

# RADMAP: Simple probes for rapid assessment of complex reactivity: A method and case studies on the reaction of hydrogen atoms with unsaturated organic molecules



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## ABSTRACT

RADMAP, an open source program, allows for rapid analysis and visualization of the earliest stages of reactions between any molecule and a monoatomic probe (*i.e.*, H<sup>\*</sup>, H<sup>+</sup>, H<sup>-</sup>, Br<sup>\*</sup>, or any other monoatomic species) using *ab initio* methods. This program creates non-planar potential energy surfaces of the initial interaction between a molecule of interest and the monoatomic probe. These surfaces can be used to both predict the site of addition as well as provide a qualitative estimate for the relative proportion of the formation of adducts; therefore, it gives insight into both the reactivity and the kinetic stability of a molecule. The program presents a way to quickly predict the number of signals anticipated in transverse field muon spin resonance spectra as well as their relative intensities.

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## 1. Introduction

Potential energy surfaces have been used for decades as a tool to describe the reactivity of molecules [1]. Unfortunately, our ability to visualize potential energy surfaces of complex molecular systems is limited. Even the simplest of molecules has a significant number of degrees of freedom in which the molecule can move and vibrate. For example, butane (C<sub>4</sub>H<sub>10</sub>) has 14 atoms and 36 degrees of freedom. It is difficult to render 36 independent variables into a form that humans can easily comprehend (2 or 3 dimensions), which limits the use of the full potential energy hypersurface.

Currently most molecular calculations performed by chemists are both computationally intensive and require a significant amount of time from the chemist. This is particularly apparent when the reactivity of a set of molecules needs to be determined, for example Carr–Parrinello molecular dynamics [2]. It is often difficult to justify applying the full breadth of techniques available due to time and money constraints. What is needed is a tool for rapid analysis that a chemist can use to quickly determine the reactivity of a system of interest.

Perhaps the simplest unbiased chemical probe is the hydrogen atom. We have been interested in this reagent to probe the reactivity of low-valent main group compounds with the hydrogen atom. We have extensively used computational chemistry to probe this reactivity and we have successfully used a hydrogen atom surrogate, muonium, to experimentally confirm our predictions. The most effective spectroscopic method to probe this reactivity is using muon spin spectroscopy (MuSR) [3,4]. MuSR is a technique that uses the short-lived muon as a “light” isotope of hydrogen to probe reactivity with typically unsaturated molecules. MuSR has been used to analyze a wide range of different molecules and systems, covering everything from liquid crystals [5] to *N*-heterocyclic carbenes [6]. Inside the spectrometer, muons are added to the target molecule where adducts form and the hyperfine coupling constant of the various adducts is then inferred from the spectroscopic signal *via* a Fourier transform. Computational methods are then used to determine which adducts correspond to a particular hyperfine coupling constant, but determining the wide variety of possible adducts is often an arduous process.

This paper describes the development of RADMAP, a program that allows for rapid analysis and visualization of the early stages of reaction between a molecule and a monoatomic probe such as the hydrogen atom. This program allows researchers to rapidly assess the most probable site of attack of a radical species such as the hydrogen atom. Experimental confirmation for the validity

Abbreviations: MuSR, muon spin resonance; PES, potential energy surface.

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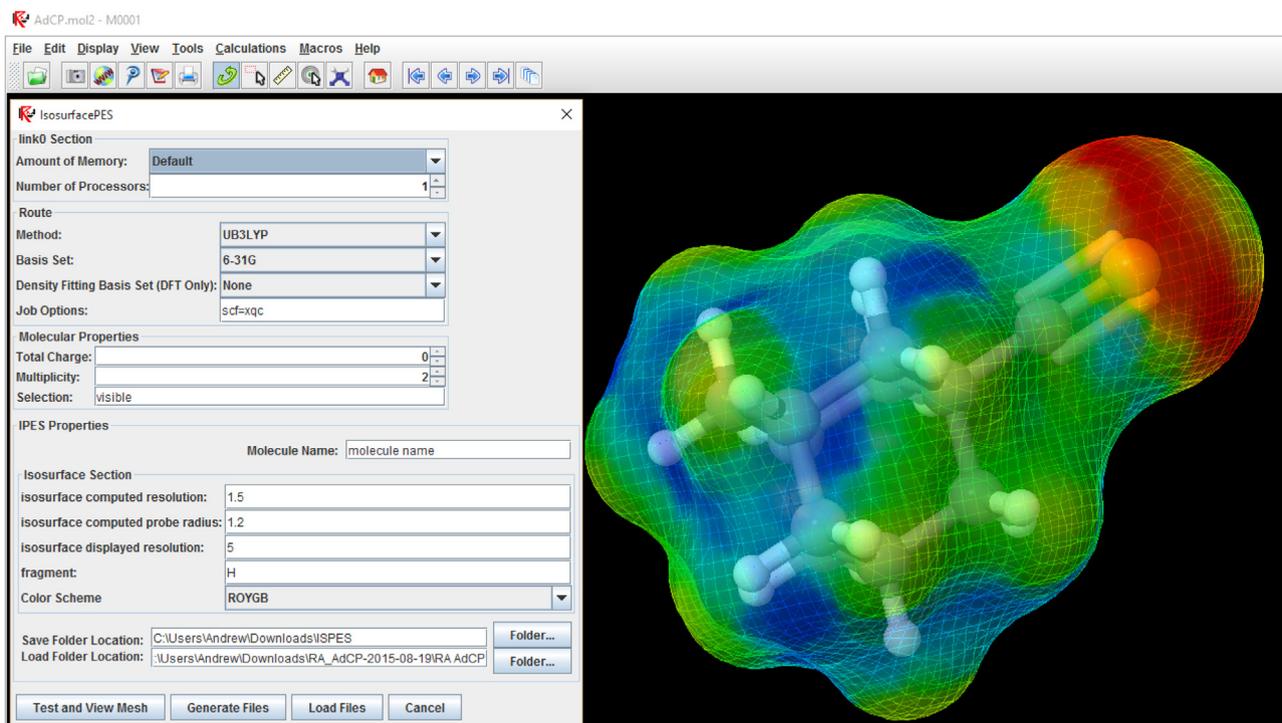


Fig. 1. The graphical user interface of RADMAP, which seamlessly integrates with Jmol, allows for the easy analysis of molecules.

of this computational approach is provided by experiments where muonium addition reactions.

## 2. Results and discussion

Chemical intuition can often be used to predict where and how a hydrogen atom (or its light surrogate, muonium) atom might add to a molecule of interest. By using knowledge of bonding and typical bond lengths, it is possible to make an informed deduction as to where a hydrogen atom might add to the molecule of interest. It is reasonable to surmise that the surface of the molecule of interest would be a realistic starting point from which all possible reaction pathways might stem. Bonding mechanics also suggest that, for a system of two atoms, there is a bond length  $r_e$  that corresponds to the lowest possible energy configuration that these two atoms can obtain. When one of the atoms is used as the origin, the possible location of the second atom when the two atoms are in the lowest energy configuration is a spherical shell of radius  $r_e$  surrounding the first atom. When this idea of a lowest energy surface is applied to a molecule, a surface or shell is formed around the molecule. This shell is mathematically similar to solvent exclusion surfaces. This surface makes for a useful tool with which to compare the potential energy barrier at this early stage of the reaction. Additionally, this first step in the reaction is often the limiting step for a particular pathway.

The RADMAP program was designed to generate an isosurface (or molecular exclusion surface) based potential energy surface and render it in three dimensions with the accompanying parent molecule (see Fig. 1). First, the structure of the molecule of interest is optimized using any standard computational package. In this work, the Gaussian suite of programs was used [7], typically with the UB3LYP method in conjunction with the 6-31G basis set. Next, Jmol [8–10] an open source molecular modeling program, was used to generate a surface around the molecule. This is typically an isosurface or a molecular exclusion surface as specified in the control panel. The molecular exclusion surface uses the Van der Waals radius to define the distance of the probe from the target molecule

and the probe typically has a radius of 1.2 Å. This probe radius was selected such that the probe would pass over the surface of aromatic rings rather than intrude on their interior. Next, points are selected along the surface to be used as the location of the hydrogen atom radical in one of the many conformations generated by RADMAP. Usually one to two thousand different points, each representing a different adduct, will be generated to create a fine mesh over the surface of the target molecule. A computational package such as Gaussian is used to calculate the single point energy of the entire set of adducts. The RADMAP program then collects all of the computed energies of the adducts and creates a potential energy surface (a heat map) of the relative energy of the various adducts, where red represents the lowest energy adduct, and blue represents the highest energy adduct. The heat map is colored based on the following formula, where the color index represents the “heat” of the heat map.

$$\text{Color index} = \frac{E_{\text{current}} - E_{\text{min}}}{E_{\text{max}} - E_{\text{min}}}$$

This formula was selected so that it presented the range of possible energies on a surface in a linear fashion in order to make the interpretation of the energy gradient easier. While an exponential color index formula might better represent the thermodynamics of the addition of hydrogen atom, for example, it causes the heat map to be more difficult to interpret. For example, the lowest energy adducts would dominate the heat map, making all other possible configurations difficult to differentiate from the background.

If a higher display resolution surface is needed than was calculated, a Gaussian-based radial interpolation function is used to estimate the additional points. Finally, the surface is displayed for the user. Essentially, this program creates a surface that is analogous to an electrostatic potential map, and it describes where and to what degree a hydrogen radical is likely to attack.

Further work has increased the usefulness and flexibility of the program. In addition to analyzing the attack of hydrogen atom radicals, it can also investigate any monoatomic fragment, including protons ( $\text{H}^+$ ), hydrides ( $\text{H}^-$ ), halides ( $\text{X}^-$ ), and halogen radicals ( $\text{X}^*$ ).

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