AMBER parameters and topology data of 2-pentylpyrrole adduct of arginine with 4-hydroxy-2-nonenal

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available to the scientific community to perform molecular dynamics simulations of modified 4-HNE proteins on arginine residue and complete the set of data parameters for nucleophilic residues with this reactive aldehyde ADDIN EN.CITE ADDIN EN.CITE.DATA [2]. Data that could be used for the researchers interested in the role of protein oxidation as mediator in cellular pathophysiological.

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### 1. Data Description

The dataset included in this article consists of 3 Tables and 3 figures. In the Table 1 the dataset of partial charges assigned to Arg-HNE is shown. Table 2 contains the dataset with the information of new obtained parameters listed as coordinates file for 4HNE-arginine pyrrole adduct; while in Table 3 is summarized the comparative data of selected bond distances and angles used in the validation step. In Fig. 1, the workflow for preparing parameter files for 2-pentylpyrrole adduct is described; while, the optimized structure for the new non-standard residue obtained with theory level HF/6-31G** is presented in Fig. 2. The running average of all atoms RMSD for non-modified and 4-HNE-modified arginine is showed in Fig. 3. Finally, supplemental Prep and Frcmod files along to their instructions to perform

### Specifications Table

| Subject | Biochemistry, Biophysics |
|---------|-------------------------|
| Specific subject area | Computational Biochemistry, Computational Biophysics |
| Type of data | Figures and tables |
| How data were acquired | Quantum Mechanics (QM), Molecular Dynamics(MD), Software used: Gaussian 09 for QM, AMBER (pmemd) for MD |
| Data format | Raw and analyzed. |
| Parameters for data collection | The 2-pentylpyrrole adduct produced by reaction between 4-Hydroxy-2-nonenal (4-HNE) and arginine was built and optimized in Gaussian D.09 version. Charges, missing bonds, angles, and dihedral angles parameters were constructed with Amber Tools 16. Missing bonds, angles, dihedral parameters and constants of 4-HNE-Arginine were calculated using parmc资源配置 |
| Description of data collection | Computational calculas with Theorical level Hartree-Fock HF/6 - 31G** for QM and Gaff2 force field and f14SB force field for MD. MD simulations were immersed in a cube of TIP3P water at 300 K and 1 bar. Values of root-mean-square deviation (RMSD). |
| Data source location | Cartagena, Colombia, Facultad de Ciencias Farmaceuticas and Facultad de Ciencias Exactas y Naturales.10°23’58.75”59.09., Cl. 6 #3’3”N, Cartagena, Bolivar. |
| Data accessibility | Data are supplied with this article. Parameter files will be available http://research.bmh.manchester.ac.uk/bryce/amber/ |
| Related research article | Antistio Anibal Alviz-Amador, Rodrigo Galindo-Murillo, Humberto Perez-Gonzalez, Erika Rodriguez-Cavallo, Ricardo Vivas-Reyes and Dario Mendez-Cuadro. Effect of 4-HNE modification on ZU5-ANK domain and the formation of their complex with β-spectrin: A Molecular dynamics simulation study [1]. https://doi.org/10.1021/acs.jcim.9b00772 |

### Value of the Data

- Dataset of new AMBER force field parameters are provided to perform Molecular Dynamics Simulation of 4-HNE carbonylated proteins with 2-pentylpyrrole adduct on arginine residues.
- A benchmark framework for constructing, parameterizing, optimizing and validating of the new non-standard 4HNE-arginine pyrrole adduct is now available.
- Our data can be used to modify, simulate and evaluate by molecular dynamic simulation the effects of 4-HNE carbonylation on arginine over any protein system.

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Table 1
Partial charges assigned to ARG-HNE.

| Atom Name | Atom Type | Partial Charge | Atom Name | Atom Type | Partial Charge |
|-----------|-----------|----------------|-----------|-----------|----------------|
| N1        | n2        | -1.318600      | H13       | h4        | 0.171000       |
| H2        | hn        | 0.128500       | C8        | c2        | -0.002400      |
| C1        | c3        | 1.179600       | C9        | c2        | -0.292500      |
| H3        | h1        | -0.410500      | H14       | ha        | 0.172900       |
| C2        | c3        | 0.067400       | C10       | c2        | -0.247500      |
| H4        | hc        | -0.094100      | H15       | ha        | 0.137100       |
| C5        | c3        | -0.431500      | C13       | c3        | 0.015700       |
| H9        | h1        | 0.137400       | H20       | hc        | 0.003900       |
| H10       | h1        | 0.137400       | H21       | hc        | 0.003900       |
| N2        | n3        | -0.318000      | C14       | c3        | 0.037200       |
| H11       | hn        | 0.239300       | H22       | hc        | -0.011200      |
| C6        | c2        | 0.631500       | H23       | hc        | -0.011200      |
| N3        | n2        | -0.904800      | C         | c3        | -0.070900      |
| H12       | hn        | 0.374300       | H24       | hc        | 0.006300       |
| N         | na        | -0.014200      | H25       | hc        | 0.006300       |
| C7        | c2        | -0.175400      | H         | hc        | 0.006300       |

Table 2
New parameters assigned to ARG-4HNE.

A. BOND

| Atom Types | Kr   | req  | note |
|------------|------|------|------|
| c3-ns      | 328.70 | 1.462 |      |
| ns-hn      | 403.20 | 1.013 |      |
| ns-c       | 427.60 | 1.379 |      |
| c3-nu      | 326.60 | 1.464 |      |
| nu-hn      | 404.60 | 1.012 |      |
| nu-c2      | 416.20 | 1.387 |      |
| C -ns      | 372.304 | 1.422 |      |
| c – N      | 282.464 | 1.512 |      |

B. ANGLE

| Atom Types | K\(\Theta\) | \(\Theta_{eq}\) | note |
|------------|------------|----------------|------|
| h1-c3-ns   | 63.390     | 117.68         |      |
| c3-ns-hn   | 49.840     | 120.69         |      |
| ns-c -o    | 74.220     | 108.88         |      |
| c3-ns-c    | 45.800     | 123.05         |      |
| ns-c -c3   | 66.790     | 115.18         |      |
| hn-ns-c    | 48.330     | 117.55         |      |
| c -c3-ns   | 67.000     | 109.06         |      |
| ns-c3-c3   | 65.910     | 111.61         |      |
| c3-c3-nu   | 66.210     | 110.46         |      |
| c3-nu-hn   | 46.070     | 115.99         |      |
| c3-nu-c2   | 62.400     | 123.71         |      |
| h1-c3-nu   | 49.570     | 109.79         |      |
| nu-c2-n2   | 71.790     | 124.27         |      |
| nu-c2-na   | 72.891     | 111.07         |      |
| hn-nu-c2   | 48.590     | 115.09         |      |
| CX-C -ns   | 68.543     | 121.53         |      |
| o -c -N    | 81.645     | 120.93         |      |
| c -N -CT   | 62.307     | 137.45         |      |
| c -N -CX   | 68.788     | 119.90         |      |

(continued on next page)
molecular dynamics simulations with Amber package software of carbonylated proteins with 4-HNE-arginine 2-pentylpyrrole adduct are available in the Amber parameter database of Bryce Group: Computational Biophysics and Drug Design (http://research.bmh.manchester.ac.uk/bryce/amber/).

2. Experimental design, materials, and methods

2.1. Parameterization

Dataset of Gaff force field parameters were established for the non-standard amino acid Arg-HNE and its use for molecular dynamics simulations of proteins [1]. In the Fig. 1 is presented the framework for derivation of missing bond, angle and dihedral parameters. First, non-standard amino acid was constructed with GaussView 5, followed by full geometry optimization of the new structure using the Hartree-Fock level (HF/6 - 31G**) [2,3]. Next, assignment of charges, missing bonds, angles, and
Table 3
Comparison between selected bond distances and angles calculated from optimized nonstandard amino acids structures.

| Validation Methods                  | Bond (Å, ± Stdev) | Angle (°, ± Stdev) |
|-------------------------------------|-------------------|--------------------|
|                                     | C5-N3             | C10-C11            |
| QM (m062x/631g(d)                   | 1.41±0.02         | 112.11±3.22        |
| MM (AMBER) aa alone                 | 1.42±0.02         | 112.11±3.22        |
| MM (AMBER) aa in the protein        | 1.41±0.02         | 112.11±3.22        |

Fig. 1. Framework for initial force field parameters and topology of the arginine adduced with 4-HNE.
Dihedral angles parameters were constructed with the antechamber and leap programs as included in AmberTools 16 [4]. Then, charges (Step 4) of the optimized structures were calculated using RESP method [5] and the partial charges assigned to individual atoms are listed in the Table 1. Missing bonds, angles, and dihedral parameters of 4-HNE modified arginine was established by homology, matching atom types automatically from the Gaff force field and using parmchk to generate the required force constants [4]. Dataset of new parameters assigned for the 2-pentylpyrrole adduct were consigned in frcmod files and they are summarized below in Table 2. Next, coordinate and topology files were created for each non-standard amino acid with the program leap.

This Arg-HNE was replaced on the proteins and the lacking parameters in frcmod files corresponding to peptide bonds, angle and torsions between the non-standard amino acids and the end nitro-terminus and the end carboxyl terminus of the nearby amino acids on proteins, were calculated using the program parmcal of Antechamber package. The improved frcmod file was loaded into tleap program from AmberTools16 to generate the libraries files (type lib files).

Finally, the optimized structure of 4HNE-arginine pyrrole adduct is showed in Fig. 2; whereas the new improved parameters were included into Table 2. There, bond parameters values are expressed as bond constants ($k_r$) in kcal-mol^{-1}Å^{-2}; distance at equilibrium ($req$) in Å; angle constant ($k_\theta$) in
kcal mol^{-1} deg^{-2}; angle at equilibrium (\Theta_{eq}) in degrees, dihedrals constants (V_{n/2}) in kcal/mol and dihedrals constants angles (\psi) in degrees.

From these datasets, the topology and coordinate of modified proteins were obtained. Hence, the applicability of the newly derived MM parameter, they were subsequently employed in 1 \mu s MD simulations of Arg-HNE as an amino acids treated following the methodology described by Refs. [1,6].

2.2. Validation

To test the generated structures from the modified arginine we performed MD simulations as described above using only the modified structure and compared selected bond distances and angles with structures obtained from DFT level of theory m062x/631g (d) (Table 3) [1]. Overall, good agreement between the data from high-level QM calculations and the generated AMBER structures were seen. Distance average error is in ~0.02 Å whereas angle error is within ~4 and 3 Å.

Data from the single modified amino acids were extracted from a 1 \mu s MD simulation using the same protocols describe before, comparisons were calculated using the DFT level of theory m062x and a basis set 6–31g.

2.3. Analysis of molecular dynamics trajectories of non-standard vs. standard amino acids

All atom root means square deviation analysis for unmodified and modified amino acids is presented in Fig. 3. Distance found in RMSD analysis for unmodified arginine was ~1.5 Å lower than that found for ARG-HNE, which was ~2.5 Å (Fig. 3). Differences observed fall into a range of 1 Å for RMSD comparisons among modified/unmodified arginine indicating that 4-HNE do not induce dramatically structural changes.

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dib.2020.105294.

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