We have investigated the potential energy surface for neutral and charged alanine and glycine chains consisting of up to 6 amino acids. For these molecules we have calculated potential energy surfaces as a function of the Ramachandran angles $\phi$ and $\psi$. Our calculations are performed within \emph{ab initio} theoretical framework based on the density functional theory and also within semi-empirical model approaches. We have demonstrated that the excessive positive charge of the system influences strongly its geometrical and conformational properties. With increasing of the excessive charge amino acid chains become unstable and decay into two or more fragments. We have analysed how the secondary structure of polypeptide chains influences the formation of the potential energy landscapes. We have calculated the energy barriers for transitions between different molecular conformations and determined the ones being energetically the most favourable.

\section{I. INTRODUCTION}

\textit{This work was presented on "The eighth European Conference on Atomic and Molecular Physics" (ECAMPVIII) (Rennes, France, July 6-10, 2004) and on the "Electronic Structure Simulations of Nanostructures" workshop (ESSN2004) (Jyväskylä Finland, June 18-21, 2004).}

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Amino acids are building blocks for proteins. Recently, it became possible to study experimentally fragments of proteins, i.e. chains of amino acids, in a gas phase with the use of the MALDI mass spectroscopy [1, 2, 3]. *Ab initio* theoretical investigations of amino acid chains began also only recently [4, 5, 6, 7, 8, 9, 10] and are still in its infancy.

We have investigated the potential energy surface for neutral and charged alanine and glycine chains consisting of up to 6 amino acids. For these molecules we have calculated potential energy surfaces as a function of the Ramachandran angles $\varphi$ and $\psi$ often used for the characterization of the polypeptide chains [11, 12]. Our calculations are performed within *ab initio* theoretical framework based on the density functional theory and also within semi-empirical model approaches. We have demonstrated that the excessive positive charge of the system influences strongly its geometrical and conformational properties. With increasing of the excessive charge amino acid chains become unstable and decay into two or more fragments. We have analysed how the secondary structure of polypeptide chains influences the formation of the potential energy landscapes. We have calculated the energy barriers for transitions between different molecular conformations and determined the ones being energetically the most favourable.

**II. THEORETICAL METHODS**

Our exploration of the potential energy surface of alanine and glycine chains is based on the density-functional theory (DFT) accounting for all electrons in the system and on the semiempirical AM1 method [13, 14, 15].

Within the DFT one has to solve the Kohn-Sham equations, which read as (see e.g. [10, 16]):

\[
\left( \frac{\hat{p}^2}{2} + U_{\text{ions}} + V_H + V_{xc} \right) \psi_i = \varepsilon_i \psi_i, \tag{1}
\]

where the first term represents the kinetic energy of the $i$-th electron, and $U_{\text{ions}}$ describes its attraction to the ions in the cluster, $V_H$ is the Hartree part of the interelectronic interaction:
\[ V_H(\vec{r}) = \int \frac{\rho(\vec{r}')}{|\vec{r} - \vec{r}'|} d\vec{r}', \tag{2} \]

and \( \rho(\vec{r}') \) is the electron density:

\[ \rho(\vec{r}) = \sum_{\nu=1}^{N} |\psi_i(\vec{r})|^2, \tag{3} \]

where \( V_{xc} \) is the local exchange-correlation potential, \( \psi_i \) are the electronic orbitals and \( N \) is the number of electrons in the cluster.

The exchange-correlation potential is defined as the functional derivative of the exchange-correlation energy functional:

\[ V_{xc} = \frac{\delta E_{xc}[\rho]}{\delta \rho(\vec{r})}, \tag{4} \]

The approximate functionals employed by DFT methods partition the exchange-correlation energy into two parts, referred to as exchange and correlation parts. Both parts are the functionals of the electron density, which can be of two distinct types: either local functional depending on only the electron density \( \rho \) or gradient-corrected functionals depending on both \( \rho \) and its gradient, \( \nabla \rho \). In literature, there is a variety of exchange correlation functionals. In our work we use the Becke’s three parameter gradient-corrected exchange functional with the gradient-corrected correlation functional of Lee, Yang and Parr (B3LYP) \[17, 18, 19]\). We utilize the standard 6-311++G(d,p) and 6-31G(2d,p) basis set to expand the electronic orbitals \( \psi_i \).

### III. RESULTS OF CALCULATION

In figure\[1\] we show the dihedral angles \( \varphi \) and \( \psi \) that are used to characterize the potential surface of the polypeptide chain.

In figure\[2\] we present the optimized geometries of the alanine and glycine polypeptide chains that have been used for the exploration of the potential energy surface. All geometries were optimized with the B3LYP density functional. We used the 6-31++G(d,p) and 6-31G(2d,p) basis sets to expand the electronic orbitals in the molecule.

In figures\[3 \text{ to } 12\] we present the potential energy surfaces for the polypeptide chains presented in figure\[2\].
In figure 13 we show the optimized structures of the alanine tripeptide. Different geometries correspond to the minima on the potential energy surface (see contour plot in figure 4).

In figure 14 we show the optimized structures of the glycine tripeptide. Different geometries correspond to the minima on the potential energy surface (see contour plot in figure 3).

In figure 15 we show the optimized structures of the glycine hexapeptide in helix conformation. Different geometries correspond to the minima on the potential energy surface (see contour plot in figure 5).

The geometries of singly charged alanine and glycine dipeptides are shown in figure 16.

The ionization of the system changes dramatically its potential energy surface and the secondary structure as it is seen from the contour plots presented in figures 17 and 18.

In figure 19 we show the distribution of observed dihedral angles \( \phi, \psi \) of non-Glycine residues in protein structures selected from the Brookhaven Protein Data Bank [11, 12]. The circles show conformations corresponding to the forbidden regions.
FIG. 1: Dihedral angles $\varphi$ and $\psi$ that are used to characterize the potential surface of the polypeptide chain
FIG. 2: Optimized geometries of the alanine and glycine polypeptide chains calculated with the B3LYP/6-31++G(d,p) (a and b) and B3LYP/6-31G(2d,p) (c-f). a) Alanine tripeptide; b) Glycine tripeptide; c) Alanine hexapeptide in sheet conformation; d) Glycine hexapeptide in sheet conformation; e) Alanine hexapeptide in helix conformation; f) Glycine hexapeptide in helix conformation. The energies below each image are given in a.u.
FIG. 3: Potential energy surface for the glycine tripeptide calculated with the B3LYP/6-31G(2d,p) method. Energies are given in eV. Numbers mark energy minima on the potential energy surface.
FIG. 4: Potential energy surface for the alanine tripeptide calculated with the B3LYP/6-31G(2d,p) method. Energies are given in eV. Numbers mark energy minima on the potential energy surface.
FIG. 5: Potential energy surface for the glycine hexapeptide in helix conformation calculated with the B3LYP/6-31G(2d,p) method. Energies are given in eV. Numbers mark energy minima on the potential energy surface.
FIG. 6: Potential energy surface for the glycine hexapeptide in helix conformation calculated with the AM1 method. Energies are given in eV.
FIG. 7: Potential energy surface for the glycine hexapeptide in sheet conformation calculated with the B3LYP/6-31G(2d,p) method. Energies are given in eV.
FIG. 8: Potential energy surface for the glycine hexapeptide in sheet conformation calculated with the AM1 method. Energies are given in eV.
FIG. 9: Potential energy surface for the alanine hexapeptide in helix conformation calculated with the B3LYP/6-31G(2d,p) method. Energies are given in eV.
FIG. 10: Potential energy surface for the alanine hexapeptide in helix conformation calculated with the AM1 method. Energies are given in eV.
FIG. 11: Potential energy surface for the alanine hexapeptide in sheet conformation calculated with the B3LYP/6-31G(2d,p) method. Energies are given in eV.
FIG. 12: Potential energy surface for the alanine hexapeptide in sheet conformation calculated with the AM1 method. Energies are given in eV.
FIG. 13: Optimized structures of the alanine tripeptide. Different geometries correspond to the minima on the potential energy surface (see contour plot in figure 4).
FIG. 14: Optimized structures of the glycine tripeptide. Different geometries correspond to the minima on the potential energy surface (see contour plot in figure 3).

1
$E_0 = -700.5011$ (a.u.)

$\varphi = 83.956$
$\psi = -71.881$

2
$\Delta E = 0.014$ (eV)

$\varphi = -180.$
$\psi = 180.$

3
$\Delta E = 0.036$ (eV)

$\varphi = -83.823$
$\psi = 63.746$
FIG. 15: Optimized structures of the glycine hexapeptide in helix conformation. Different geometries correspond to the minima on the potential energy surface (see contour plot in figure 5).
FIG. 16: Optimized geometries of singly charged alanine (a) and glycine (b) tripeptides calculated with the B3LYP/6-31G(2d,p) method. Energies below each image are given in a.u.
FIG. 17: Potential energy surface for the singly charged alanine tripeptide calculated with the AM1 method. Energies are given in eV.
FIG. 18: Potential energy surface for the singly charged glycine tripeptide calculated with the B3LYP/6-31G(2d,p) method. Energies are given in eV.
FIG. 19: Distribution of observed dihedral angles $\phi, \psi$ of non-Glycine residues in protein structures selected from the Brookhaven Protein Data Bank [11, 12].
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