**Ruwan Silva**
**DL**
**GXB**

**What are Nuclear Magnetic Resonance (NMR) ring currents and why are they useful?**
**Physics/Chemistry**
**Word Count: 3,897 (excluding references and bibliography)**

**Ruwan Silva**

# What are Nuclear Magnetic Resonance (NMR) ring currents and why are they useful?

The world around us is governed by nature's laws. Some of these we understand, and others we do not. In the case of electron movements and thus currents, whether in the form of particles or waves, Maxwell's Equations create a framework to understand these. One of these equations deals with the connectivity between currents and magnetism. This is Ampère's law, where when charges are subject to a changing magnetic field it induces a current. If the said charges are confined to a race-track like arena, the electrons involved are free to circulate. This idea of delocalised electrons in bonds, responding to a strong magnetic field, led to the whole field of ring currents. Now if the magnetic field is directed perpendicular to the plane of an aromatic system, a ring current induced in the delocalised $\pi$ electrons of the aromatic ring can be used for understanding the fundamentals of the material as well as its surrounding. But, let us start at the beginning and first understand how and why aromatic currents were connected to magnetic resonance.

In the middle of the 18th century a class of compounds was discovered that displayed an unusually low level of chemical reactivity. Several of these had distinctive odours, unlike pure saturated hydrocarbons, and so were given the term 'aromatic' by August Wilhelm Hofmann in 1855 in his article about a group of benzene compounds[1]. Later in the 1930s, Erich Hückel produced a set of rules for determining whether a compound is aromatic[2]. He stated that the molecule must be cyclic, nearly planar, and possess a p-orbital as well as have (4n+2) $\pi$ electrons, where n is an integer. Today the Encyclopaedia Britannica defines an aromatic compound as: 'any of a large class of unsaturated chemical compounds characterized by one or more planar rings of atoms joined by covalent bonds of two different kinds. The unique stability of these compounds is referred to as aromaticity.' It also states that aromaticity results from specific bonding arrangements, which result in particular $\pi$ electrons within a molecule being strongly held. Along with this it is also associated with low reactivity.
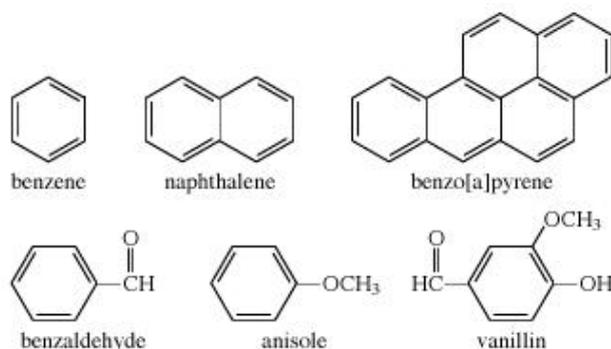


*Figure 1: Diagrams of various aromatic compounds (From: Encyclopedia Britannica http://www.xxxx.xxxx.xxxx)*

Many regard benzene as the molecule central to aromatic chemistry and so it is known as the 'parent aromatic compound'. August Kekulé is best known for his work on the structure of benzene. According to Kekule, the structure of benzene was 'apparently' revealed in a dream. The empirical formula of benzene had been known for a long time, but owing to its highly unsaturated structure it was a challenge to determine. Archibald Scott Couper had suggested a possible structure in 1858, containing multiple double bonds and multiple rings, but there was too little evidence available to organic chemists to confirm any structures and so their suggestions didn't survive[3]. By the year 1865 more evidence was available, specifically on the relationships of aromatic isomers. Kekulé's proposed structure was based on the consideration of the number of isomers observed for derivatives of benzene. For every mono-substituted derivative of benzene, where a hydrogen atom was replaced by a different functional group ($C_6H_5X$ where X is NH2, OH, Cl, etc.), only one isomer was ever found, suggesting that the six carbons are equivalent. So that replacing any carbon gives one product. For di-substituted derivatives three isomers were observed, which gave rise to isomers named ortho, meta, and para. Kekulé's new understanding of benzene resulted in the German Chemical Society organising an elaborate appreciation in Kekulé's honour in 1890 to celebrate the 25th anniversary of his first benzene paper[4]. It was here that he revealed the details of the creation of his theory. He stated that he discovered the ring shape of benzene from a daydream of a snake biting its own tail. This vision was said to have come to him after years of studying the nature of carbon-carbon atoms. Owing to his considerable contribution to benzene, Kekulé has cemented his name in history as the 'founder of aromaticity' as stated in a New Scientist article written by Jeff Hecht[5] about the discovery of Buckminsterfullerenes.

The discoveries on aromaticity and aromatic ring currents that formed its foundations in Chemistry in the 1860's, corresponded almost coincidently with the foundations of the theory of electromagnetism in Physics, and the work of Maxwell. As a result when a magnetic field was directed perpendicular to the plane of an aromatic system, it resulted in a ring current induced in the delocalised $\pi$ electrons of the aromatic ring. This is due to Ampère's law, with the electrons involved now free to circulate, and resonate based on the bonding within and external to the aromatic compounds. At the same time, Lord Kelvin subsequent to proposing his fundamental insights to absolute temperature, was looking to promote the practical applications of electromagnetism via the Atlantic Telegraph Company should have looked into the exploitation of ring currents too. But, this happened over a century later, once a better understanding of aromacity and spectroscopy came together.
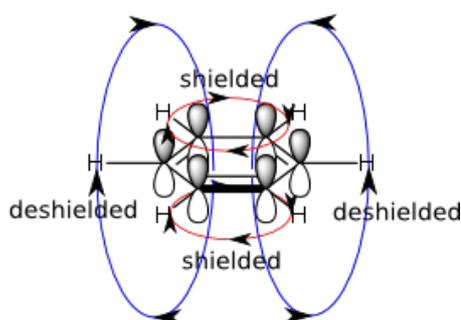


*Figure 2: Diagram showing the effect of ring currents (From: Organic Spectroscopy Easyochem www.xxxx.xxxx.xxxx/xxxx).*

The Ring Current Model (RCM) proposed by J. A. Pople in 1956[6] and was later updated into a more detailed classical description by Waugh and Fessenden, suggests that, for a (4n+2) $\pi$ electron system, the diatropic ring current will form an induced magnetic field, that is flipped in the opposite direction of the external field found at the centre of the current. Outside the ring the magnetic field is acting in the same direction as the external field (Figure 2). The protons outside the ring experience a downfield shift, while protons inside experience an upfield shift. The protons inside and outside the ring experience opposing shifts. This is a Nuclear Magnetic Resonance (NMR) chemical shift. It can be used to identify aromatic and anti-aromatic compounds.

Aromatic ring currents are relevant to NMR spectroscopy, due to the dramatic effects they exert on the chemical shifts of 1H nuclei in aromatic molecules. This helps distinguish between the nuclear environments and so are helpful in determining molecular structure. Isidor Rabi discovered NMR when he noticed how nuclei could be induced to flip their principal magnetic orientation by an oscillating magnetic field in 1938[7]; this led to him being awarded the Nobel Prize for physics in 1944. Today NMR is known as the most direct method to observe the effects of ring currents and is the default experimental method to identifying aromatic and antiaromatic moieties in molecules. NMR is a property of the nucleus, associated with a property called nuclear spin. This is similar to imagining the nucleus is a miniature bar magnet. When a nucleus is placed in a magnetic field it can either align itself with the field (low energy state) or align itself against the field (high energy state). If a radio wave is applied, nuclei in the low-energy state can absorb it and flip to the high-energy state. Once this radio wave is removed we can observe the nuclei flip back to the lower energy state as it 'relaxes' and emits energy, which can be detected. In aromatic systems, protons outside the cycle will experience a downfield shift while protons inside the cycle will experience an upfield shift. An example of this is in benzene where the ring protons experience de-shielding because the induced magnetic field is aligned with the external field. Any proton inside the aromatic ring experiences shielding because the fields are unaligned.

Over the years there have been many attempts to quantify aromaticity with respect to the induced ring current. One method is diamagnetic susceptibility exaltation, which is the difference between the measured magnetic susceptibility of a compound and a devised value taken from group additivity tables. Large negative values such as benzene (-13.4) indicate an aromatic compound while values near zero are non-aromatic (cyclohexane: +1.1). Also large positive values are antiaromatic, for example cyclobutadiene (+18). Another measurable quantity is the chemical shift of lithium ions (Li+) in aromatic compounds containing lithium, as it tends to bond as a $\pi$-coordinate complex to the face of the aromatic rings. Both methods have their faults as both suffer from the fact that they depend on ring size and the second is only valid for compounds containing lithium.

The Nucleus Independent Chemical Shift (NICS) method was conceived in 1996[8] and has been continuously refined and improved. It is a simple tool that can be used to assess the magnetic field at any desired location and its major use is for the evaluation of aromatic compounds. As explained before, an aromatic compound placed in an external magnetic field creates induced ring currents, which in turn produce an induced magnetic field. The induced magnetic field affects the chemical shift of the compound, which can be used as an indicator of the direction and magnitude of the induced magnetic field. This idea was previously used with

bridgehead atoms and Li+ ions, but because the nucleus of the probe itself affects the calculated chemical shift, the results were questionable. However, the NICS probe has no nucleus and therefore is present as a spectator. All different NICS methods determine aromaticity by harnessing this indicative change in aromaticity.

Schleyer and coworkers noted the difficulty in using NICS on three-membered rings due to the local shielding of nearby $\sigma$ bonds. A year after their first publication, the developers of NICS made two modifications. They raised the benzene quinionine 1 Å above the molecular plane and named this NICS. It soon became apparent that their original claims were false and the original form of NICS contained a lot of $\sigma$ contributions. The movement of the benzene quinionine reduced $\sigma$ contributions due to their short ranged nature. The second change was to separate the total NICS value into $\sigma$ and $\pi$ contributions. Since aromaticity results from the $\pi$ system of a compound, the developers attempted to calculate the sole $\pi$ contribution to the NICS value. NICS was soon chosen as a better aromaticity index based on a 2D grid study (single point NICS). This was soon termed 'dissected NICS'. Owing to the separation of $\pi$ and $\sigma$ contributions this method is only useful for planar systems, as non-planar systems will have 'contaminated' $\pi$ orbitals.

After a second version of dissected NICS was developed, named MO-NICS (Molecular Orbital-NICS) and later CMO-NICS (Canonical Molecular Orbital-NICS), Steiner and Fowler brought up the issue of using the isotropic value of NICS[9] as it disguises significant features of the different components. They stated that aromaticity is a $\pi$ system property and the $\pi$ system is found perpendicular to the molecular plane and so a far more suitable indicator is the out-of-plane component of the shielding tensor. For planar compounds found in the XY plane, this is the ZZ component and so this value has been termed NICSzz. What should be mentioned though is that NICSzz is not free from $\sigma$ contributions, even in planar systems. This resulted in the most refined index, NICS$\pi$zz, which combines the two fundamental modifications to NICS mentioned above. It does this by considering solely the $\pi$ contribution (using LMO or CMO methods), and only the ZZ component of the chemical shift tensor. Following this there have been several comparisons between the different NICS versions. From this research the most refined indices (NICS$\pi$zz and NICS zz) have been shown to be more accurate because they clarify the contribution of the $\pi$ electrons to the NICS value, which is the only relevant effect of aromaticity or antiaromaticity.
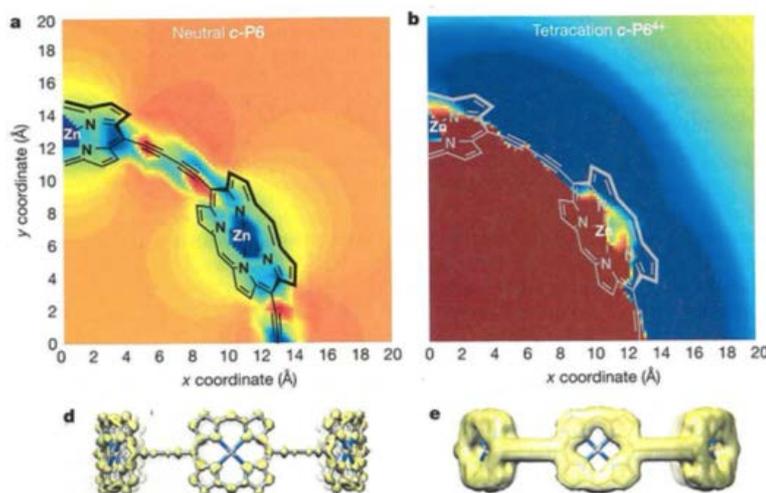


*Figure 3: Computational Data showing the splitting of the Nuclear energy bands when ring currents are induced within the molecules (From Martin D. Peeks, Timothy D.W. Claridge, and Harry L. Anderson, Nature, (2017), 541: 201)*

There have been many variations of single-point NICS methods utilised with varying levels of success to investigate aromatic character of many systems such as inorganic rings, annulenes and all-metal clusters. It has also been used to investigate mechanistic pathways and transition states. Although NICS is widely used it is also known to be misleading in some cases when it contradicts other indices of aromaticity.

Klod and Kleinpeter first introduced multi-dimensional NICS in 2001[10] when they used a 3D grid of NICS probes and presented the iso-chemical-shielding-surfaces. This produced colourful maps that enable quantitative calculation of anisotropy effects of functional groups and the ring current effect of aromatic and antiaromatic systems (See Figure 3). Their aim was to assign chemical shifts of stereoisomers. This method was later used to provide the anisotropies of a large group of compounds. The authors did not move to expand their research into the assignment of aromatic/antiaromatic compounds. However, their NICS values that were calculated were isotropic, which are not appropriate for aromatic assignment.

Later in 2006 the NICS-Scan method was unveiled[11] and alongside this Solà and coworkers produced a similar methodology, but applied to inorganic compounds. The thought behind both methods was that single-point NICS measurements were not enough to identify the aromatic behaviour of a compound. However, due to the physics of the induced magnetic field being known to researchers, a one-dimensional scan above the centre of the system is enough to calculate the properties of the induced magnetic field. The NICS values obtained by this are then isolated into the two groups of in-plane and out-of-plane components and plotted on a graph against the distance from the molecular plane. The nature of the curve on the graph provides a far more complete picture of the system than a single NICS value. From this characteristic shapes can be interpreted as diatropic or paratropic ring currents. This also displayed that the diamagnetic and paramagnetic contributions to the in-plane component are similar for 4n $\pi$ electron and $(4n+\pi)$ electron. Another similarity found was the paramagnetic contribution to the out-of-plane component. In aromatic compounds this contribution is smaller than the diamagnetic one and rapidly decreases with increasing distance. The NICS-Scan provides a qualitative analysis of the magnetic behaviour of studied systems, however, the values cannot be used for quantitative comparison, which was demonstrated by A. Stranger in one of his studies from 2006.

In 2010, A. Stranger produced the $\sigma$-Only Model[12]. This was designed to enable quantitative analysis by utilising the NICS-Scan to imitate the contribution of $\sigma$ electrons to the NICS value. Like the LMO and CMO systems, this model works on separating the $\pi$ effects from the $\sigma$ effects of a compound. However, this model is not based on mathematical treatment of orbitals, but instead a model in which the $\pi$ electrons are used to bind hydrogens. $\sigma$-Only Model obtains its NICS values by subtracting its values from the delocalised system, which results in the $\pi$ contribution. This agrees with the Current Density Analysis (CDA) of the given compound. This method enables the comparison between ring currents of different systems and treatment of non-planar systems.

Despite the improvements to NICS methods that enable a more accurate determination of the diatropicity and paratropicity of the $\pi$ electron, the inability of NICS to determine the origin of the induced ring currents and magnetic fields has not been addressed. This information becomes vital in polycyclic systems, where current density analysis shows that generally the currents are spread over the

whole system rather than found at one point inside each ring. The solution to this was to coin the term 'local aromaticity' in order to use NICS or Harmonic Oscillator Model of Aromaticity (HOMA) for single ring systems.

Most recently in 2014, R. Gershoni Poranne and A. Stranger introduced the NICS-XY-Scan[13]. This method enables the identification of local and global ring currents in polycyclic systems, by utilising the NICS tool. This method's basis comes from one or more 1D scan(s) of NICS along a path that crosses the axis/axes of the compound at a constant height above the system. These scans display a far more complete picture of the behaviour of the induced magnetic field of the compound. The NICS-XY-Scan can be quantitatively used alongside NICS $\pi$ zz values, but can also be used in a qualitative manner for NICSzz at a height of 1.7 Å above the molecular plane. The NICS-XY-Scan are in agreement with CDA results when they are available and in some cases provide additional information.

NICS has undergone much criticism for it being a 'virtual' index as it is unable to corroborate results via experimental work. Despite this it still remains a very popular tool, which is used for many different applications. This can be seen very frequently in literature involving assignment of aromaticity/antiaromaticity to different systems. It has been used with other methods to help obtain a better understanding of the substituent effect, the effect of distortion and the effect of bending on the aromaticity of benzene and benzenoids. They have also been used in the study of antiaromaticity, especially on fluorenyl- and fluorenylidene-containing compounds by the Mills group[14], who found correlations between NICS values and other experimental and computational methods such as Aromatic Stabilisation Energies (ASE) and HOMA. As well as this they calculated and measured the chemical shifts of 1H and 13C. NICS is not limited to organic compounds. It can be used to assign aromaticity to inorganic compounds. Liu and Xu[15,16] demonstrated this on the compound Si2BX (X=H, Li, K, O and S) and on X3+ (X=H, Li, Na, K and Cu) respectively. However, these studies used isotropic NICS values, which are problematic because they can cause loss of information about the ring currents.

Ring current shifts are also utilised for the study of the human body. One area of focus has been membrane proteins, which Dongsheng Liu and Kurt Wüthrich published a research paper on in 2016[16]. They used Fluorine-19 NMR markers due to their high sensitivity to chemical shifts in non-covalent environments. Their study focused on G protein-coupled receptors (GPCR), which are the largest and most diverse group of membrane receptors in eukaryotes, where they encountered situations where 19F chemical shifts were unresponsive to conformational changes that had been implicated by other methods. There studies resulted in the promise of being able to identify labelling sites for future 19F-NMR studies of GPCR activation.

Other biological research has been done comparing experimental secondary shifts and calculated ring current shifts on the aromatic protons of the enzyme called lysozyme. Lysozyme is an enzyme that protects the human body from bacterial infection by attacking the protective cell walls of bacteria. This work was carried out in a study in 1983[17], which compared results using 3 different ring current shift models: the classical dipolar equation, the Johnson-Bovey equation and the Haigh-Mallion equation. Tests were also carried out on the bovine pancreatic trypsin inhibitor and cytochrome c. The results showed that for all test subjects the Root Mean Square difference (RMS) was similar for all the ring current models used. As much as this assignment was done for the comparison of ring

current models, it did also yield useful insight into the imaging of each molecule tested.

Research using NMR ring currents has even been done on RNA bases using chemical shifts and joint electric field and ring current effects. Aleksandr B. Sahakyan and Michele Vendruscolo published this research in 2013[18]. To study the ring current effects in molecular structures that are similar to nucleic acids, they created a database of the structures of RNAs that reflected the inter-base arrangement of RNA structures in high-resolution X-rays. They studied these bases using the simplistic Pople model and the more accurate Haigh-Mallion model. Along with this they created a database of dibase arrangements observed from high-resolution RNA structures. They then carried out hybrid-DFT calculations on these structures, which estimated the charge in local electric fields and nuclear shielding constants in the vicinity of conjugated rings. Furthermore, they used linear model fitting to derive ring currents and electric field based models for explaining the chemical shift changes induced by neighbouring conjugated rings. This process allowed them to access the hierarchy ring current and electric field effects on both hydrogen (1H) and non-hydrogen nuclei (13C, 15N and 17O). From this they found that hydrogen-bonding-induced electric field effects are very well captured by the geometric factors of ring current models, which is a useful property to help account for modelling hydrogen-bonding effects on chemical shifts in nucleic acid bases. One use of NMR that could in theory become a common use is the imaging of different bacteria. R. Shulman compiled and edited a book about the 'Biological Applications of Magnetic Resonance'[19]. In this book he reports the calculation of the NMR spectrum of E. coli. He used a molecule of yeast to base his hypothetical atomic coordinates of E. coli and along with optimised ring currents and intrinsic positions he calculated the NMR spectrum of E. coli. The result was similar, but not perfect when compared to an experimental spectrum of E. coli. He stated that the differences in the two spectra were most likely because of the assumption that the yeast and E. coli are identical in structure and that in the future this procedure should be done with highly refined coordinates. It is almost 40 years since this book was published and while NMR ring currents have been used in biology for imaging bacteria, there has not been much follow up work on the imaging of bacteria since the 1990s. As a result of NMR providing unambiguous structural information, I believe that for future strains of bacteria or even viruses, NMR ring currents could be used to image and pinpoint weaknesses in pathogens and help provide valuable information that could lead to cures.

Another future application could the study of metabolic processes of biodegradation pathways. Many examples have shown the potential of the 19F NMR technique, including the work of M.G Boersma who illustrated this for metabolic characterisation of newly isolated microorganisms and also for identification of relatively unstable pathway intermediates such as fluoromuconolactones and fluoromaleylacetates in 2001[20]. In 2010 S. Durand used NMR and Liquid Chromatography (LC) to complement Liquid Chromatography - Mass Spectrometry (LC-MS) to define the biodegradation pathway of mesotrione (herbicide)[21]. The side act of NMR and LC identified six out of the ten metabolites, while LC-MS identified four. From this NMR discovered the presence of a new metabolic pathway. From research like this we could further understand biodegradation of our waste and possibly help reduce pollution caused by non-biodegradable waste by finding ways to make this waste biodegradable.

NMR ring currents have many uses in science today and have come a long way since the likes Kekulé, Isidor Rabi and J.A. Pople. Even today there are still

further developments in techniques that implement this idea and hopefully will be for many more years to come. With this better understanding there should be far more to come from NMR ring currents and maybe, just maybe, some ideas that I have suggested might become a reality in the near future.

According to Lord Kelvin who saw the importance of the applications of natural sciences to engineering in the latter part of his life 'nearly all the grandest discoveries of science have been but the rewards of accurate measurement and patient long-continued labour". It has taken over a hundred years for practical applications to follow the natural discoveries of aromaticity. We should therefore expect more applications to follow with the progress of careful research and measurement in the field of NMR ring currents.

## References:

1. Hofmann, A. W. (1855). "On Insolinic Acid". Proceedings of the Royal Society. 8: 1–3.
2. NMR Spectroscopy Of Aromatic Compounds. 1st ed. New Mexico: University of New Mexico, 2017.
3. Archibald S. Couper (1858) "On a new chemical theory," Philosophical Magazine, 4th series, 16: 104-116.
4. Kekulé, F. A. (1865). "Sur la constitution des substances aromatiques". Bulletin de la Societe Chimique de Paris, 3: 98–110.
5. Hecht, Jeff. (1985). "Football Molecule May Pervade The Universe". *New Scientist,* 1482: 24.
6. Pople, J.A. (1958). "Molecular Orbital Theory Of Aromatic Ring Currents". Molecular Physics, 1.2: 175-180.
7. Rabi II, Zacharias JR, Millman S, Kusch P. (1938). "A new method of measuring nuclear magnetic moment." Phys. Rev., 53: 318.
8. Schleyer P. v. R., Maerker C., Dransfeld A., Jiao H. and van Eikema N. J. R., Hommes, (1996). J. Am. Chem. Soc., 118, 6317–6318.
9. Steiner E., and Fowler P. W., (2001). Chem. Commun. 21: 2220–2221.
10. Klod S. and Kleinpeter E., J. (2001). Chem. Soc., Perkin Trans. 2: 34: 1893–1898.
11. Stanger A., (2006) J. Org. Chem., 71: 883–893
12. Stanger A., (2010). J. Org. Chem., 75: 2281–2288.
13. Gershoni-Poranne, R. and Stanger A. (2015) "Magnetic Criteria Of Aromaticity". Chem. Soc. Rev., 44.18: 6597-6615.
14. Mills Group paper
15. Xu W. G., Zhang R. C., Lu S. X. and Zhang Y. C., (2008). THEOCHEM, 864: 1–5.
16. Liu, D. and Wüthrich K. (2016). "Ring Current Shifts In 19F-NMR Of Membrane Proteins". Journal of Biomolecular NMR 65.1: 1-5. Web.
17. Redfield, C, Hoch J. C., and Dobson C. M. (1983). "Chemical Shifts Of Aromatic Protons In Protein NMR Spectra". FEBS Letters 159.1-2: 132-136.
18. Sahakyan, A. B. and Vendruscolo M. (2013). "Analysis Of The Contributions Of Ring Current And Electric Field Effects To The Chemical

Shifts Of RNA Bases". The Journal of Physical Chemistry B 117.7: 1989-1998.

19. Schulman, R. Biological Applications Of Magnetic Resonance. 1st ed. Elsevier (2017).

20. Boersma, M. G. et al. (2001). "19 F NMR Metabolomics For The Elucidation Of Microbial Degradation Pathways Of Fluorophenols". Journal of Industrial Microbiology and Biotechnology 26.1-2: 22-34.

21. Durand S. et al. (2010). "Biodegradation Pathway Of Mesotrione: Complementarities Of NMR, LC–NMR And LC–MS For Qualitative And Quantitative Metabolic Profiling". Chemosphere 81.3: 372-380.

22.

23. **Bibliography**

24. Abraham, Raymond J. and Reid M. "1H Chemical Shifts In NMR. Part 18.1 Ring Currents And П-Electron Effects In Hetero-Aromatics". Journal of the Chemical Society, Perkin Transactions 2 6 (2002): 1081-1091.

25. Aromatic Compounds. 1st ed. Dallas: University of Texas at Dallas, (2017). Web. 12 Mar. 2017.

26. "Aromatic Compounds - Learn Chemistry Wiki". Rsc.org. N.p., 2017. Web. 12 Mar. 2017.

27. "Aromaticity - New World Encyclopedia". Newworldencyclopedia.org. N.p., (2017). Web. 12 Mar. 2017.

28. Gomes, J. A. N. F. and Mallion R. B. "Aromaticity And Ring Currents". (2017).

29. "Magnetic Resonance Imaging (MRI)". Science.jrank.org. N.p., (2017). Web. 12 Mar. 2017.

30. Marco D. Metagenomics. 1st ed. Norfolk: Caister Acad. Press, (2011).

31. Rahman, A. and Choudhry M. I. Applications Of NMR Spectroscopy:, Volume 1. 1st ed. Bentham Science Publishers, (2017).

32. Revolvy, LLC. ""Aromatic Ring Current" On Revolvy.Com". Revolvy.com. N.p., (2017). Web. 12 Mar. 2017.

33. Victora, A., Moller H. M., and Exner T. E. "Accurate Ab Initio Prediction Of NMR Chemical Shifts Of Nucleic Acids And Nucleic Acids/Protein Complexes". Nucleic Acids Research 42.22 (2014): e173-e173.

34. Williams, A., Martin G., and Rovnyak D. Modern NMR Approaches To The Structure Elucidation Of Natural Products: Volume 2: Data Acquisition And Applications To Compound Classes. 1st ed. Royal Society of Chemistry, (2017).

35. "5.1: The Origin Of The NMR Signal". Chemistry LibreTexts. N.p., (2017). Web. 12 Mar. 2017.

36. "5.2 Chemical Shift". Chem.wisc.edu. N.p., (2017). Web. 12 Mar. 2017.

37. Chemical Shifts. 1st ed. London: University College London, (2017). Web. 12 Mar. 2017.

38. "Nuclear Magnetic Resonance". Hyperphysics.phy-astr.gsu.edu. N.p., (2017). Web. 12 Mar. 2017.

39. Wannere, C. S. and Schleyer P. V. R. "How Do Ring Currents Affect1h NMR Chemical Shifts?". Organic Letters 5.5 (2003): 605-608. Web.