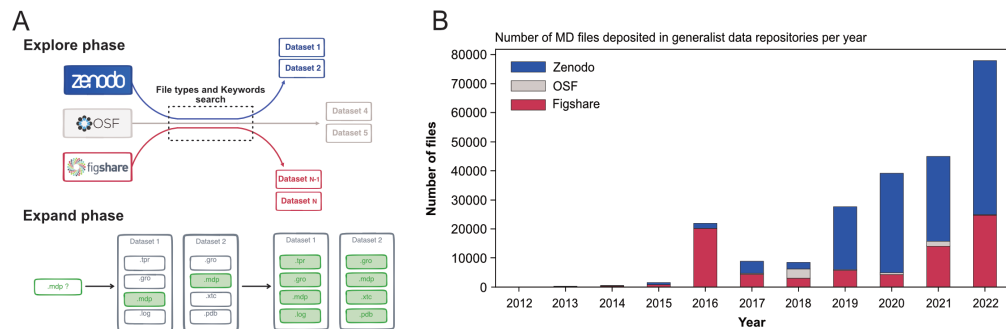


Figure 1. (A) Explore and Expand (E_x^2) strategy used to index and collect MD-related files. Within the explore phase, we search in the respective data repositories for datasets that contain specific keywords (e.g. "molecular dynamics", "md simulation", "namd", "martini"...) in conjunction with specific file extensions (e.g. ".mdp", ".psf", ".parm7"...), depending on their uniqueness and level of trust to not report false-positives (i.e. not MD related). In the expand phase, the content of the identified datasets is fully cataloged, including files that individually could result in false positives (such as e.g. ".log" files). (B) Number of deposited files in generalist data repositories, identified by our E_x^2 strategy.

140 a few thousands files in 2018 to almost 50,000 files in 2022 (see Fig. 1-B). In 2018, the number of
 141 MD files deposited in OSF was similar to those in the two other data repositories, but did not take
 142 off as much as the other data repositories. Zenodo seems to be favored by the MD community
 143 since 2019, even though Figshare in 2022 also saw a sharp increase in deposited MD files. The
 144 preference for Zenodo could also be explained by the fact that it is a publicly funded repository de-
 145 veloped under the European OpenAIRE program and operated by CERN (*European Organization*
 146 *For Nuclear Research and OpenAIRE, 2013*). Overall, the trend showed a rise of deposited data with
 147 a steep increase in 2022 (Fig. 1-B). We believe that this trend will continue in future years, which
 148 will lead to a greater amount of MD data available. It is thus urgent to deploy a strategy to index
 149 this vast amount of data, and to allow the MD community to easily explore and reuse such gigantic
 150 resource. The following describes what is already feasible in terms of meta analysis, in particular
 151 what types of data are deposited in data repositories and the simulation setup parameters used
 152 by MD experts that have deposited their data.

153 With our E_x^2 strategy (see Fig. 1-A), we assigned the deposited files to the MD packages: AMBER
 154 (*Ferrer et al., 2012*), DESMOND (*Bowers et al., 2006*), Gromacs (*Berendsen et al., 1995; Abraham*
 155 *et al., 2015*), and NAMD/CHARMM (*Phillips et al., 2020; Brooks et al., 2009*), based on their corre-
 156 sponding file types (see Materials and Methods section). In the case of NAMD/CHARMM, file exten-
 157 sions were mostly identical, which prevented us from distinguishing the respective files from these
 158 two MD programs. With 87,204 files deposited, the Gromacs program was most represented (see
 159 Fig. 2-A), followed by NAMD/CHARMM, AMBER, and DESMOND. This statistic is limited as it does not
 160 consider more specific databases related to a particular MD program. For example, the DE Shaw
 161 Research website contains a large amount of simulation data related to SARS-CoV-2 that has been
 162 generated using the ANTON supercomputer ([https://www.deshawresearch.com/downloads/download_](https://www.deshawresearch.com/downloads/download_trajectory_sarscov2.cgi/)
 163 [trajectory_sarscov2.cgi/](https://www.deshawresearch.com/downloads/download_trajectory_sarscov2.cgi/)) or other extensively simulated systems of interest to the community. How-
 164 ever, this in itself might also serve as a good example, since few automated search strategies will
 165 be able to find custom stand-alone web servers as valuable repositories. Here, our goal was not

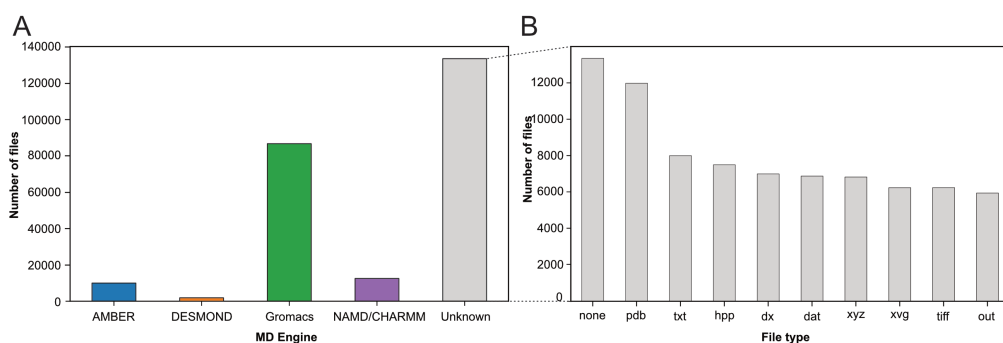


Figure 2. Categorization of index files based on their file types and assigned MD engine. (A) Distribution of files among MD simulation engines (B) Expansion of (A) MD Engine category "Unknown" into the 10 most observed file types.

166 to compare the availability of all data related to each MD program but to give a snapshot of the
167 type of data available at a given time (*i.e.* March 2023) in generalist data repositories. Interest-
168 ingly, many files (> 133,000) were not directly associated to any MD program (see Fig. 2-A label
169 'Unknown'). We categorized these files based on their extensions (see Fig. 2-B). While 10 % of these
170 files were without file extension (Fig. 2-B, column *none*), we found numerous files corresponding
171 to structure coordinates such as .pdb (~12,000) and .xyz (~6,800) files. We also got images (.tiff
172 files) and graphics (.xvg files). Finally, we found many text files such as .txt, .dat, and .out which can
173 potentially hold details about how simulations were performed. Focusing further on files related
174 to the Gromacs program, being currently most represented in the studied data repositories, we
175 demonstrated in the following present possibilities to retrieve numerous information related to
176 deposited MD simulations.

177 First, we were interested in what file types researchers deposited and thereby find potentially
178 of great value to share. We therefore quantified the types of files generated by Gromacs (Fig. 3-A).
179 The most represented file type is the .xtc file (28,559 files, representing 8.6 TB). This compressed
180 (binary) file is used to store the trajectory of an MD simulation and is an important source of in-
181 formation to characterize the evolution of the simulated molecular system as a function of time.
182 It is thus logical to mainly find this type of file shared in data repositories, as it is of great value
183 for reuse and new analyses. Nevertheless, it is not directly readable but needs to be read by a
184 third-party program, such as Gromacs itself, a molecular viewer like VMD (*Humphrey et al., 1996*)
185 or an analysis library such as MDAnalysis (*Michaud-Agrawal et al., 2011; Gowers et al., 2016*). In
186 addition, this trajectory file can only be of use in combination with a matching coordinates file, in
187 order to correctly access the dynamics information stored in this file. Thus, as it is, this file is not
188 easily mineable to extract useful information, especially if multiple .xtc and coordinate files are
189 available in one dataset. Interestingly, we found 1,406 .trr files, which contain trajectory but also
190 additional information such as velocities, energy of the system, etc. While this file is especially use-
191 ful in terms of reusability, the large size (can go up to several 100 GB) limits its deposition in most
192 data repositories. For instance, a file cannot usually exceed 50 GB in Zenodo, 20 GB in Figshare
193 (for free accounts) and 5 GB in OSF. Altogether, Gromacs trajectory files represented about 30,000
194 files in the three explored generalist repositories (34% of Gromacs files). This is a large number
195 in comparison to existing trajectories stored in known databases dedicated to MD with 1,700 MD
196 trajectories available in MoDEL, 1,737 trajectories (as of November 2022) available in GPCRmd,
197 5,971 (as of January 2022) trajectories available in MemProtMD and 726 trajectories (as of March
198 2023) available in the NMRlipids Databank. Although fewer in count, these numbers correspond to
199 manually or semi-automatically curated trajectories of specific systems, mostly proteins and lipids.
200 Thus, ~30,000 MD trajectories available in generalist data repositories may represent a wider spec-
201 trum of simulated systems but need to be further analyzed and filtered to separate usable data

202 from less interesting trajectories such as minimization or equilibration runs.

203 Given the large volume of data represented by .xtc files (see above), we could only scratch the
204 surface of the information stored in these trajectory files by analyzing a subset of 779 .xtc files -
205 one per dataset in which this type of file was found. We were able to get the size of the molecular
206 systems and the number of frames available in these files (Fig. 3-B). Of note, the frames do not
207 directly translate to the simulation runtime - more information deposited in other files (e.g. .mdp
208 files) is needed to determine the complete runtime of the simulation. The system size was up
209 to more than one million atoms for a simulation of the TonB protein (*Virtanen et al., 2020*). The
210 cumulative distribution of the number of frames showed that half of the files contain more than
211 10,000 frames. This conformational sampling can be very useful for other research fields besides
212 the MD community that study, for instance, protein flexibility or protein engineering where diverse
213 backbones can be of value. We found an .xtc file containing more than 5 million frames, where the
214 authors probe the picosecond–nanosecond dynamics of T4 lysozyme and guide the MD simulation
215 with NMR relaxation data (*Kümmerer et al., 2021*). Extending this analysis to all 28,559 .xtc files
216 detected would be of great interest for a more holistic view, but this would require an initial step
217 of careful checking and cleaning to be sure that these files are analyzable.

218 These results bring a first explanation on why there is not a single special-purpose repository
219 for MD trajectory files. Databases dedicated to molecular structures such as the Protein Databank
220 (*Berman et al., 2000; Kinjo et al., 2017; Armstrong et al., 2019*), or even the recent PDB-dev (*Bur-*
221 *ley et al., 2017*), designed for integrative models, cannot accept such large-size files, even less if
222 complete trajectories without reducing the number of frames would be uploaded. This would also
223 require implementing extra steps of data curation and quality control. In addition, the size of the
224 IT infrastructure and the human skills required for data curation represents a significant cost that
225 could probably not be supported by a single institution.

226 Subsequently, our interest shifted towards exploring which systems are being investigated by
227 MD researchers who deposit their files. We found 9,718 .gro files which are text files that contain
228 the number of particles and the Cartesian coordinates of the system modelled. By parsing the
229 number of particles and the type of residue, we were able to give an overview of all Gromacs sys-
230 tems deposited (Fig. 3-C,D). In terms of system size, they ranged from very small - starting with
231 two coarse-grain (CG) particles of graphite (*Piskorz et al., 2019*), followed by coordinates of a water
232 molecule (3 atoms) (*Ivanov et al., 2017*), CG model of benzene (3 particles) (*Dandekar and Mondal,*
233 *2020*) and atomistic model of ammonia (4 atoms) (*Kelly and Smith, 2020*) — to go up to atomistic
234 and coarse-grain systems composed of more than 3 million particles (*Duncan et al., 2020; Schae-*
235 *fer and Hummer, 2022*) (Fig. 3-C). Interestingly, the system sizes in .gro files exceeded those of the
236 analyzed .xtc files (Fig. 3-B). Even if we cannot exclude that the limited number of .xtc files analyzed
237 (779 .xtc files selected from 28,559 .xtc files indexed) could explain this discrepancy, an alternate
238 hypothesis is that the size of an .xtc file also depends on the number of frames stored. To reduce
239 the size of .xtc files deposited in data repositories, besides removing some frames, researchers
240 might also remove parts of the system, such as water molecules. As a consequence for reusability,
241 this solvent removal could limit the number of suitable datasets available for researchers inter-
242 ested in re-analysing the simulation with respect to, in this case, water diffusion. While the size of
243 systems extracted from .gro files was homogeneously spread, we observed a clear bump around
244 system sizes of circa 8,500 atoms/particles. This enrichment of data could be explained by the de-
245 position of ~340 .gro files related to the simulation of a peptide translocation through a membrane
246 (Fig. 3-C) (*Kabelka et al., 2021*). Beyond 1 million particles/atoms, the number of systems is, for the
247 moment, very limited.

248 We then analyzed residues in .gro files and inferred different types of molecular systems (see
249 Fig. 3-D). Two of the most represented systems contained lipid molecules. This may be related to
250 NMRlipids initiative (<http://nmrlipids.blogspot.com>). For several years, this consortium has been ac-
251 tively working on lipid modelling with a strong policy of data sharing and has contributed to share
252 numerous datasets of membrane systems. As illustrated in Fig 3-C, a variety of membrane sys-

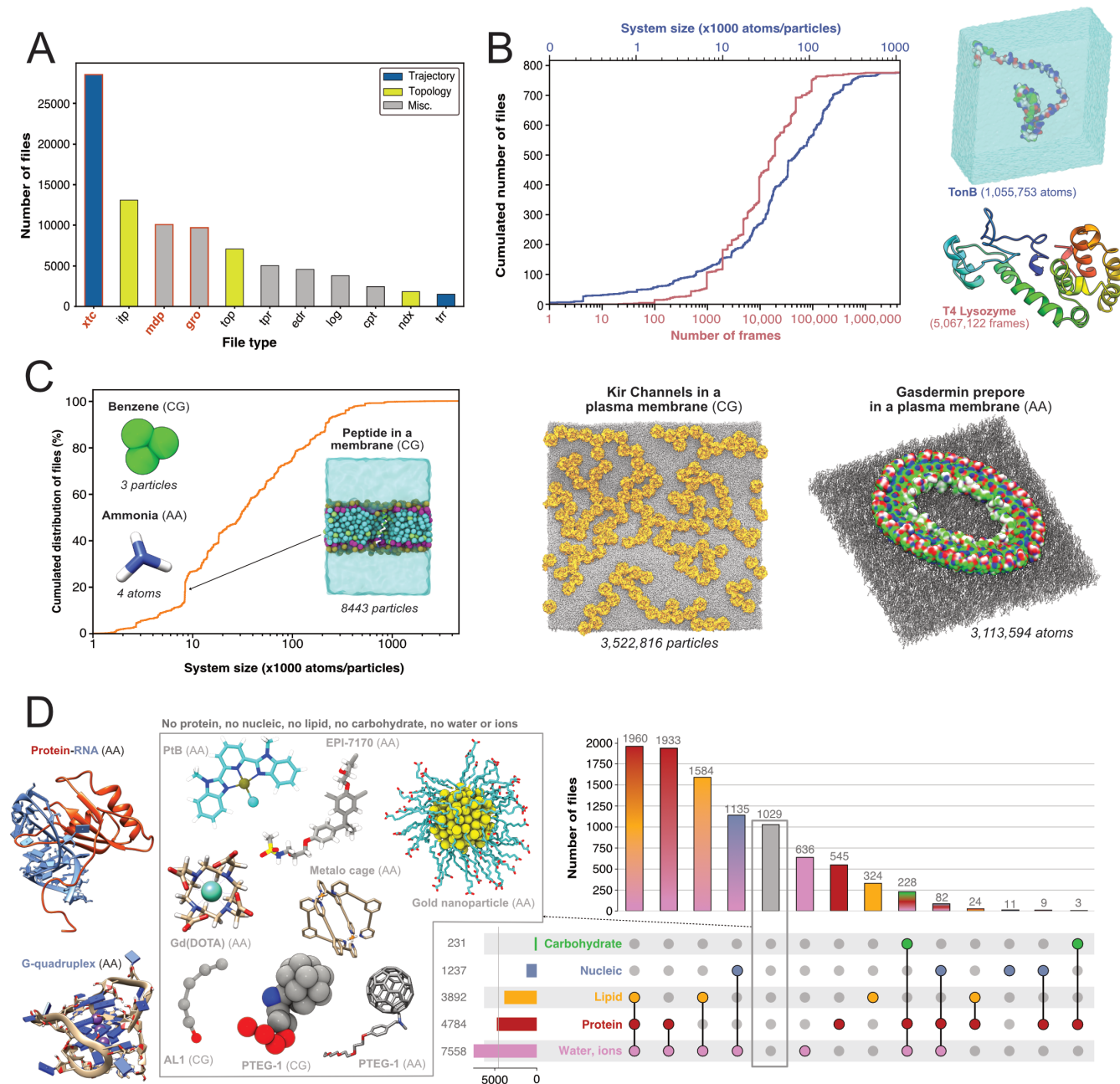


Figure 3. Content analysis of .xtc and .gro files. (A) Number of Gromacs-related files available in searched data repositories. In red, files used for further analyses. (B) Simple analyze of a subset of .xtc files with the cumulative distribution of the number of frames (in green) and the system size (in orange). (C) Cumulative distribution of the system sizes extracted from .gro files. (D) Upset plot of systems grouped by molecular composition, inferred from the analysis of .gro files. For this figure, 3D structures of representative systems were displayed, including soluble proteins such as TonB and T4 Lysozyme, membrane proteins such as Kir Channels and the Gasdermin prepore, Protein-/RNA and G-quadruplex and other non-protein molecules.

tems, especially membrane proteins, were deposited. This highlights the vitality of this research field, and the will of this community to share their data. We also found numerous systems containing solvated proteins. This type of data, combined with .xtc trajectory files (see above), could be invaluable to describe protein dynamics and potentially train new artificial intelligence models to go beyond the current representation of the static protein structure (Lane, 2023). There was also a good proportion of systems containing nucleic acids alone or in interaction with proteins (1237 systems). At this time, we found only few systems containing carbohydrates that also contained proteins and corresponded to one study to model hyaluronan-CD44 interactions (Vuorio et al., 2017). Maybe a reason for this limited number is that systems containing sugars are often modelled using AMBER force field (Ferrer et al., 2012), in combination with GLYCAM (Kirschner et al., 2008-03). A future study on the ~10,200 AMBER files deposited could retrieve more data related to carbohydrate containing systems. Given the current developments to model glycans (Fadda, 2022), we expect to see more deposited systems with carbohydrates in the coming years.

Finally, we found 1,029 .gro files which did not belong to the categories previously described. These files were mostly related to models of small molecules, or molecules used in organic chemistry (Young et al., 2020) and material science (Zheng et al., 2022; Piskorz et al., 2019) (see central panel, Fig. 3-D). Several datasets contained lists of small molecules used for calculating free energy of binding (Aldeghi et al., 2015), solubility of molecules (Liu et al., 2016), or osmotic coefficient (Zhu, 2019). Then, we identified models of nanoparticles (Kyrychenko et al., 2012; Pohjolainen et al., 2016), polymers (Sarkar et al., 2020; Karunasena et al., 2021; Gertsen et al., 2020), and drug molecules like EPI-7170, which binds disordered regions of proteins (Zhu et al., 2022). Finally, an interesting case from material sciences was the modelling of the PTEG-1 molecule, an addition of polar triethylene glycol (TEG) onto a fulleropyrrolidine molecule (see central panel, Fig. 3-D). This molecule was synthesized to improve semiconductors (Jahani et al., 2014). We found several models related to this peculiar molecule and its derivatives, both atomistic (Qiu et al., 2017; Sami et al., 2022) and coarse grained (Alessandri et al., 2020). With a good indexing of data and appropriate metadata to identify modelled molecules, a simple search, which was previously to this study missing, could easily retrieve different models of the same molecule to compare them or to run multi-scale dynamics simulations.

Another important category of deposited files are those containing information about the topology of the simulated molecules, including file extensions such as .itp and .top. Further, they are often the results of long parametrization processes (Wang et al., 2004; Vanommeslaeghe and Mackereel, 2012; Souza et al., 2021) and therefore of significant value for reusability. Based on our analysis, we indexed almost 20,000 topology files which could spare countless efforts to the MD community if these files could be easily found, annotated and reused. Interestingly, the number of .itp files was elevated (13,058 files) with a total size of 2 GB, while there were less .top files (7,009 files) with a total size of 17 GB. Thus, .itp files seemed to contain much less information than the .top files. Among the remaining file types, .tpr files contain all the information to potentially directly run a simulation. Here, we found 4,987 .tpr files, meaning that it could virtually be possible to re-run almost 5,000 simulations without the burden of setting up the system to simulate. Finally, the 3,730 .log files are also a source of useful information as it is relatively easy to parse this text file to extract details on how MD simulations were run, such as the version of Gromacs, which command line was used to run the simulation, etc.

Our next step was to gain insight into the parameter settings employed by the MD community, which may aid us in identifying preferences in MD setups and potential necessity for further education to avoid suboptimal or outdated configurations. We therefore analyzed 10,055 .mdp files stored in the different data repositories. These text files contain information regarding the input parameters to run the simulations such as the integrator, the number of steps, the different algorithms for barostat and thermostat, etc. (for more details see: <https://manual.gromacs.org/documentation/current/user-guide/mdp-options.html>).

We determined the expected simulation time corresponding to the product of two parameters

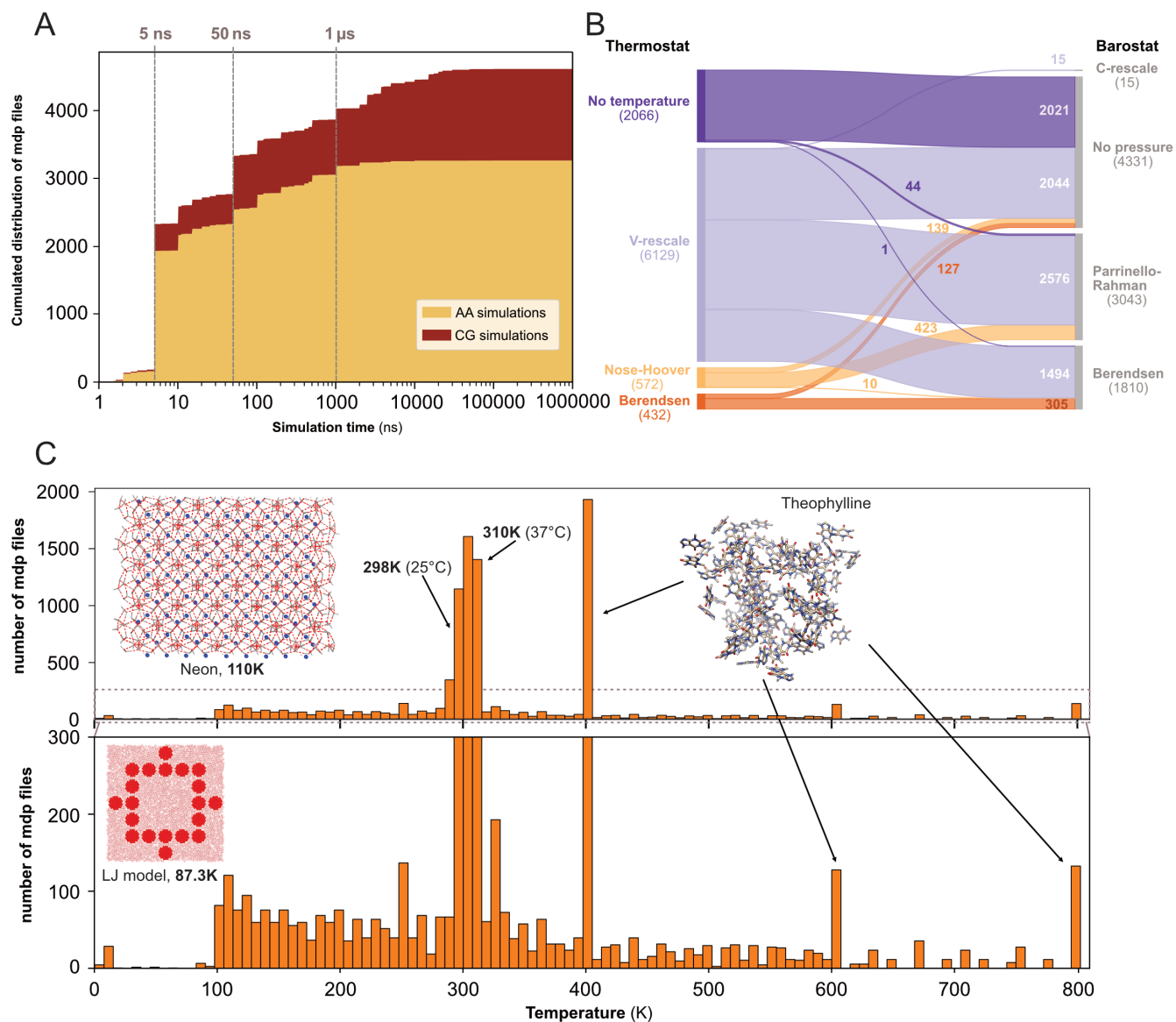


Figure 4. Content analysis of .mdp files. (A) Cumulative distribution of .mdp files versus the simulation time for all-atom and coarse-grain simulations. (B) Sankey graph of the repartition between different values for thermostat and barostat. (C) Temperature distribution, full scale in upper panel and zoom-in in lower panel.

304 found in .mdp files: the number of steps and the time step. Here, we acknowledge that one can
305 set up a very long simulation time and stop the simulation before the end or, on contrary, use
306 a limited time (especially when calculations are performed on HPC resources with wall-time) and
307 then extend the simulation for a longer duration. Using only the .mdp file, we cannot know if the
308 simulation reached its term. To do so, comparison with an .xtc file from the same dataset may
309 help to answer this specific question. However, in this study, we were interested in MD setup
310 practices, in particular what simulation time researchers would set up their system with - likely in
311 the mindset to reach that ending time. We restricted this analysis to the 4,623 .mdp files that used
312 the *md* or *sd* integrator, and that have a simulation time above 1 ns. We found that the majority of
313 the .mdp files were used for simulations of 50 ns or less (see Fig. 4-A). Further, 697 .mdp files with
314 simulations times set-up between 50 ns and 1 μ s and 585 .mdp files with simulation time above
315 1 μ s were identified. As analyzing .gro files showed a good proportion of coarse-grained models
316 (Fig. 3-B,C), we discriminated simulations setups for these two types of models using the time step
317 as a simple cutoff. We considered that a time step greater than 10 fs (*i.e.* dt=0.01) corresponded
318 to MD setups for coarse grained models (*Ingólfsson et al., 2014*). Globally, we found that over all
319 simulations, the setups for atomistic simulations were largely dominant. However, for simulations
320 with a simulation time above 1 μ s specifically, coarse-grain simulations represented 86 % of all.

321 We then looked into the combinations of thermostat and barostat (see Fig. 4-B) from 9,199 .mdp
322 files. The main thermostat used is by far the V-rescale (*Bussi et al., 2007*) often associated with the
323 Parrinello-Rahman barostat (*Parrinello and Rahman, 1981*). This thermostat was also used with
324 the Berendsen barostat (*Berendsen et al., 1984*). In a few cases, we observed the use of the V-
325 rescale thermostat with the very recently developed C-rescale barostat (*Bernetti and Bussi, 2020*).
326 A total of 2,021 .mdp files presented neither thermostat nor barostat, which means they would
327 not be used in production runs. This could correspond to setups used for energy minimization,
328 or to add ions to the system (with the genion command), or for molecular mechanics with Pois-
329 son-Boltzmann and surface area solvation (MM/PBSA) and molecular mechanics with generalised
330 Born and surface area solvation (MM/GBSA) calculations (*Genheden and Ryde, 2015*).

331 Finally, we analyzed the range of starting temperatures used to perform simulations (see Fig. 4-
332 C). We found a clear peak around the temperatures 298 K - 310 K which corresponds to the range
333 between ambient room (298 K - 25 °C) and physiological (310 K - 37 °C) temperatures. Nevertheless,
334 we also observed lower temperatures, which often relate to studies of specific organic systems or
335 simulations of Lennard-Jones models (*Jeon et al., 2016*). Interestingly, we noticed the appearance
336 of several pikes at 400 K, 600 K, and 800 K, which were not present before the end of the year 2022.
337 These peaks corresponded to the same study related to the stability of hydrated crystals (*Dybeck
338 et al., 2023*). Overall, this analysis revealed that a wide range of temperatures have been explored,
339 starting mostly from 100 K and going up to 800 K.

340 To encourage further analysis of the collected files, we shared our data collection with the com-
341 munity in Zenodo (see Data and code availability section). The data scrapping procedure and data
342 analysis is available on GitHub with a detailed documentation. To let researchers having a quick
343 glance and explore this data collection, we created a prototype web application called *MDverse data
344 explorer* available at <https://mdverse.streamlit.app/> and illustrated in Fig. 5-A. With this web applica-
345 tion, it is easy to use keywords and filters to access interesting datasets for all MD engines, as well
346 as .gro and .mdp files. Furthermore, when available, a description of the found data is provided
347 and searchable for keywords (Fig. 5-A, on the left sidebar). The sets of data found can then be
348 exported as a tab-separated values (.tsv) file for further analysis (Fig. 5-B).

349 **Towards a better sharing of MD data**

350 With this work, we have shown that it was possible to not only retrieve MD data from the gen-
351 eralist data repositories Zenodo, Figshare and OSF, but to shed light onto the *dark matter of MD*
352 data in terms of learning current scientific practice, extracting valuable topology information, and
353 analysing how the field is developing. Our objective was not to assess the quality of the data but

354 only to show what kind of data was available. The Ex^2 strategy to find files related to MD sim-
355 ulations relied on the fact that many MD software output files with specific file extensions. This
356 strategy could not be applied in research fields where data exhibits non-specific file types. We
357 experienced this limitation while indexing zip archives related to MD simulations, where we were
358 able to decide if a zip archive was pertinent for this work only by accessing the list of files contained
359 in the archive. This valuable feature is provided by data repositories like Zenodo and Figshare, with
360 some caveats, though.

361 As of March 2023, we managed to index 245,756 files from 1,979 datasets, representing alto-
362 gether 14 TB of data. This is a fraction of all files stored in data repositories. For instance, as of
363 December 2022, Zenodo hosted about 9.9 million files for ~ 1.3 PB of data (*Panero and Benito,*
364 *2022*). All these files are stored on servers available 24/7. This high availability costs human re-
365 sources, IT infrastructures and energy. Even if MD data represents only 1 % of the total volume
366 of data stored in Zenodo, we believe it is our responsibility, as a community, to develop a better
367 sharing and reuse of MD simulation files - and it will neither have to be particularly cumbersome
368 nor expensive. To this end, we are proposing two solutions. First, improve practices for sharing
369 and depositing MD data in data repositories. Second, improve the FAIRness of already available
370 MD data notably by improving the quality of the current metadata.

371 **Guidelines for better sharing of MD simulation data**

372 Without a community-approved methodology for depositing MD simulation files in dataposito-
373 ries, and based on the current experience we described here, we propose a few simple guidelines
374 when sharing MD data to make them more FAIR (Findable, Accessible, Interoperable and Reusable):

- 375 • Avoid zip or tar archives whose content cannot be properly indexed by data repositories. As
376 much as possible, deposit original data files directly.
- 377 • Describe the MD dataset with extensive metadata. Provide adequate information along your
378 dataset, such as:
 - 379 - The scope of the study, e.g. investigate conformation dynamics, benchmark force field,
380 ...
 - 381 - The method on a basic (e.g. quantum mechanics, all-atom, coarse-grain) or advanced
382 (accelerated, metadynamics, well-tempered) level.
 - 383 - The MD software: name, version (tag) and whether modifications have been made.
 - 384 - The simulation settings (for each of the steps, including minimization, equilibration and
385 production): temperature(s), thermostat, barostat, time step, total runtime (simulation
386 length), force field, additional force field parameters.
 - 387 - The composition of the system, with the precise names of the molecules and their num-
388 bers, if possible also PDB, UniProt or Ensemble identifiers and whether the default struc-
389 ture has been modified.
 - 390 - Give information about any post-processing of the uploaded files (e.g. truncation or
391 stripping of the trajectory), including before and after values of what has been modified
392 e.g. number of frames or number of atoms of uploaded files
 - 393 - Highlight especially valuable data, e.g. excessively QM-based parameterized molecules,
394 and their parameter files.

395 Store this metadata in the description of the dataset. An adaptation of the Minimum Infor-
396 mation About a Simulation Experiment (MIASE) guidelines (*Waltemath et al., 2011*) in the
397 context of MD simulations would be useful to define required metadata.

- 398 • Link the MD dataset to other associated resources, such as:
 - 399 - The research article (if any) for which these data have been produced. Datasets are
400 usually mentioned in the research articles, but rarely the other way around, since the
401 deposition has to be done prior to publication. However, it is eminently possible to

A

MDverse data explorer

gro files quick search

Enter search term. For instance: Covid, POPC, Gromacs, CHARMM36, 1402417

9780 elements found

Show 20 entries

Index	Dataset	ID	Title	Creation date	Authors	Description	File name	Atom number	Protein	Lipid
1	zenodo	1468560	C36 POPC simulation with 17 lipids per leaflet, 300K	2018-10-22	Hanne ...	POPC bilayer with 30 waters per lipid (17+17), at 300K, si...	whole17.gro	7616	false	true
2	zenodo	6526243	Amyloid-beta 16-22 peptide dimer simulation (150nM Na...	2022-05-07	Kav, Ba...	Amyloid-beta 16-22 peptide dimer simulation with the CH...	prod.gro	32020	true	false
3	zenodo	838641	Large DPPC monolayer simulations with Charmm36+OPC ...	2017-08-03	Javanai...	DPPC monolayers simulated at a varying area per lipid in t...	DPPC-31...	232488	false	true
4	zenodo	838641	Large DPPC monolayer simulations with Charmm36+OPC ...	2017-08-03	Javanai...	DPPC monolayers simulated at a varying area per lipid in t...	DPPC-31...	232488	false	true
5	zenodo	838641	Large DPPC monolayer simulations with Charmm36+OPC ...	2017-08-03	Javanai...	DPPC monolayers simulated at a varying area per lipid in t...	DPPC-31...	232488	false	true
6	zenodo	838641	Large DPPC monolayer simulations with Charmm36+OPC ...	2017-08-03	Javanai...	DPPC monolayers simulated at a varying area per lipid in t...	DPPC-31...	232488	false	true
7	zenodo	838641	Large DPPC monolayer simulations with Charmm36+OPC ...	2017-08-03	Javanai...	DPPC monolayers simulated at a varying area per lipid in t...	DPPC-31...	232488	false	true
8	zenodo	838641	Large DPPC monolayer simulations with Charmm36+OPC ...	2017-08-03	Javanai...	DPPC monolayers simulated at a varying area per lipid in t...	DPPC-31...	232488	false	true
9	zenodo	838641	Large DPPC monolayer simulations with Charmm36+OPC ...	2017-08-03	Javanai...	DPPC monolayers simulated at a varying area per lipid in t...	DPPC-31...	232488	false	true
10	zenodo	838641	Large DPPC monolayer simulations with Charmm36+OPC ...	2017-08-03	Javanai...	DPPC monolayers simulated at a varying area per lipid in t...	DPPC-31...	232488	false	true

B

Example of outputs for mdp files

	dataset_origin	dataset_id	file_name	dt	nsteps	temperature	thermostat	barostat	dataset_url
0	zenodo	1043926	mono.mdp	0.002	100000000.0	298.0	v-rescale	no	https://zenodo.org/record/1043926
1	zenodo	1043946	mono.mdp	0.002	100000000.0	298.0	v-rescale	no	https://zenodo.org/record/1043946
2	zenodo	3463130	md.mdp	0.020	25000000.0	310.0	v-rescale	parrinello-rahman	https://zenodo.org/record/3463130
3	zenodo	1167532	md.mdp	0.002	100000000.0	298.0	nose-hoover	parrinello-rahman	https://zenodo.org/record/1167532
4	zenodo	3434100	1-POPC512_ECC-lipid14-CaCL_978mM_md_moutout.mdp	0.002	NaN	313.0	v-rescale	parrinello-rahman	https://zenodo.org/record/3434100

Example of outputs for gro files

	dataset_origin	dataset_id	file_name	atom_number	has_protein	has_nucleic	has_lipid	has_glucid	has_water_ion	dataset_url	k_particles
1706	zenodo	7125315	3b_START.gro	5583.0	False	False	False	False	False	https://zenodo.org/record/7125315	5.583
1707	zenodo	7125315	3c_START.gro	5844.0	False	False	False	False	False	https://zenodo.org/record/7125315	5.844
1708	zenodo	7125315	4a_START.gro	4374.0	False	False	False	False	False	https://zenodo.org/record/7125315	4.374
1709	zenodo	7125315	4b_START.gro	4410.0	False	False	False	False	False	https://zenodo.org/record/7125315	4.410
1710	zenodo	7125315	DMF.gro	12.0	False	False	False	False	False	https://zenodo.org/record/7125315	0.012
...
8666	osf	4aghb	PtB-b-force field/em4_nojump.gro	18432.0	False	False	False	False	False	https://osf.io/4aghb/	18.432
8667	osf	4aghb	PtB-b-force field/pr_nvt.gro	18432.0	False	False	False	False	False	https://osf.io/4aghb/	18.432
8668	osf	4aghb	PtB-b-force field/pr_nvt_nojump.gro	18432.0	False	False	False	False	False	https://osf.io/4aghb/	18.432
8669	osf	4aghb	PtB-b-force field/Production_10ns_PTI_noVs.gro	18432.0	False	False	False	False	False	https://osf.io/4aghb/	18.432
8670	osf	4aghb	Pt-free-force field/MOL_GMX.gro	61.0	False	False	False	False	False	https://osf.io/4aghb/	0.061

Figure 5. Snapshots of the MDverse data explorer, a prototype search engine to explore collected files and datasets. (A) General view of the web application. (B) Focus on the .mdp and .gro files sets of data exported as .tsv files. The web application also includes links to their original repository.

- 402 submit a revised version, and providing a link to the related research paper in updated
403 metadata of the MD dataset will ease the reference to the original publication upon data
404 reuse.
- 405 – The code used to analyze the data, ideally deposited in the repository to guarantee avail-
406 ability, or in a GitHub or GitLab repository.
 - 407 – Any other datasets that belong to the same study.
- 408 • Provide sufficient files to reproduce simulations and use a clear naming convention to make
409 explicit links between related files. For instance, for the Gromacs MD engine, trajectory .xtc
410 files could share the same names as structure .gro files (e.g. proteinA.gro & proteinA.xtc).
 - 411 • Revisit your data deposition after paper acceptance and update information if necessary. Zen-
412 do and Figshare provide a DOI for every new version of a dataset as well as a 'master' DOI
413 that always refers to the latest version available.

414 These guidelines are complementary to the reliability and reproducibility checklist for molecular
415 dynamics simulations (*Commun Biol*, 2023). Eventually, they could be implemented in machine
416 actionable Data Management Plan (maDMP) (*Miksa et al.*, 2019). So far, MD metadata is formalized
417 as free text. We advocate for the creation of a standardized and controlled vocabulary to describe
418 artifacts and properties of MD simulations. Normalized metadata will, in turn, enable scientific
419 knowledge graphs (*Auer*, 2018; *Färber and Lamprecht*, 2021) that could link MD data, research
420 articles and MD software in a rich network of research outputs.

421 **Improving metadata of current MD data**

422 While indexing about 2,000 MD datasets, we found that title and description accompanying these
423 datasets were very heterogeneous in terms of quality and quantity and were difficult for machines
424 to process automatically. It was sometimes impossible to find even basic information such as the
425 identity of the molecular system simulated, the temperature or the length of the simulation. With-
426 out appropriate metadata, sharing data is pointless, and its reuse is doomed to fail (*Musen*, 2022).
427 It is thus important to close the gap between the availability of MD data and its discoverability and
428 description through appropriate metadata. We could gradually improve the metadata by following
429 two strategies. First, since MD engines produce normalized and well-documented files, we could
430 extract parameters of the simulation by parsing specific files. We already explored this path with
431 Gromacs, by extracting the molecular size and composition from .gro files and the simulation time
432 (with some limitations), thermostat and barostat from .mdp files. We could go even further, by
433 extracting for instance Gromacs version from .log file (if provided) or by identifying the simulated
434 system from its atomic topology stored in .gro files. This strategy can in principle be applied to
435 files produced by other MD engines. A second approach that we are currently exploring uses data
436 mining and named entity recognition (NER) methods (*Perera et al.*, 2020) to automatically identify
437 the molecular system, the temperature, and the simulation length from existing textual metadata
438 (dataset title and description), providing they are of sufficient length. Finally, the possibilities af-
439 forded by large language models supplemented by domain-specific tools (*Bran et al.*, 2023) might
440 help interpret the heterogenous metadata that is often associated with the simulations.

441 **Future works**

442 In the future, it is desirable to go further in terms of analysis and integrate other data repositories,
443 such as Dryad and Dataverse instances (for example [Recherche Data Gouv](#) in France). The collab-
444 orative platform for source code GitHub could also be of interest. Albeit dedicated to source code
445 and not designed to host large-size binary files, GitHub handles small to medium-size text files like
446 tabular .csv and .tsv data files and has been extensively used to record cases of the Ebola epidemic
447 in 2014 (*Perkel*, 2016) and the Covid-19 pandemic (<https://github.com/CSSEGISandData/COVID-19>).
448 Thus, GitHub could probably host small text-based MD simulation files. For Gromacs, we already
449 found 70,000 parameter .mdp files and 55,000 structure .gro files. Scripts found along these files

450 could also provide valuable insights to understand how a given MD analysis was performed. Fi-
451 nally, GitHub repositories might also be an entry point to find other datasets by linking to simu-
452 lation data, such as institutional repositories (see for instance (*Pesce and Lindorff-Larsen, 2023*)).
453 However, one potential point of concern is that repositories like GitHub or GitLab do not make any
454 promises about long-term availability of repositories, in particular ones not under active develop-
455 ment. Archiving of these repositories could be achieved in Zenodo (for data-centric repositories)
456 or Software Heritage (*Di Cosmo and Zacchioli, 2017*) (for source-code-centric repositories).

457 An obvious next step is the enrichment of metadata with the hope to render open MD data
458 more findable, accessible and ultimately reusable. Possible strategies have already been detailed
459 previously in this paper. We could also go further by connecting MD data in the research ecosystem.
460 For this, two apparent resources need to be linked to MD datasets: their associated research pa-
461 pers to mine more information and to establish a connection with the scientific context, and their
462 simulated biomolecular systems, which ultimately could cross-reference MD datasets to reference
463 databases such as UniProt (*Consortium, 2022*), the PDB (*Berman et al., 2000*) or Lipid Maps (*Sud
464 et al., 2007*). For already deposited datasets, the enrichment of metadata can only be achieved
465 via systematic computational approaches, while for future depositions, a clear and uniformly used
466 ontology and dedicated metadata reference file (as it is used by the PLUMED-NEST: *Bonomi et al.
467 (2019)*) would facilitate this task.

468 Eventually, front-end solutions such as the MDverse data explorer tool can evolve being more
469 user-friendly by interfacing the structures and dynamics with interactive 3D molecular viewers (*Tie-
470 mann et al., 2017; Kampfrath et al., 2022; Martinez and Baaden, 2021*).

471 **Conclusion**

472 In this work, we showed that sharing data generated from MD simulations is now a common prac-
473 tice. From Zenodo, Figshare and OSF alone, we indexed about 250,000 files from 2,000 datasets,
474 and we showed that this trend is increasing. This data brings incentive and opportunities at differ-
475 ent levels. First, for researchers who cannot access high-performance computing (HPC) facilities,
476 or do not want to rerun a costly simulation to save time and energy, simulations of many sys-
477 tems are already available. These simulations could be useful to reanalyze existing trajectories, to
478 extend simulations with already equilibrated systems or to compare simulations of a dedicated
479 molecular system modelled with different settings. Second, building annotated and highly curated
480 datasets for artificial intelligence will be invaluable to develop dynamic generative deep-learning
481 models. Then, improving metadata along available data will foster their reuse and will mechan-
482 ically increase the reproducibility of MD simulations. At last, we see here the occasion to push for
483 good practices in the setup and production of MD simulations.

484 **Methods and Materials**

485 **Initial data collection**

486 We searched for MD-related files in the data repositories Zenodo, Figshare and Open Science
487 Framework (OSF). Queries were designed with a combination of file types and optionally keywords,
488 depending on how a given file type was solely associated to MD simulations. We therefore built a
489 list of manually curated and cross-checked file types and keywords ([https://github.com/MDverse/
490 mdws/blob/main/params/query.yml](https://github.com/MDverse/mdws/blob/main/params/query.yml)). All queries were automated by Python scripts that utilized Ap-
491 plication Programming Interfaces (APIs) provided by data repositories. Since APIs offered by data
492 repositories were different, all implementations were performed in dedicated Python(*van Rossum,
493 1995*) (version 3.9.16) scripts with the NumPy(*Oliphant, 2007*) (version 1.24.2), Pandas(*Wes McKin-
494 ney, 2010*) (version 1.5.3) and Requests (version 2.28.2) libraries.

495 We made the assumption that files deposited by researchers in data repositories were coherent
496 and all related to a same research project. Therefore, when an MD-related file was found in a
497 dataset, all files belonging to this dataset were indexed, regardless of whether their file types were

498 actually identified as MD simulation files. This is the core of the Explore and Expand strategy (Ex^2)
499 we applied in this work and illustrated in Fig 1.

500 When a zip file was found in a dataset, its content was extracted from a preview provided by
501 Zenodo and Figshare. This preview was not provided through APIs, but as HTML code, which we
502 parsed using the Beautiful Soup library (version 4.11.2). Note that the zip file preview for Zenodo
503 was limited to the first 1,000 files. To avoid false-positive files collected from zip archives, a final
504 cleaning step was performed to remove all datasets that did not share at least one file type with
505 the file type list mentioned above. In the case of OSF, there was no preview for zip files, so their
506 content has not been retrieved.

507 **Gromacs files**

508 After the initial data collection, Gromacs .mdp and .gro files were downloaded with the Pooch
509 library (version 1.6.0). When a .mdp or .gro file was found to be in a zip archive, the latter was
510 downloaded and the targeted .mdp or .gro file was selectively extracted from the archive. The same
511 procedure was applied for a subset of .xtc files that consisted of about one .xtc file per Gromacs
512 datasets.

513 Once downloaded, .mdp files were parsed to extract the following parameters: integrator, time
514 step, number of steps, temperature, thermostat, and barostat. Values for thermostat and barostat
515 were normalized according to values provided by the Gromacs documentation. For the simulation
516 time analysis, we selected .mdp files with the *md* or *sd* integrator and with simulation time above
517 1 ns to exclude most minimization and equilibrating simulations. For the thermostat and barostat
518 analysis, only files with non-missing values and with values listed in the Gromacs documentation
519 were considered.

520 The .gro files were parsed with the MDAnalysis library (*Michaud-Agrawal et al., 2011*) to ex-
521 tract the number of particles of the system. Values found in the residue name column were also
522 extracted and compared to a list of residues we manually associated to the following categories:
523 protein, lipid, nucleic acid, glucid and water or ions ([https://github.com/MDverse/mdws/blob/main/
524 params/residue_names.yml](https://github.com/MDverse/mdws/blob/main/params/residue_names.yml)).

525 The .xtc files were analyzed using the `gmxcheck` command ([https://manual.gromacs.org/current/
526 onlinehelp/gmx-check.html](https://manual.gromacs.org/current/onlinehelp/gmx-check.html)) to extract the number of particles and the number of frames.

527 **MDverse data explorer web app**

528 The MDverse data explorer web application was built in Python with the Streamlit library. Data was
529 downloaded from Zenodo (see the Data and code availability section).

530 **System visualization and molecular graphics**

531 Molecular graphics were performed with VMD (*Humphrey et al., 1996*) and Chimera (*Pettersen
532 et al., 2004*). For all visualizations, .gro files containing molecular structure were used. In the case
533 of the two structures in Fig. 3-B, .xtc files were manually assigned to their corresponding .gro (for
534 the TonB protein) or .tpr (for the T4 Lysozyme) files based on their names in their datasets.
535 Origin of the structures displayed in this work:

536 **TonB**

537 Dataset URL: <https://zenodo.org/record/3756664>

538 Publication (DOI): <https://doi.org/10.1039/D0CP03473H>

539 **T4 Lysozyme**

540 Dataset URL: <https://zenodo.org/record/3989044>

541 Publication (DOI): <https://doi.org/10.1021/acs.jctc.0c01338>

542 **Benzene**

543 Dataset URL: https://figshare.com/articles/dataset/Capturing_Protein_Ligand_Recognition_Pathways_

- 544 [in_Coarse-Grained_Simulation/12517490/1](#)
545 Publication (DOI): <https://doi.org/10.1021/acs.jpcltt.0c01683>
- 546 **Ammonia**
547 Dataset URL: https://figshare.com/articles/dataset/Alchemical_Hydration_Free-Energy_Calculations_Using_Molecular_Dynamics_with_Explicit_Polarization_and_Induced_Polarity_Decoupling_An_On_the_Fly_Polarization_Approach/11702442
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549 [the_Fly_Polarization_Approach/11702442](#)
550 Publication (DOI): <https://doi.org/10.1021/acs.jctc.9b01139>
- 551 **Peptide with membrane**
552 Dataset URL: <https://zenodo.org/record/4371296>
553 Publication (DOI): <https://doi.org/10.1021/acs.jcim.0c01312>
- 554 **Kir channels**
555 Dataset URL: <https://zenodo.org/record/3634884>
556 Publication (DOI): <https://doi.org/10.1073/pnas.1918387117>
- 557 **Gasdermin**
558 Dataset URL: <https://zenodo.org/record/6797842>
559 Publication (DOI): <https://doi.org/10.7554/eLife.81432>
- 560 **Protein-RNA**
561 Dataset URL: <https://zenodo.org/record/1308045>
562 Publication (DOI): <https://doi.org/10.1371/journal.pcbi.1006642>
- 563 **G-quadruplex**
564 Dataset URL: <https://zenodo.org/record/5594466>
565 Publication (DOI): <https://doi.org/10.1021/jacs.1c11248>
- 566 **Ptb**
567 Dataset URL: <https://osf.io/4aghb/>
568 Publication (DOI): <https://doi.org/10.1073/pnas.2116543119>
- 569 **EPI-7170**
570 Dataset URL: <https://zenodo.org/record/7120845>
571 Publication (DOI): <https://doi.org/10.1038/s41467-022-34077-z>
- 572 **Gold nanoparticle**
573 Dataset URL: https://acs.figshare.com/articles/dataset/Fluorescence_Probing_of_Thiol_Functionalized_Gold_Nanoparticles_Is_Alkylthiol_Coating_of_a_Nanoparticle_as_Hydrophobic_as_Expected_/2481241
574 [Gold_Nanoparticles_Is_Alkylthiol_Coating_of_a_Nanoparticle_as_Hydrophobic_as_Expected_/2481241](#)
575 Publication (DOI): <https://doi.org/10.1021/jp3060813>
- 576 **Gd(DOTA)**
577 Dataset URL: https://acs.figshare.com/articles/dataset/Modeling_Gd_sup_3_sup_Complexes_for_Molecular_Dynamics_Simulations_Toward_a_Rational_Optimization_of_MRI_Contrast_Agents/20334621
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579 Publication (DOI): <https://doi.org/10.1021/acs.inorgchem.2c01597>
- 580 **Metallo cage**
581 Dataset URL: https://acs.figshare.com/articles/dataset/Rationalizing_the_Activity_of_an_Artificial_Diels-Alderase_Establishing_Efficient_and_Accurate_Protocols_for_Calculating_Supramolecular_Catalysis/11569452
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583 [11569452](#)
584 Publication (DOI): <https://doi.org/10.1021/jacs.9b10302>
- 585 **AL1**
586 Dataset URL: https://acs.figshare.com/articles/dataset/Nucleation_Mechanisms_of_Self-Assembled_Physisorbed_Monolayers_on_Graphite/8846045
587 [Physisorbed_Monolayers_on_Graphite/8846045](#)
588 Publication (DOI): <https://doi.org/10.1021/acs.jpcc.9b01234>

589 **PTEG-1 (all-atom)**

590 Dataset URL: https://figshare.com/articles/dataset/PTEG-1_PP_and_N-DMBI_atomistic_force_fields/5458144

592 Publication (DOI): <https://doi.org/10.1039/C7TA06609K>

593 **PTEG-1 (coarse-grain)**

594 Dataset URL: https://figshare.com/articles/dataset/Neat_and_P3HT-Based_Blend_Morphologies_for_PCBM_and_PTEG-1/12338633

596 Publication (DOI): <https://doi.org/10.1002/adfm.202004799>

597 **Theophylline**

598 Dataset URL: https://figshare.com/articles/dataset/A_Comparison_of_Methods_for_Computing_Relative_Anhydrous_Hydrate_Stability_with_Molecular_Simulation/21644393

600 Publication (DOI): <https://doi.org/10.1021/acs.cgd.2c00832>

601 **Data and code availability**

602 Data files produced from the data collection and processing are shared in Parquet format in the
603 Zenodo repository: <https://zenodo.org/record/7856806>

604 Python scripts to search and index MD files, and to download and parse .mdp and .gro files are
605 open-source, freely available on GitHub (<https://github.com/MDverse/mdws>) and archived in Soft-
606 ware Heritage ([swh:1:dir:4d30b00345a732dc9f79d3c8bfae38b35b8f2c4](https://swh.1:dir:4d30b00345a732dc9f79d3c8bfae38b35b8f2c4)). A detailed documenta-
607 tion is provided along the scripts to easily reproduce the data collection and processing.

608 Jupyter notebooks used to analyze results and create the figures of this paper are open-source,
609 freely available on GitHub (<https://github.com/MDverse/mdda>) and archived in Software Heritage
610 ([swh:1:dir:1f8497f72134cef0a9724c955bb03c751f52cccd](https://swh.1:dir:1f8497f72134cef0a9724c955bb03c751f52cccd)).

611 The code of the MDverse data explorer web application is open-source, freely available on
612 GitHub (<https://github.com/MDverse/mdde>) and archived in Software Heritage ([swh:1:dir:1fc8b8eaabf4a9087e](https://swh.1:dir:1fc8b8eaabf4a9087e)).

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624 **Author contributions**

625 The original idea was conceived by EL together with JKST, MC, RH and LD. JKST, MC and PP super-
626 vised the project. JKST, PP, MC and SG conceived the search strategy. PP, JKST and LB implemented
627 the search strategy. PP performed the analysis and interpreted the results with MS, JKST, MC and
628 KL-L. PP and MO generated the MDverse web interface. JKST, PP and MC discussed all designs and
629 results. MC and PP designed the figures. JKST, MB, MC and PP wrote the manuscript with input
630 from all authors.

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