

UNIVERSITY OF SOUTH BOHEMIA

FACULTY OF SCIENCE



RNDr. thesis

**Effect of Local Sugar and Base Geometry on  $^{13}\text{C}$  and  $^{15}\text{N}$   
Magnetic Shielding Anisotropy in DNA Nucleosides**

Mgr. Eva Brumovská

České Budějovice

2009

BRUMOVSKÁ E., 2009: Effect of Local Sugar and Base Geometry on  $^{13}\text{C}$  and  $^{15}\text{N}$  Magnetic Shielding Anisotropy in DNA Nucleosides. RNDr. thesis (in English) - 14 p. The University of South Bohemia, Faculty of Science, České Budějovice, Czech republic.

### **Annotation**

An accurate knowledge of  $^{13}\text{C}$  and  $^{15}\text{N}$  chemical shift anisotropy (CSA) in nucleotides is important for the interpretation of solution-state NMR data in terms of local dynamic properties of DNA and RNA. It allows structural analysis of biologically important nucleic acid motifs such as Z-DNA, DNA triplexes and quadruplexes, or unusual DNA duplex and hairpin motifs. A DFT-based computational approach was applied to extract the information about CSA tensor values for carbon and nitrogen atoms in DNA nucleosides under different nucleoside conformations (glycosidic torsion angle  $\chi$  and sugar pucker). Our calculations have revealed that not only sugar carbons and nitrogen atoms involved in glycosidic bond but also C6 atom in pyrimidines and C8 atom in purines are strongly dependent on  $\chi$ . In the case the information would not be included into the structure determination it could lead to errors. On the other hand, this dependence may be very useful for determining preferred glycosidic bond conformations.

Prohlašuji, že jsem svoji rigorózní práci vypracovala samostatně pouze s použitím uvedené literatury.

Prohlašuji, že v souladu s § 47b č. zákona 111/1998 Sb. v platném znění souhlasím se zveřejněním své rigorózní práce, a to v úpravě vzniklé vypuštěním vyznačených částí archivovaných Přírodovědeckou fakultou elektronickou cestou ve veřejně přístupné části databáze STAG provozované Jihočeskou Univerzitou v Českých Budějovicích na jejích internetových stránkách.

V Českých Budějovicích 29.5.2009

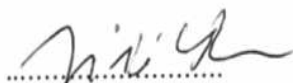
Eva Brumovská

## Author agreement

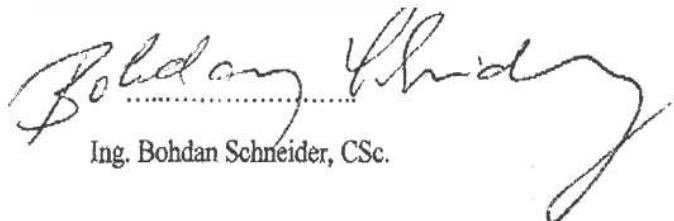
Manuscript title: **Effect of Local Sugar and Base Geometry on  $^{13}\text{C}$  and  $^{15}\text{N}$  Magnetic Shielding Anisotropy in DNA Nucleosides.**

Authors: **Eva Brumovská, Vladimír Sychrovský, Zuzana Vokáčová, Jiří Šponer, Bohdan Schneider, Lukáš Trantírek**

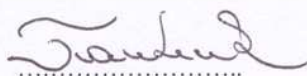
We, the undersigned, confirm that Eva Brumovská contributed substantially to this publication.



Prof. RNDr. Jiří Šponer, DrSc.



Ing. Bohdan Schneider, CSc.



Mgr. Lukáš Trantírek, Ph.D.

## Effect of local sugar and base geometry on $^{13}\text{C}$ and $^{15}\text{N}$ magnetic shielding anisotropy in DNA nucleosides

Eva Brumovská · Vladimír Sychrovský · Zuzana Vokáčová · Jiří Šponer · Bohdan Schneider · Lukáš Trantířek

Received: 12 September 2008 / Accepted: 17 September 2008 / Published online: 14 October 2008  
© Springer Science+Business Media B.V. 2008

**Abstract** Density functional theory was employed to study the dependence of  $^{13}\text{C}$  and  $^{15}\text{N}$  magnetic shielding tensors on the glycosidic torsion angle ( $\chi$ ) and conformation of the sugar ring in 2'-deoxyadenosine, 2'-deoxyguanosine, 2'-deoxycytidine, and 2'-deoxythymidine. In general, the magnetic shielding of the glycosidic nitrogens and the sugar carbons was found to depend on both the conformation of the sugar ring and  $\chi$ . Our calculations indicate that the magnetic shielding anisotropy of the C6 atom in pyrimidine and the C8 atom in purine bases depends strongly on  $\chi$ . The remaining base carbons were found to be insensitive to both sugar pucker and  $\chi$  re-orientation. These results call into question the underlying assumptions of currently established methods for interpreting residual chemical shift anisotropies and  $^{13}\text{C}$  and  $^{15}\text{N}$  auto- and cross-correlated

relaxation rates and highlight possible limitations of DNA applications of these methods.

**Keywords** Magnetic shielding · Chemical shift anisotropy · DNA · RNA

### Introduction

Knowledge of the magnitude and orientation of  $^{13}\text{C}$  and  $^{15}\text{N}$  magnetic shielding (MS)/chemical shift (CS) tensors in DNA and RNA nucleosides is essential for the interpretation of NMR relaxation data and for the analysis of residual chemical shift anisotropy (RCSA) resulting from weak alignment (Akke et al. 1997; Boisbouvier et al. 2000; Duchardt et al. 2004; Duchardt and Schwalbe 2005; Femer et al. 2008; Grishaev et al. 2006; Hansen and Al-Hashimi 2006; Ravindranathan et al. 2003; Ravindranathan et al. 2005; Schoffberger et al. 2006; Shajani and Varani 2007; Sychrovský et al. 2005; Trantířek et al. 2007). Large chemical shift anisotropies (CSAs) of  $^{13}\text{C}$  and  $^{15}\text{N}$  nuclei in nucleic acids have been found useful for constraining bases relative to the molecular alignment tensor (Grishaev et al. 2006; Hansen and Al-Hashimi 2006), glycosidic torsion angle (Duchardt et al. 2004), sugar ring conformation (Boisbouvier et al. 2000), and the evaluation of conformational dynamics around a glycosidic bond (Ravindranathan et al. 2003). Until quite recently, the only available experimental data on the  $^{13}\text{C}$  and  $^{15}\text{N}$  CS-tensor magnitude and orientation in nucleic acids originated from solid-state NMR measurements and were limited to model compounds such as nucleic acid bases (Ha et al. 1998) or nucleosides (Staeber and Grant 2002).

In a recent report, Duchardt and Schwalbe simultaneously analyzed relaxation measurements for all protonated base carbons in the nucleosides of a small RNA hairpin, using

**Electronic supplementary material** The online version of this article (doi:10.1007/s10858-008-9278-7) contains supplementary material, which is available to authorized users.

E. Brumovská · L. Trantířek (✉)  
Faculty of Science, University of South Bohemia and Biology Centre AS CR v.v.i., Branšovská 31, 370 05 České Budějovice, Czech Republic  
e-mail: trant@pau.cas.cz

V. Sychrovský · Z. Vokáčová  
Institute of Organic Chemistry and Biochemistry, AS CR v.v.i., Flemingovo náměstí 2, 166 10 Prague, Czech Republic

J. Šponer  
Institute of Biophysics, AS CR v.v.i., Královopolská 135, 612 65 Brno, Czech Republic

B. Schneider  
Biotechnological Institute AS CR, Vítězská 1083, 142 20 Prague, Czech Republic

## Abstrakt

Tenzory magnetického stínění atomů  $^{13}\text{C}$  a  $^{15}\text{N}$  v molekulách 2'-deoxyadenosinu, 2'-deoxyguanosinu, 2'-deoxycytidinu a 2'-deoxytymidinu byly spočítány pomocí metody DFT (Density Functional Theory) v závislosti na orientaci glykosidického torzního úhlu ( $\chi$ ) a konformaci cukerného kruhu. Nedávno bylo prokázáno, že magnetické stínění dusíků, které jsou zapojeny do glykosidické vazby, a uhlíků na cukerném kruhu se mění podle konformace cukru a torzního úhlu  $\chi$ . Naše výpočty ukázaly, že také tenzor magnetického stínění atomů C6 u pyrimidinů a C8 u purinů je silně závislý na  $\chi$ . Ostatní uhlíkové atomy ležící na bázi nukleosidu zůstávají orientací cukru a reorientací glykosidického torzního úhlu  $\chi$  neovlivněny. Tyto výsledky ale naznačují, že předpoklady, které byly do této doby používány pro interpretaci reziduálních posunů chemické anizotropie (residual chemical shift anisotropies) a  $^{13}\text{C}$  a  $^{15}\text{N}$  auto- a cros- korelovaných relaxačních rychlostí (auto- and cross-correlated relaxation rates) nemají absolutní platnost a ukazují možné limitace těchto metod pro DNA aplikace.