

Bachelor Thesis

Chemistry Grade.

Theoretical Chemistry.

Computational study of aromaticity with electron delocalization indices.

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In chemistry, aromaticity refers to the unique stability and reactivity of certain cyclic compounds. These compounds are characterized by having a ring of atoms with the alternation of σ and π bonds, which creates a delocalized system of electrons that is particularly stable.

While aromaticity is a well-established concept in organic chemistry, there has been some debate about the precise definition and use of the etiquette. Some authors argue that aromaticity is not a fundamental property of molecules, but rather a useful shorthand for describing certain chemical phenomena.

Additionally, the concept of aromaticity has been applied to systems that do not fit the traditional definition of an aromatic compound, leading some to question the validity of the concept.[1] Furthermore, there have been some discrepancies between experimental observations and theoretical predictions regarding the behavior of aromatic compounds.[2]

Kimikan, aromatizitateak erreferentzia egiten dio egonkortasun eta errektibitate berezia erakusten duten molekula batzuei. Molekula hauen ezaugarritzen dira eraztun formako molekuletan atomoen artean σ eta π loturak txandatzeko dituztela, zeinek deslokalizatutako sistema elektroniko bat osatzen duen, egonkortasun berezia erakutsiz.

Naiz eta kimika organikoaren arloan aromatizitate kontzeptua ongi finkatuta egon, kimikaren arloan eztabaida handia dago kontzeptua zehazki definitzeko orduan. Aditu batzuek diote aromatizitatea ez dela molekulen funtsezko propietate bat, baizik eta zenbait fenomeno kimiko erraz sailkatzeko etiketa.

Gainera, azken urteetan aromatizitate kontzeptua tradizionalik aromatikotzat kontsideratu ez diren molekulei aplikatu zaie, kontzeptuaren baliagarritasuna zalantzan jarriz.[1] Hau gutxi balitz, behaketa esperimentalen eta iragarpen teorikoen artean desadostasunak daude konposatu aromatikoek erakutsi beharko luketen portaeran.[2]

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Introduction

1.1 From quantum mechanics to computational chemistry.

At the end of the 19th century, many scientists believed that the field of physics was dead, they thought that everything had already been discovered and that they only had to explain some meaningless phenomena. In 1878, Philipp von Jolly wrote a letter to a student, advising against studying physics because:

“In this field, almost everything is already discovered, and all that remains is to fill a few unimportant holes.”[3]

One of these “unimportant holes” was the black body radiation. Max Planck, a German physicist, discovered a way to explain the experimental observations of black body radiation by proposing that the energy of each electromagnetic oscillator is limited to discrete quantities proportional to the frequency ν of the light, with the magnitude $h\nu$. The constant of proportionality h , known as Planck’s constant, has a value of $6.62607015 \cdot 10^{-34} \text{ Js}$. [4] This limitation of energies to discrete values is known as the quantization of energy. Planck’s discovery revolutionized the field of physics and paved the way for the development of quantum mechanics.[5]

In 1905, Einstein was working on the photoelectric effect. In this experiment, a metal layer was illuminated with light and the electrons from the surface absorbed the energy, causing them to be emitted. He observed that a minimum threshold frequency, ν_0 , was required for the emission of electrons to begin. Furthermore, as the intensity of the light increased, the number of emitted electrons also increased, but their energy remained constant. It was only with an increase in the frequency of the applied light that the energy of the emitted electrons increased. This phenomenon could not be explained by classical theory. Therefore, building upon Planck’s earlier work, he proposed that light possessed particle properties in addition to its wave properties. He postulated that the energy of a light particle, known as a photon, could be determined by the equation $E_{\text{photon}} = h\nu$.

Some years later, in 1911, Rutherford discovered the structure of atoms. He found that the atom's nucleus was made up of small, heavy particles with a positive charge, while the extra-nuclear region was composed of small particles with a negative charge. Classical mechanics was unable to explain this atomic model. According to classical mechanics, the acceleration of a charged particle would lead to an emission of light(energy) with the frequency of the orbit, with the emission of this energy, the radius of the electron's orbit would decrease and the frequency would change. But this is not what was observed, hydrogen emitted light in sharply defined frequencies. In 1913, Bohr inspired by Einstein's work postulated the existence of stationary state E_0 and that the transition from one energetic state E_1 to another energetic state E_2 was done by the absorption or emission of light with frequency ν described by:[4]

$$\nu = \frac{E_2 - E_1}{h} \quad (1.1)$$

In 1923, De Broglie[6] proposed that matter had a dual nature, behaving both as a wave and a particle. Where matter could only vibrate to certain discrete frequencies.

$$\lambda = \frac{h}{mv} = \frac{h}{p} \quad (1.2)$$

This equation describes that the wave length, λ , of any particle is given by the division of the Planck's constant, h , by its momentum, p . This describes that wave properties are significant when the mass of the particles is very small.

In 1927, Werner Heisenberg[7] proposed that it is impossible to simultaneously specify, with arbitrary precision, both the momentum and position of a particle. Heisenberg's uncertainty principle can be formulated as

$$\Delta p_x \Delta x \geq \frac{h}{4\pi}, \quad (1.3)$$

where Δp_x and Δx are the uncertainty in momentum and position.

With these discovered phenomena and the inability of classical physics to explain them, the necessity of a new physical formulation was needed. The first one to develop a formulation for quantum mechanics was Werner Heisenberg in 1925; because of the use of matrices it is usually called matrix mechanics. A year later, Erwin Schrödinger developed another formulation based on the wavefunction. His method was rapidly adopted by other scientists and became more popular than matrix mechanics. This theory relied on the following postulates:

1) Every physical system has a wave function $\Psi(\vec{r}, t)$ that defines its state depending on spacial coordinates \vec{r} and time t . This wavefunction $\Psi(\vec{r}, t)$ does not have a physical meaning. But $|\Psi|^2$ has a physical meaning and describes the probability density, which corresponds to the probability of finding a particle in a certain region of the space.

2) Physical observables are represented by linear hermitian operators: $\hat{A}\Psi = \Psi'$

3) A wavefunction Ψ will be the eigenvalue of operator \hat{A} if, $\hat{A}\Psi = a\Psi$. Where a is the eigenvalue, the value of the physical property measured by the operator \hat{A}

4) Ψ , is a superposition of states, thus, $\Psi = \sum c_i \Psi_i$. Then, a single measurement of an observable will return an eigenvalue a_i , with a $|c_i|^2$ probability. As a consequence of the measurement, the system will collapse to that Ψ_i state.

5) To obtain the wave function that describes the system we have to solve the Schrodinger equation.

$$\hat{H}\Psi = E\Psi \quad (1.4)$$

6) Spin can take on either integer values (corresponding to bosons) or half-integer values (corresponding to fermions). The wave functions of bosons will be symmetric and the fermions wavefunction antisymmetric with respect to any exchange between two particles. $\Psi(q_1, \dots, q_i, q_j, \dots, q_n) = \pm \Psi(q_1, \dots, q_j, q_i, \dots, q_n)$.

The evolution of this theory settled the basis and the tools for a better description of the microscopical world and brought more insight into molecular phenomena, such as the chemical bond, ionization potentials, and atomic orbitals.

Its main problem practical problem is that the Schrödinger equation can only be solved analytically for one particle system. If we write the molecular Hamiltonian in atomic units,

$$\hat{H} = - \sum_{i=1}^N \frac{1}{2} \nabla_i^2 - \sum_{A=1}^M \frac{1}{2M_A} \nabla_A^2 - \sum_{i=1}^N \sum_{A=1}^M \frac{Z_A}{r_{iA}} + \sum_{i=1}^N \sum_{j>i}^N \frac{1}{r_{ij}} + \sum_{A=1}^M \sum_{B>A}^M \frac{Z_A Z_B}{R_{AB}} \quad (1.5)$$

Where N is the total number of electrons, M is the total number of nuclei, M_A is the mas of nuclei A, r_{iA} is the distance between electron i and nuclei A and R_{AB} is the distance between nuclei A and nuclei B. The first term of the equation describes the kinetic energy of the electrons, the second term is the kinetic energy of the nuclei, the third term is the potential energy of the attraction between the nuclei and the electrons, the fourth term is the potential energy of the repulsion between electrons, and the fifth term is the potential energy of the repulsion between the nuclei.

Due to the cross-term, $\vec{r}_{iA} = |\vec{r}_i - \vec{R}_A|$, the Schrödinger equation does not render itself and the separation of variables and hence cannot be solve analytically. To study more complex systems is necessary to use approximations, like the Born-Oppenheimer approximation. This approximation assumes that since nuclei are much more heavy than electrons, they move more slowly. Hence, for a good approximation, one can consider the electrons in a molecule to be moving in the field of fixed nuclei. Then, the kinetic energy of the nuclei can be neglected and the repulsion between nuclei can be considered constant, and allowing the separation of the Schrödinger into an electronic equation and a nuclear equation. The electronic equation and Hamiltonian are:

$$\hat{H}_{elec} \Phi_{elec}(\vec{r}_A; \vec{R}_A) = E_{elec} \Phi_{elec} \quad (1.6)$$

$$\hat{H}_{elec} = - \sum_{i=1}^N \frac{1}{2} \nabla_i^2 - \sum_{i=1}^N \sum_{A=1}^M \frac{Z_A}{r_{iA}} + \sum_{i=1}^N \sum_{j>i}^N \frac{1}{r_{ij}} \quad (1.7)$$

Once the electronic equation is solved, you obtain the electronic energy which depends on the nuclear coordinates $E_{elec}(\{\vec{R}_A\})$. This energy is introduced in the Hamiltonian of the nuclear equation.

$$\hat{H}_{Nuc} \Phi_{Nuc}(\vec{R}_A) = E_{tot} \Phi_{Nuc} \quad (1.8)$$

$$\hat{H}_{Nuc} = - \sum_{A=1}^M \frac{1}{2M_A} \nabla_A^2 + E_{elec}(\{\vec{R}_A\}) + \sum_{A=1}^M \sum_{B>A}^M \frac{Z_A Z_B}{R_{AB}} \quad (1.9)$$

After solving the nuclear equation, we obtain the wavefunction of the system and the total energy.[8] Eigenfunctions of an operator form a vector space, the Hilbert space. Any function in this space can be represented as a linear combination of eigenfunctions. This allow us to write any orbital wavefunctions as a linear combination of other wavefunctions.

$$\Psi = \sum_i^N c_i \phi(i) \quad (1.10)$$

This allows to write the Schrödinger equation in a matrix form and through iterative processes to minimize the electronic energy in order to obtain the ground state. One of the methods that uses this kind of iterative procedure is the Hartree Fock Self Consistent Field method. (Figure 1.1).[8]

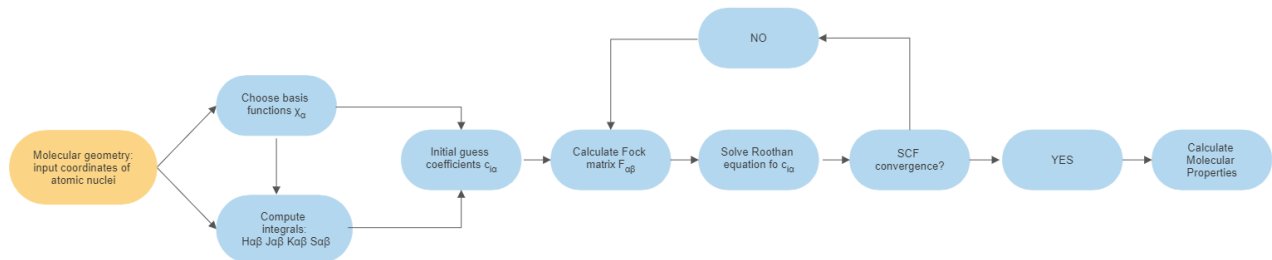


Figure 1.1: Hartree Fock Self Consistent Field flow chart.

The tedious work of solving the Schrödinger equation requires the use of computers (Figure 1.2). The tremendous evolution of computer science in the last decades has allowed us to study more and more complex systems with higher precision, giving birth to computational chemistry.

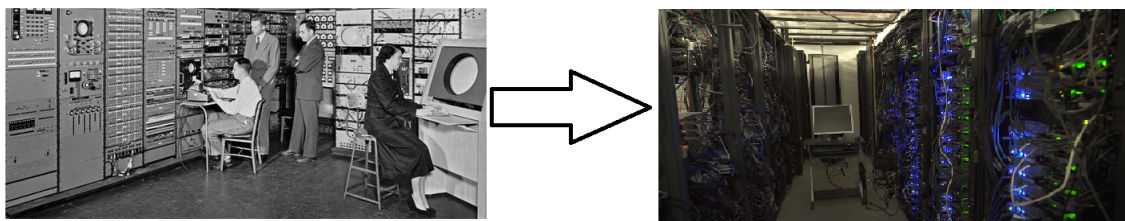


Figure 1.2: On the left a 50s computer and on the right nowadays ATLAS supercomputer.

In this framework, quantum mechanics are the laws of physics that describe the behaviour of small particles, while quantum chemistry is the application of the laws of quantum mechanics to chemical problems,[9] and computational chemistry is the application of computer science to solve problems posed by quantum chemistry. Nowadays, computational chemistry plays a key role in chemical research, allowing a better understanding of the experimental results obtained in the laboratory.

1.2 The aromaticity problem.

1.2.1 History of aromatic compounds.

In the first half of the 19th century, there was no specific category for aromatic compounds because few compounds of this family were discovered at the time. The earliest member of this family was benzoic acid, which was commercialized as a component of a balsamic fragrance called "gum Benzoin".

In 1825, Michael Faraday isolated benzene for the first time. Gradually, more and more compounds related to benzene were found. In 1855, Hoffmann introduced the term "aromatic" to indicate the sweet smell of this group of compounds.[10].

Some years later, in 1865, Kekule proposed the famous structure of benzene. Here below a quote of how Kekule came up with the idea of the benzene structure.[11]

" long rows, sometimes more closely fitted together all twining and twisting in snake-like motion. But look! What was that? One of the snakes had seized hold of its own tail, and the form whirled mockingly before my eyes. As if by a flash of lightning I awoke." (Figure 1.3)

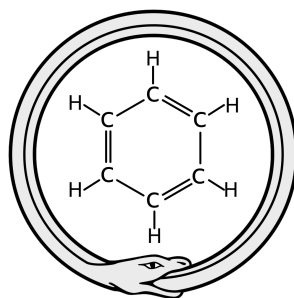


Figure 1.3: Ouroboros and benzene structure.

But it was not until 1931 when Erich Hückel,[12, 13] based on the quantum mechanics formulation, came up with his rule to predict if a planar ring molecule would have aromatic properties.

In 1938, Evans and Warhurts stated that during pericyclic reactions, a cyclic system is formed through a transition state that can be aromatic or antiaromatic. Based on this statement, they explained that ethylene prefers to react with butadiene to produce cyclohexene because the transition state formed is aromatic, rather than reacting with ethylene to give cyclobutane.[14]

During the second half of the 20th century, many new types of aromaticity were discovered, e.g. homoaromaticity, three-dimensional aromaticity, Möbius Aromaticity, among others. In 2001, Boldyrev characterized the first all-metal aromatic cluster, Al_4^{2-} . [15] In 2007, Anderson synthesized a six-porphyrin nanoring.[16] This porphyrin nanoring was the first of a series of similar large macrocyclic structures exhibiting (anti)aromaticity. In 2015, Li reported that $[Zn^1]_8$ is a multicenter-bonded cluster with cubic aromaticity.[17]

The discovery of all these new compounds led to different types of aromaticity (Figure 1.4). In 2017, Jörg Grunenberg pointed out that he collected up to 45 different types of aromaticities.[18]

1.2.2 Aromaticity, the unicorn of chemistry.

Chemistry has evolved from its beginning essentially as an experimental science. Based on experimental observations, chemists have built a series of empirically proved laws and models. On the other hand, quantum mechanics relies on postulates builded from a solid theory. However, due to its mathematical description, quantum mechanics can predict the electronic structure of matter, replacing the laws and models of chemistry with physically sound theories. In the words of Paul Dirac:

" The underlying physical laws necessary for the mathematical theory of a large part of physics and the whole of chemistry are thus completely known"[19]

But some scientists point out that, many of the concepts that chemists use daily (chemical bonding, bond order, aromaticity, etc.) will most likely not find a solid root in the quantum

1.2. The aromaticity problem.

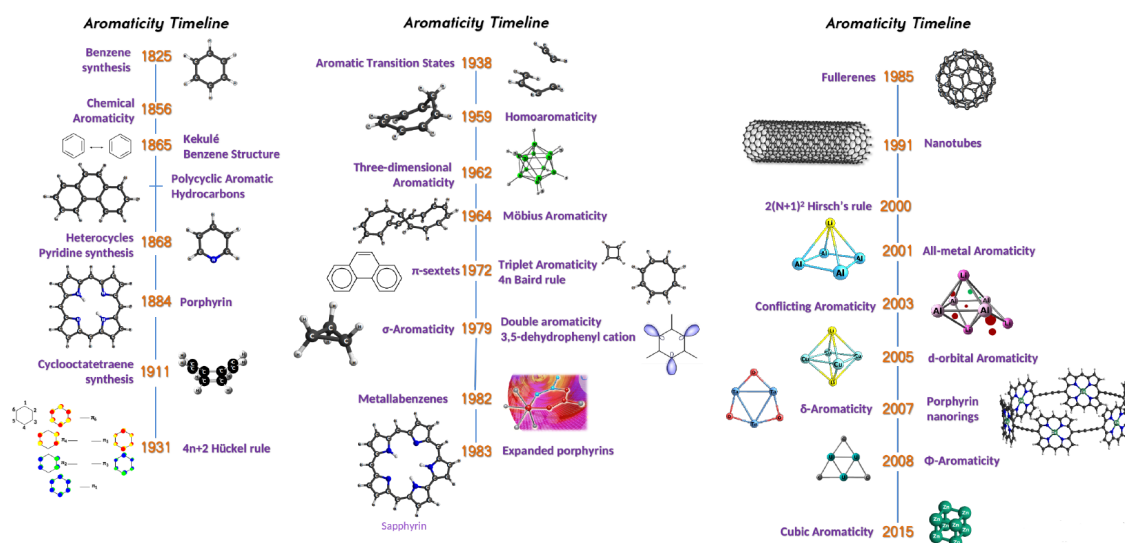


Figure 1.4: Aromaticity time line. [17]

theory because there is no observable behind them.[20] Among these concepts, one of the most used, but also one of the most controversial, is aromaticity.

The problem with aromaticity is that it is ill-defined, because it is not a physical observable that can be directly quantified. Aromaticity is said to be a multidimensional phenomenon, meaning that it is the manifestation of many properties. Aromaticity is related to cyclic electron delocalization in closed circuits, energy stabilization, bond length equalization, large magnetic anisotropies, and abnormal chemical shifts.[21]

All these manifestations can be quantified and used as aromatic indices to elucidate if a molecule is aromatic or not. But Miquel Solà points out that there are too many indices, and not all of them give the same ordering by aromaticity of a series of rings or molecules, adding confusion to the field. Also, because most of the methods were developed for the classical aromatic organic molecules (such as benzene, cyclobutadiene or pyridine) cannot be directly applied to the newly discovered aromatic metallic clusters.[22]

Furthermore, with the evolution of the field, many different types of aromaticity have been described: Hückel aromaticity, Möbius aromaticity, excited state aromaticity, metalloaromaticity, chelatoaromaticity, quasiaromaticity... increasing the complexity of the topic.

From an experimentalist's perspective, one of the most used methodology to determine if a molecule is aromatic or not, is studying the reactivity of the compound. Due to their stability, aromatic molecules show characteristic reactions such as the electrophilic aromatic substitution. This kind of reactivity can suggest the aromatic nature of the molecule. However, this criteria is difficult to apply in general because it needs a reference molecule to measure the stabilization energy.

Apart from reactivity, aromaticity can also be determined through analysis using ^1H-NMR

spectroscopy. In $^1H - NMR$, a strong magnetic field is applied to the sample, causing most nuclei to align with the field. However, certain nuclei do not align and create an energy gap between the aligned state (lower in energy) and the non-aligned state (higher in energy). When the sample is exposed to radio frequencies, the nuclei absorb energy, resulting in transitions between these states. The necessary energy for a transition to happen is related with the electronic environment of the nuclei. This allows to differentiate one nucleus from the other in a molecule. Aromatic molecules show a very characteristic chemical shift, this is due to the electric current induced in the ring. In aromatic molecules, this ring current induces another magnetic field opposite to the external magnetic field changing the total magnetic field that nuclei feel.

To quantify the magnitude of the induced electric current, the chemical shift of a nucleus is measured. But this chemical shift is not only due to the current but also chemical environment affects it. In order to isolate the effect of the current from other sources, another nucleus, that is not affected by the current, is used as a reference. Once the chemical shift due to the induced current is known, it is possible to know the magnitude of the induced magnetic field in the nuclei, from the Biot-Savart law. This method has clear limitations, including the challenge of isolating the effect of the current on the chemical shift from other influences and identifying a nucleus that should not be affected by the current.

In 2007, Anderson and their team synthesized a six-porphyrin nanoring. They conducted theoretical calculations and performed NMR measurements, confirming the aromatic nature of the molecule.^[23] However, the methods they utilized were subsequently discussed and cast into doubt.^[24, 25]

Even this said, aromaticity is still a central concept of chemistry despite all the challenges that go with it. The continuous increase in the bibliometric impact of the terms aromaticity and antiaromaticity throughout this century (Figure 2.4) demonstrates the significance and utility of these concepts.

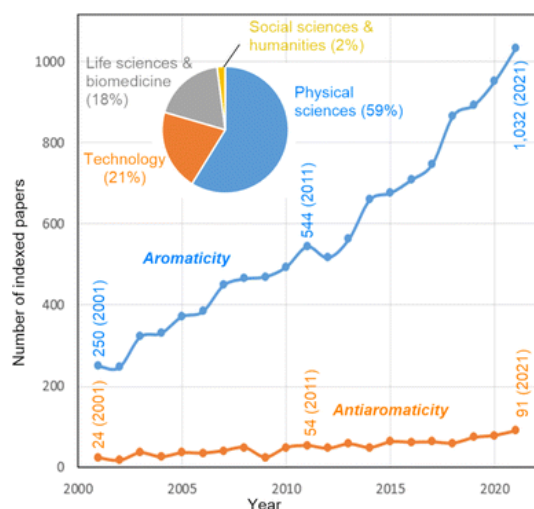


Figure 1.5: Evolution of the number of indexed papers including the words aromaticity and antiaromaticity in their abstract and keywords along the first half of the twenty-first century (Source: web of Science. Data download on October 28,2022)

1.3 Previous works and goals.

This project is inspired by previous works about the study of aromaticity in large molecules.[24][25][26]

- The main goal of this thesis is to understand the concept of aromaticity and how two facets of aromaticity, electron delocalization and magnetic response, are connected between them. To this end, the four following particular objectives are considered.

- Familiarizing oneself with computational chemistry tools is for studying and characterizing the aromaticity in organic molecules.
- Study classical organic molecules, computing various indices that assess intrinsic properties, as well as indices that quantify the response induced by an external magnetic field.
- Proceed with similar calculations for larger systems, such as annulenes, to investigate the impact of ring size on both intrinsic and response properties.
- Assess the most adequate computational approximation to study aromaticity.

Methodology

2.1 From chemical bonding analysis to aromaticity indices.

2.1.1 The electron density.

The electron density is the central quantity of density functional theory (DFT) and the quantum theory of atoms in molecules (QTAIM). The density function is a simpler quantity than the wavefunction, as it only depends on three Cartesian coordinates. Additionally, the density is an observable.

Based on Born's interpretation, the probability of finding one electron at position $\mathbf{1}$ (at position \vec{r}_1 with spin σ_1) regardless the other (N-1) electrons is given by:

$$P(\mathbf{1})d_1 = \int d_2 \int d_3 \dots \int d_N |\Psi(\mathbf{1}, \mathbf{2}, \dots, \mathbf{N})|^2 d_1, \quad (2.1)$$

where $\Psi(\mathbf{1}, \mathbf{2}, \dots, \mathbf{N})$ is the wavefunction describing an N-electron system. From here, we can define the density at position $\mathbf{1}$ as

$$\rho(\mathbf{1}) = NP(\mathbf{1}) = N \int d_2 \int d_3 \dots \int d_N |\Psi(\mathbf{1}, \mathbf{2}, \dots, \mathbf{N})|^2, \quad (2.2)$$

where N is the total number of electron in the system. This density can be understood as the amount of particles that are found on average at position $\mathbf{1}$.

The integration of $\rho(\mathbf{1})$ over the whole space gives the total number of electrons. By integrating $\rho(\mathbf{1})$ over an arbitrary space Ω , we obtain the average number of electrons in that region,

$$N_\Omega \equiv \langle N(\Omega) \rangle = \int_\Omega d_1 \rho(\mathbf{1}) = N \int_\Omega d_1 P(\mathbf{1}). \quad (2.3)$$

2.1.2 The pair density.

Extending further Born's interpretation, the probability of finding two electrons, one at $\mathbf{1}$ and the other at $\mathbf{2}$, regardless the position of the other $N-2$ electrons is given by:

$$P(\mathbf{1}, \mathbf{2})d_1d_2 = \int d_3 \dots \int d_N |\Psi(\mathbf{1}, \mathbf{2}, \dots, \mathbf{N})|^2 d_1 d_2 \quad (2.4)$$

with this we can express the pair density as:

$$\rho(\mathbf{1}, \mathbf{2}) = N(N-1)P(\mathbf{1}, \mathbf{2}) = N(N-1) \int d_3 \dots \int d_N |\Psi(\mathbf{1}, \mathbf{2}, \dots, \mathbf{N})|^2 \quad (2.5)$$

The expected number of electron pairs at an arbitrary position Ω is given by:

$$\begin{aligned} N_{\Omega\Omega} &\equiv \langle N^2(\Omega) \rangle = N_{\Omega} + \int_{\Omega} \int_{\Omega} d_1 d_2 \rho(\mathbf{1}, \mathbf{2}) = \\ &= N_{\Omega} + N(N-1) \int_{\Omega} \int_{\Omega} d_1 d_2 P(\mathbf{1}, \mathbf{2}) \end{aligned} \quad (2.6)$$

where N_{Ω} is the number of self-pairing electrons. We include this term to compensate for the Pauli's principle, that excludes the possibility of self-pairing in the wavefunction. In this way, $N_{\Omega\Omega}$ can attain its maximum value, N_{Ω}^2 .

In the case of two regions Ω_1 and Ω_2 , the expected number of electron pairs, one at Ω_1 and the other at Ω_2 , is given by:

$$N_{\Omega_1\Omega_2} \equiv \langle N_{\Omega_1} N_{\Omega_2} \rangle = N_{\Omega_1 \cap \Omega_2} + \int_{\Omega_1} \int_{\Omega_2} d_1 d_2 \rho(\mathbf{1}, \mathbf{2}), \quad (2.7)$$

where $N_{\Omega_1 \cap \Omega_2}$ are the electron pairs in the overlapping region.

2.1.2.1 Bonding Analysis.

Now using some statistical tools we can explain the bonding by analysing how electrons are shared between two regions. We will define the variance in a region as:

$$\sigma^2[N_{\Omega}] = N_{\Omega\Omega} - N_{\Omega}^2 = N_{\Omega} + \int_{\Omega} \int_{\Omega} d_1 d_2 \rho(\mathbf{1}, \mathbf{2}) - \left(\int_{\Omega} d_1 \rho(\mathbf{1}) \right)^2 \quad (2.8)$$

If electrons in region Ω are never outside Ω , then $N_{\Omega}^2 = N_{\Omega\Omega}$ and the variance will be 0. In this case, the uncertainty is minimal, the electrons are totally localized. But if electrons from Ω are sometimes outside Ω , then the variance will take positive values. In this case, the uncertainty on the position of the electrons will increase.

The variance gives an idea of the electron fluctuation in a region. The larger the fluctuation, the larger the variance. Large variances are related with covalent bonding, Whereas small variance occur in closed-shell fragments and hence it is connected to ionic bonding and non-covalent interactions.

Similarly, the covariance between two regions, Ω_1 and Ω_2 can be defined as:

$$\begin{aligned} cov(\Omega_1, \Omega_2) &= N_{\Omega_1\Omega_2} - N_{\Omega_1}N_{\Omega_2} = \\ &= N_{\Omega_1\cap\Omega_2} + \int_{\Omega_1} \int_{\Omega_2} d_1d_2\rho(\mathbf{1}, \mathbf{2}) - \left[\left(N \int_{\Omega_1} d_1\rho(\mathbf{1}) \right) \left(N \int_{\Omega_2} d_1\rho(\mathbf{2}) \right) \right] \end{aligned} \quad (2.9)$$

the covariance measures the dependency of the electrons from both regions. It gives the idea of how many electrons from Ω_1 and Ω_2 are shared between them.

Zero covariance between Ω_1 and Ω_2 is attained when these regions do not overlap and form the maximum possible number of electron pairs, $N_{\Omega_1} \cdot N_{\Omega_2}$. This means that electrons from Ω_1 are independent from Ω_2 . In this case, we will say that there is no a chemical bond between these two regions.

For example, if we see that the variance in the regions of the two nuclei, A and B, have a positive value (meaning that electrons in regions A and B are shared with other regions) and the covariance between A and B has a negative value (meaning that regions A and B share electrons), we could say that there is a covalent bonding between nucleus A and nucleus B. On the other hand, if the variance in the two regions and the covariance between the two regions is zero and $N_A > Z_A$, $N_B < Z_B$ (meaning that in region A there are more electrons than protons and in region B are more protons than electrons), this would indicate an ionic bond between A and B having opposite charges.

2.1.3 Quantum Theory of Atoms in Molecules (QTAIM).

To compute N_Ω its necessary to define an atom in a molecule (also known as an atom partition); there are many atom partitions, here we choose QTAIM because its one of the most reliable ones.[27]

This theory uses as a central concept the electron density and it defines the atom in a molecule through the topological analysis of the charge distribution in the molecule.

The density is a continuous non negative function defined at every point of the real (Cartesian) space. Here, the critical points, r_c , of the electron density are defined as the points that present a zero value of the gradient of density function.

$$\nabla\rho(\mathbf{r}_c) = 0 \quad (2.10)$$

These critical points are characterized by the analysis of the second derivatives of the density function at the position of these critical points. All the second derivatives of the density are

collected in the so-called Hessian matrix.

$$\mathbf{H}[\rho](\mathbf{r}_c) = \nabla_{\mathbf{r}}^T \nabla_{\mathbf{r}} \rho(\mathbf{r})|_{\mathbf{r}=\mathbf{r}_c} = \begin{pmatrix} \frac{\partial^2 \rho(r)}{\partial^2 x} & \frac{\partial^2 \rho(r)}{\partial x \partial y} & \frac{\partial^2 \rho(r)}{\partial x \partial z} \\ \frac{\partial^2 \rho(r)}{\partial y \partial x} & \frac{\partial^2 \rho(r)}{\partial^2 y} & \frac{\partial^2 \rho(r)}{\partial y \partial z} \\ \frac{\partial^2 \rho(r)}{\partial z \partial x} & \frac{\partial^2 \rho(r)}{\partial z \partial y} & \frac{\partial^2 \rho(r)}{\partial^2 z} \end{pmatrix}_{\mathbf{r}=\mathbf{r}_c} \quad (2.11)$$

Since $\frac{\partial^2 f}{\partial a \partial b} = \frac{\partial^2 f}{\partial b \partial a}$, \mathbf{H} is a real symmetric matrix and can be diagonalized through a unitary transformation, \mathbf{L} ,

$$\mathbf{H}[\rho]\mathbf{L} = \mathbf{L}\Lambda, \quad (2.12)$$

where Λ is

$$\Lambda = \begin{pmatrix} \frac{\partial^2 \rho(r)}{\partial^2 x} & 0 & 0 \\ 0 & \frac{\partial^2 \rho(r)}{\partial^2 y} & 0 \\ 0 & 0 & \frac{\partial^2 \rho(r)}{\partial^2 z} \end{pmatrix}_{\mathbf{r}=\mathbf{r}_c} = \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{pmatrix} \quad (2.13)$$

where λ_1 , λ_2 , and λ_3 are the eigenvalues of the Hessian matrix.

If the three eigenvalues are negative, we will have an Attractor Critical Point (ACP), a maximum of $\rho(r)$. This point usually coincides with an atomic position. An atom-in-molecule within QTAIM is characterized by one and only one ACP.

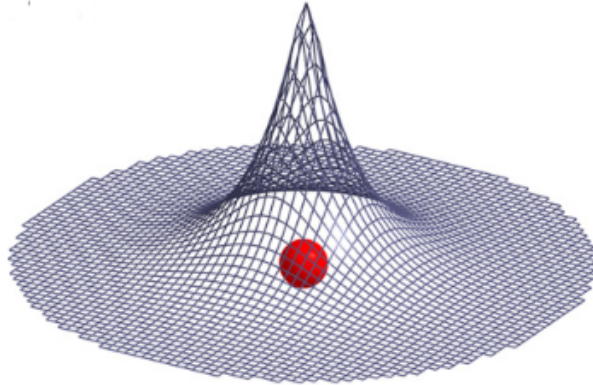


Figure 2.1: Example of an Attractor Critical Point.(Source: Revisiting the foundations of the quantum theory of atoms in molecules: Some open problems by Shahbazian and Shant.[28])

If one of the eigenvalues is positive while others negative, a Bond Critical Point (BCP) is obtained. A BCP presents two negative curvatures and a positive one. BCPs are found between two ACPs.

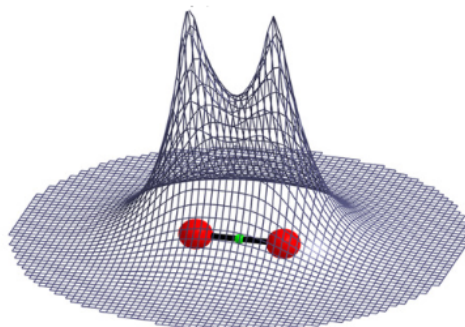


Figure 2.2: Example of a Bond Critical Point (green point).(Source: Revisiting the foundations of the quantum theory of atoms in molecules: Some open problems by Shahbazian and Shant.[28])

A Ring Critical Point (RCP) presents one negative eigenvalue and the others are positive. A RCP has two positive curvatures; its presence indicates a ring structure in the plane formed by the positive eigenvalues. If the molecule is planar, the RCP is located at the minimum of the electron density inside the ring structure.

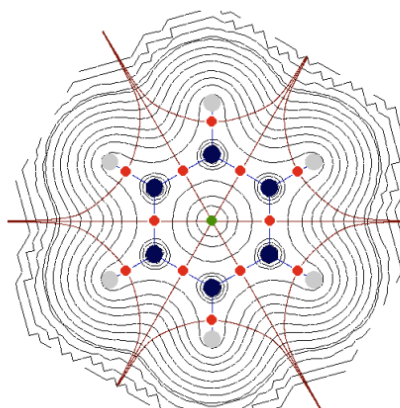


Figure 2.3: Example of a Ring Critical Point (green point) at the center of the benzene molecule.(Source: New tools for chemical bonding analysis by E. Matito.[29])

If all three eigenvalues are positive, we will have a Cage Critical Point (CCP), which is a minimum of the electron density.

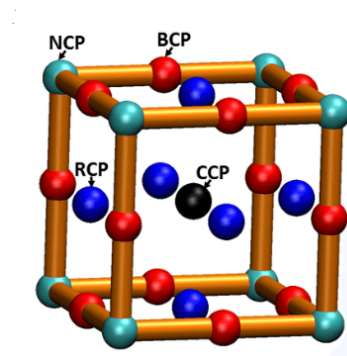


Figure 2.4: Example of a Cage Critical Point (black point) at the center of the cube. (Source: A review of geometric, topological and graph theory apparatuses for the modeling and analysis of biomolecular data by Kelin Xia.[30])

In this bachelor thesis, we will employ Bader's definition of an atom in a molecule, defined as an attractor of $\rho(r)$ surrounded by a zero flux surface of the density or by infinity (see figure 2.3), these are the atom definition we will employ to compute the quantities of section 2.1.1 and 2.1.2

2.1.4 Aromaticity indices.

Aromaticity is considered to be a multidimensional phenomenon, meaning that is the manifestation of many properties like electron delocalization, energy stabilization, bond length equalization, and magnetic properties. Hence, a plausible methodology to determine if a novel molecule is aromatic or not results from measuring these properties and compare them with those obtained from well-established and reported aromatic molecules. If the values are similar it can also be considered aromatic.

For this purpose different indices were invented. These indices are categorized based on the properties they measure.[17] An interesting classification that can be made among all indices is the distinction between those that measure intrinsic properties and those that measure induced properties. Intrinsic properties are the properties that a molecule show without any external perturbation, on the other hand, induced properties are the ones a molecule shows when an external perturbation is applied.

Aromaticity descriptors formula are associated to a molecule with n atoms denoted by the string $A = \{A_1, A_2, \dots, A_n\}$ whose components are arranged following the connectivity of the atoms in the ring.

2.1.4.1 Geometrical indices.

This type of indices measures the bond length equalization and molecular symmetry, signatures of the aromatic character.

Harmonic Oscillator Model of Aromaticity (HOMA).

HOMA relies on the similitude between the bond distances of the studied molecule to the reference one. For instance, in C-C bonds, the r_{opt} is obtained from the benzene, 1.388 Å. When HOMA yields value close to one, it indicates an aromatic character.[31]

$$\begin{aligned} HOMA(A) &= 1 - \frac{1}{n} \sum_i^n \alpha_i (r_{opt} - r_{A_i, A_{i+a}})^2 = \\ &= 1 - (EN + GEO) \end{aligned} \quad (2.14)$$

HOMA can be decomposed into EN (energetic) and GEO (geometric) components, where EN measures the deviation of the bond distances from a tabulated reference one and GEO evaluates the variance of the bond distances. Both quantities are near zero for aromatic molecules.

The biggest limitation of this descriptor is the dependence on reference values. These reference values are limited to few types of bonds (C-C, C-N, C-O, C-P, C-S, N-N, N-O) for which a reference molecule could be found.

Bond Length Alternation.

This index was developed to analyze conjugated chains.[32] It was defined as the difference between the mean bond length of odd bonds and the mean bond length of even bonds:

$$BLA(A) = \bar{r}_{\text{oddbonds}} - \bar{r}_{\text{evenbonds}}, \quad (2.15)$$

depending the dominance of the resonant structures drawn from the conjugated form, BLA will give a positive value or negative (see figure 2.5).

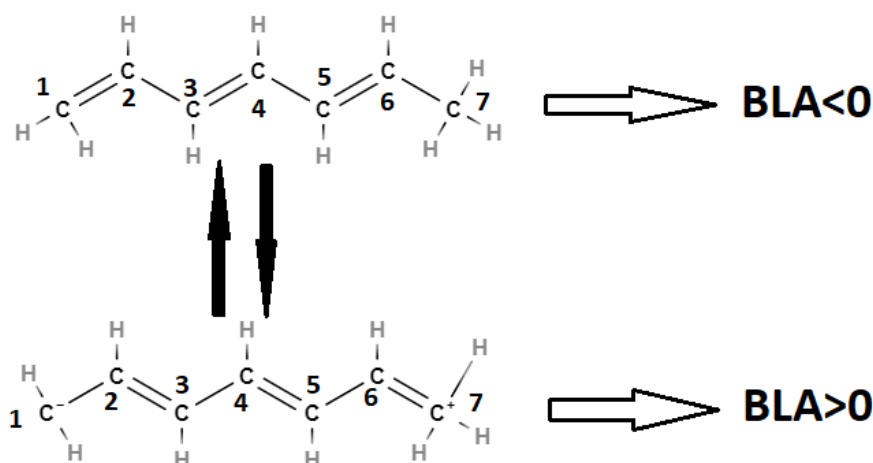


Figure 2.5: The value of BLA for different resonant forms of 1,3,5-heptatriene.

Later, BLA was applied also to cyclic molecules. But the direct application of the index brought an error. For some molecules, there is a possibility that the differences cancel out, giving $BLA=0$, even if bonds are not all identical, this happens, for example for 1,4-cyclohexadiene.

To avoid this problem, $BLA(1)$ was proposed.[26] This descriptor computes the average of the bond lengths of consecutive bonds in a ring.

$$BLA(A) = \frac{1}{2n} \sum_{i=1}^n |r_{A_i, A_{i+1}} - r_{A_{i+1}, A_{i+2}}| \quad (2.16)$$

BLA and $BLA(1)$ measures the bond length equalization expected in aromatic molecules. For aromatic molecules BLA and $BLA(1)$ give values near to zero. However, one should keep in mind that molecules where the bond distances are equal will also give $BLA=0$, even if there is no π conjugation, as in cyclohexane.

We also have to take into account that sometimes the average value does not give us the whole picture. For this, it is interesting to look to the maximum, minimum, and the variance of the values.

2.1.4.2 Electronic Indices.

Electronic indices measure the electronic delocalization of the molecule. They can be distinguished between the ones that measure intrinsic electronic properties (without applying any external perturbation), such as FLU, BOA, Iring, MCI, and AV1245, and the ones that measure induced electronic properties (applying an external perturbation), such as the ring current.

Electron Sharing Index (ESI).

The bond order or ESI is a key concept in chemistry. In QTAIM context, ESI arises from the population covariance and it is also called the delocalization index (DI):

$$\delta(A, B) = -2cov(N_A, N_B) \quad (2.17)$$

(See equation 2.9) since the ESI is defined from the covariance between atoms A and B, it is a measure of the number of electrons simultaneously fluctuating between these atoms. It is common to take this value as the number of electron pairs shared between atoms A and B, a quantity commonly known as the order of the bond. The ESI will be used to define electronic aromaticity indices.

The Aromatic Fluctuation Index (FLU).

It is the analogue of HOMA for electronic descriptors. This electronic descriptor only employs the electronic delocalization of the bonds in the ring and compares them with the cyclic electron delocalization of an aromatic molecule of reference.[33]

$$FLU(A) = \frac{1}{n} \sum_{i=1}^n \left[\left(\frac{\delta(A_i)}{\delta(A_{i-1})} \right)^\alpha \left(\frac{\delta(A_i, A_{i-1}) - \delta_{ref}(A_i, A_{i-1})}{\delta_{ref}(A_i, A_{i-1})} \right) \right]^2 \quad (2.18)$$

where α ensures that the first term of equation is always greater than or equal to 1, $\delta_{ref}(A, B)$ is the DI of the aromatic molecule of reference, and n is the number of atoms. If the delocalization values of the bonds are similar to the reference (for C-C bonds is benzene, for C-N is pyrimidine) the value of FLU will be near to zero.

Bond Order Alternation (BOA).

Is the electronic counterpart of BLA(1)(see equation 2.16). It compares the bond order of the consecutive bonds.

$$BOA(A) = \frac{1}{n_1} \sum_{i=1}^{n_1} \delta(A_{2i-1}, A_{2i}) - \frac{1}{n_2} \sum_{i=1}^{n_2} \delta(A_{2i}, A_{2i+1}) \quad (2.19)$$

Similarly to BLA, BOA is not suitable for molecules with an odd number of atoms. To avoid this problem, BOA(1) was developed.

$$BOA(A) = \frac{1}{2n} \sum_{i=1}^n |\delta(A_i, A_{i+1}) - \delta(A_{i+1}, A_{1+2})|, \quad (2.20)$$

Bond orders are much less dependent on the method and the basis set used.[34][35] Therefore, aromaticity indices based on bond order are not highly dependent on the level theory employed. Aromatic molecules give BOA values near zero, but as with BLA, molecules like cyclohexane present similar values.

Multi center indices: I_{ring} and MCI.

Multi center indices are an extension of the DI. They quantify the electron delocalization along a given ring.[36]

$$I_{ring}(A) = \sum_{i_1 i_2 \dots i_n}^{occ} S_{i_1 i_2}(A_1) S_{i_2 i_3}(A_2) \dots S_{i_n i_1}(A_n) \quad (2.21)$$

where the $S_{ij}(A)$ is the overlap of molecular orbitals i and j in the atom A . The higher the overlap between molecular orbitals, the higher the delocalization, and the higher will be the value of I_{ring} . Aromatic molecules will give large I_{ring} values. The greatest limitation of I_{ring} is that it can not be used in large cyclic molecules. This occurs because the value of I_{ring} is determined by the sum of the multiplication between many orbital overlaps, since the orbital overlap values are smaller than one, their multiplication leads to a decrease in the value of I_{ring} . Hence, the values of I_{ring} for large rings accumulate errors that are of the order of magnitude of I_{ring} . It is worth saying that rings of different size should be compared using $I_{ring}^{1/N}$, N being the number of atoms in the ring, rather than I_{ring} .

MCI is the sum of all of different delocalization patterns generated by permuting the position of all the atoms in the ring A . In other words, to consider the contribution of all the structures that arise from taking into account all possible permutations of the atomic positions in the ring

$$MCI(A) = \frac{1}{2n} \sum_{P(A)} \sum_{i_1 i_2 \dots i_n}^{occ} S_{i_1 i_2}(A_1) S_{i_2 i_3}(A_2) \dots S_{i_n i_1}(A_n) \quad (2.22)$$

MCI presents large values for aromatic molecules, and for antiaromatic molecules often gives negative values. Its limitation is the high computational cost, because it takes into account all permutations, increasing the computational cost and numerical error exponentially. This makes the computation of MCI very complex for rings that present more than twelve atoms. MCI and I_{ring} have been proved to be the most reliable indices of aromaticity.[37]

AV1245 and AVmin.

To solve the high cost of MCI, AV1245 was proposed.[38, 39] This electronic index is an arithmetic average of four-center MCI between relative positions 1-2 and 4-5, constructed from each five-atom fragment along the perimeter of a ring.

The advantages of AV1245 are that it does not need any reference value, does not produce huge precision errors, does not present any limitation with respect to the atoms or the geometries and the computational cost increases linearly with the amount of atoms. A disadvantage could be, that it represents the arithmetic average, that could hide some characteristics of the system. To solve this problem AVmin (gives the value of the section composed of 5 atoms with the

smallest MCI value), AVmax (gives the value of the section composed of 5 atoms with the biggest MCI value), and AVvar (display the variance of MCI values for sections along the ring) are used to have a better picture of the system. Another drawback is that, is not possible to study rings with less than 6 atoms.

Ring Current.

The ring current is an induced property that aromatic and antiaromatic molecules show when an external magnetic field is applied. The physical basis of this phenomenon is explained by the Ring Current Model (RCM), which compares a cyclically conjugated molecule to a circular wire, with π electrons being analogous to the freely moving electrons in the metal wire. Just as electrons in a wire loop move in a circular motion through the wire when an external magnetic field is applied, RCM assumes that cyclically delocalized electrons in the conjugated cyclic system also have circular motion. As it is described by Ampere's circuit law and Maxwell equations, this motion generates another magnetic field with opposite direction.[40]

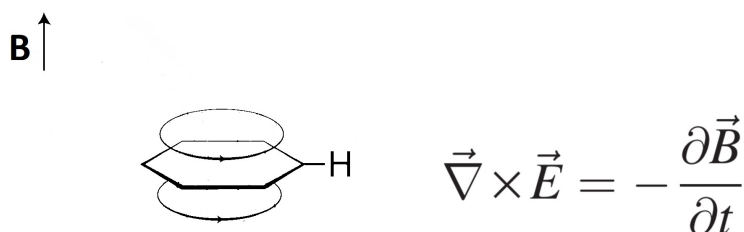


Figure 2.6: The induced current in a benzene molecule and the Faraday's differential equation.

In figure 2.6, $B\uparrow$ indicates a changing magnetic field in the direction perpendicular to the plane form by the atoms of benzene. Faraday's equation describes that when an external varying magnetic field ($\frac{\partial \vec{B}}{\partial t}$) generates a curl in the electric field ($\vec{\nabla} \times \vec{E}$) perpendicular to the magnetic field orientation. If there is a closed circuit with electric charges, these charges will feel the force of the induced electric field and will generate an electric current.

If the electrons in a molecule are very localized in bonds, they can not move freely along the ring and the induced current will be negligible. On the other hand, in molecules where the electrons are very delocalized, they can move with more freedom increasing the magnitude of the induced current.

The ring current will have a positive sign when the induced current has a diatropic nature (meaning that the current rotates clockwise), this is a characteristic of aromatic molecules. On the other hand, the ring current will have a negative sign when the induced current has a paratropic nature (meaning that the current rotates counterclockwise), this is a characteristic of antiaromatic molecules.

2.1.4.3 Magnetic Indices.

Magnetic indices evaluate the induced properties of molecules by measuring the response magnetic properties that appear when an external field is applied.

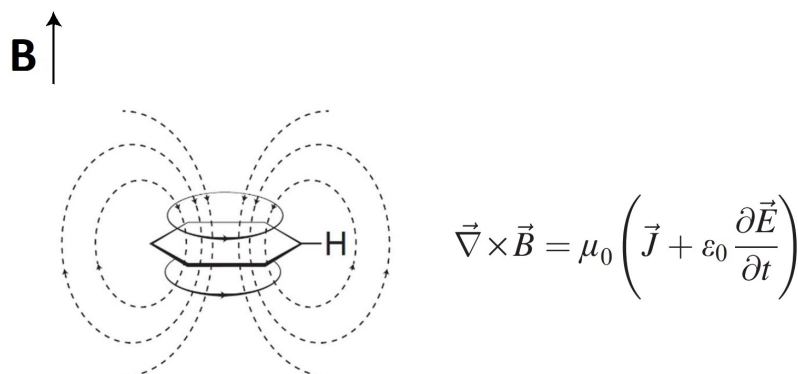


Figure 2.7: The induced magnetic in a benzene molecule and the Ampere's differential equation.

Ampere's law describe that a circuit with current (\vec{J}) will produce a perpendicular curl in the magnetic field ($\vec{\nabla} \times \vec{B}$).

Nucleus Independent Chemical Shift (NICS).

NICS is one of the most popular index that follows the magnetic criteria. NICS shows the magnetic response of a cyclic molecule to an external magnetic field.

NICS is a computational tool that evaluates aromaticity indirectly, by reporting the negative value of the absolute shielding computed on a point, thereby indicating the strength of the induced magnetic field at that point. There are different NICS depending on the point is calculated, the most common one is NICS(0), which is calculated at the center of the ring. But there is also NICS(1), wick is computed one angstrom above or below the ring plane. Some authors recommend to calculate NICS not at the geometric center but where the electron density is the lowest in the ring plane, on the Ring Critical Point.[41] This is, because in some types of molecules such as heterocyclic or metalaaromatic, RCP is usually displaced from the geometric ring center.

Negative values of NICS indicate a diatropic current, this is related with aromatic molecules. The more aromatic the molecule, the more negative the value for NICS will be. On the other hand, positive values of NICS indicate a paratropic current, this is related with antiaromatic molecules. The more positive the value of NICS, the more antiaromatic the molecule will be.[40]

2.2 Computational details.

2.2.1 Electronic structure calculations.

To perform the geometry optimization and frequency evaluations, we utilized Gaussian 16.[42] This program allowed us to obtain the wavefunction of the optimized geometry. For the calculation of both homocyclic and heterocyclic molecules, the CAM-B3LYP functional was employed.[43] However, for the annulenes, a variety of functionals were utilized including B3LYP,[44, 45] M06-2X,[46] and CAM-B3LYP as well as the Hartree-Fock (HF) method (with the unrestricted form used for triplet states of the molecules). For all calculation the basis aug-cc-pVDZ was used.[47]

2.2.2 QTAIM anylisis.

To proceed with the QTAIM analysis of the density function we used AIMALL 17.11.14B.[48] With this software, we obtained the critical points of the molecule and the atomic overlap matrices, S_{ij} .

2.2.3 Aromatic Indices.

2.2.3.1 Intrinsic properties indices.

To obtain the different intrinsic aromatic indices we used ESI.[49] This program uses the atomic overlap matrices to calculate the value of various indices.

2.2.3.2 Induced properties indices.

In order to obtain the value for NICS(0), first we need to obtain the Ring Critical Point (RCP) for that we used AIMALL. Then, the RCP Cartesian coordinates are added in the xyz Gaussian input as a ghost atoms, and finally, a NMR calculation is performed using the Gauge-Independent Atomic Orbital (GIAO) method.

To calculate the magnitude of the induced current we used AIMALL 19.10.12 [50] and ParaView.[51] To obtain the images of the current we follow the same procedure but the plane was placed over the molecule and parallel to the plane formed by the atoms of the molecule.

2.2.4 Studied molecules.

Benzene, cyclohexane, cyclohexene, cyclopropenylidene, cyclobutadiene, 1,3-cyclohexadiene, 1,4-cyclohexadiene, 0.7cyclohexatriene, 0.8cyclohexatriene, 0.9cyclohexatriene, pyridine, pyridazine, pyrimidine, pyrazine, triazine, $C_{12}H_{12}$ triplet state, $C_{14}H_{14}$, $C_{14}H_{14}$ planar, $C_{16}H_{16}$, and $C_{16}H_{16}$ triplet.

Results and Discussion

3.1 Carbocyclic compounds.

For a better understanding of how indices work, we will first discuss the values of the indices for various popular organic molecules.

3.1.1 Analysis of geometric indices.

Table 3.1: Values of geometric indices for different carbocyclic molecules. In the series of cyclohexatrienes, the number indicates the difference in the bond length between the double and single bonds, $\frac{R_{C=C}}{R_{C-C}}$.

Molecules	HOMA	BLA	BLA(1)
Benzene	0.992	0.000	0.000
Cyclohexane	-4.158	0.000	0.000
Cyclohexene	-2.882	0.048	0.066
Cyclopropenylidene	0.521	2.037	0.061
Cyclobutadiene	-3.719	0.237	0.237
1,3-Cyclohexadiene	-1.572	0.091	0.107
1,4-Cyclohexadiene	-1.528	0.000	0.114
0.7Cyclohexatriene	-50.534	0.622	0.622
0.8Cyclohexatriene	-31.266	0.408	0.408
0.9Cyclohexatriene	-18.024	0.204	0.204

The obtained values for the whole series of molecules align with the expected ones. For benzene, HOMA provides a value close to one. This occurs because HOMA uses the bond length C-C of benzene as a reference (see eq.(2.14)). Additionally, BLA and BLA(1) yield values close

to zero. This is because BLA compares the average of bond lengths of consecutive bonds in a ring (see eq.(2.16)), since benzene molecule's bonds are all equal, BLA gives values near zero.

For cyclohexane, HOMA shows a substantial negative value, -4.158, indicating the large deviation of its bond lengths from the reference one. On the other hand, for BLA and BLA(1) give the same value as benzene, this is because all bonds of the cyclohexane molecule are also equal. Hence, BLA alone is not a fully reliable aromaticity index.

For cyclohexene, HOMA yields a negative value pointing out a significant deviation of the bond lengths from the reference value. On the other hand, BLA and BLA(1) are small because of the double bond in the molecule.

In the case of cyclopropenylidene, HOMA provides a value of 0.521, indicating a noteworthy deviation from the reference one. BLA yields a value of 2.037 indicating also a considerable difference between the bond lengths, but if we look to BLA(1) it yields a value of 0.061, suggesting the opposite of what BLA indicates. As it is explained in the previous section, BLA was developed to study open chains, and later, BLA(1) was developed to study cyclic molecules. In this way, it is preferable to utilize BLA(1) when studying aromaticity.

In the case of cyclobutadiene, HOMA yields a significant negative value of -3.719 pointing to a large deviation from the reference bond distance. Also, BLA shows a value of 0.237, pointing out some disparity among the bond lengths.

For 1,3-cyclohexadiene and 1,4-cyclohexadiene, HOMA reveals negative values of -1.572 and -1.528, suggesting a substantial deviation of their bond lengths from the reference value. For 1,4-cyclohexadiene, BLA gives a value of 0.000, this problem was mentioned in the methodology, but if we look to BLA(1) we can see that both molecules give similar values, 0.107 and 0.114, indicating that not all bonds are equal.

For the series of cyclohexatriene, we can see that HOMA gives extremely large negative values. It is normal because we distorted externally the bond lengths, but we can also see that while the differences between the bond lengths decrease the values tend to 1. Also for the index BLA and BLA(1), as expected, the three molecules suggest a great bond alternance.

Based on the HOMA index, only benzene is characterized as aromatic. Cyclopropenylidene provides a value that raises doubt and does not allow us to ensure its aromatic nature. The remaining molecules exhibit notable deviations from the reference values, indicating their distinct characteristics. Notice that with HOMA is difficult to distinguish between nonaromatic and aromatic molecules.

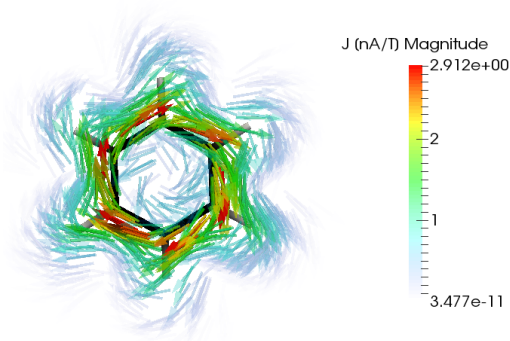
Based on the index BLA(1), only benzene and cyclohexane are categorized as aromatic. Cyclohexene and cyclopropenylidene give unclear values. The rest of the molecules are categorized as nonaromatic.

3.1.2 Analysis of electronic indices.

Table 3.2: Values of electronic indices for different carbocyclic molecules.

Molecules	FLU	BOA	BOA(1)	I_{ring}	MCI	AV1245	$ AV_{min} $	Current[nA/T]
Benzene	0.000	0.001	0.001	0.047	0.071	10.415	10.414	12.402
Cyclohexane	0.093	0.000	0.000	0.000	0.000	0.000	0.000	0.385
Cyclohexene	0.085	0.246	0.272	0.000	0.000	-0.024	0.088	2.126
Cyclopropenylidene	0.021	2.337	0.257	0.375	0.375	—	—	12.566
Cyclobutadiene	0.100	0.884	0.884	0.005	0.010	—	—	-81.794
1,3-Cyclohexadiene	0.069	0.446	0.469	0.001	0.002	0.098	0.147	-0.353
1,4-Cyclohexadiene	0.078	0.000	0.521	0.001	0.001	0.159	0.046	-0.336
0.7Cyclohexatriene	0.136	1.030	1.030	0.007	0.007	1.714	1.714	5.251
0.8Cyclohexatriene	0.085	0.814	0.814	0.012	0.013	2.914	2.911	5.064
0.9Cyclohexatriene	0.033	0.504	0.504	0.031	0.043	7.213	7.212	8.476

Benzene is the most known aromatic molecule. For benzene, FLU exhibits a value of 0.000, which is reasonably expected since FLU utilizes the electron delocalization of the benzene ring as a reference (see eq.2.18). Moreover, BOA and BOA(1) yield values close to zero, specifically 0.001, indicating that the electron delocalization among consecutive bonds is equally distributed, implying that all bonds possess the same bond order (see eq.2.20). I_{ring} reveals a substantial value of 0.047, suggesting a significant orbital overlap along the ring. Additionally, upon examining MCI, we observe a noticeable increase in its value, reaching 0.071 when compared to I_{ring} . This implies that the contributions from various delocalization patterns across the ring are also noteworthy. Analyzing the values of AV1245 and $|AV_{min}|$, 10.415 and 10.414, confirms the significant delocalization along the ring. Furthermore, upon considering the response to an external magnetic field, we find that the value of the induced ring current is 12.402 nA/T, which is remarkably significant. Looking to Figure 3.1, we can see a very clear clockwise rotation, consistent with the diatropic current expected in an aromatic molecule.

**Figure 3.1:** Benzene's induced current vector field over the molecule in a parallel plane.

In the case of cyclohexane, FLU exhibits a value of 0.093, indicating a significant deviation from the reference electron delocalization. Conversely, BOA and BOA(1) give 0.000, which is understandable since all bonds in cyclohexane are equal. When considering I_{ring} , AV1245, and $|AV_{min}|$, values of 0.000 are obtained, revealing that the delocalization along the ring is zero. Furthermore, upon analyzing MCI, a value of 0.000 is observed, indicating that the contribution of the across pattern is nonexistent. Additionally, when examining the response to the external magnetic field, the induced current is found to be 0.385 nA/T, which is negligible. Figure 3.2 shows that the response is small and the direction of the current is not that clear.

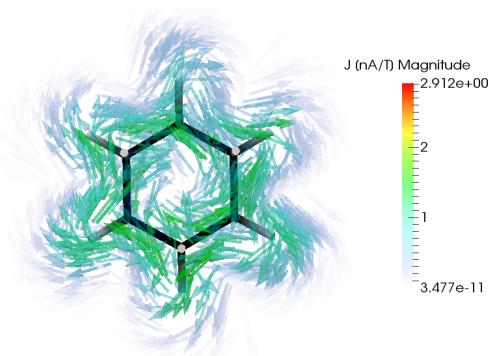


Figure 3.2: Cyclohexane's induced current vector field over the molecule in a parallel plane.

In the case of cyclohexene, FLU gives 0.085, indicating a different ESI (bond order) pattern than in benzene. Also, BOA and BOA(1) give a significant value, 0.246 and 0.272, showing that not all bonds are equal. If we examine the values of I_{ring} and MCI, 0.000 and 0.000, we see that the delocalization along and across the ring is null. Analyzing the values of AV1245 and $|AV_{min}|$, -0.024 and 0.088, pointing to negligible electron delocalization. If we explore the response of the molecule to the external magnetic field, we see that the magnitude of the induced current is small, 2.126 nA/T. Looking at Figure 3.3 shows that the induced current magnitude is not homogeneous along the ring, also the direction is not that clear.

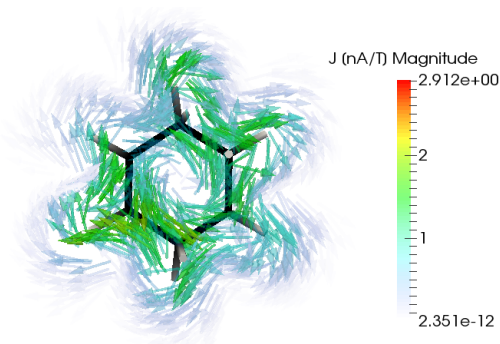


Figure 3.3: Cyclohexene's induced current vector field over the molecule in a parallel plane.

For cyclopropenylidene, FLU presents a value of 0.021, indicating a slight deviation from the reference electron delocalization. Furthermore, both BOA and BOA(1) yield values of 2.337 and 0.257, respectively. As explained in section 2.1.4.2, BOA has similar limitations as BLA, because of this BOA(1) was developed. This suggests an uneven distribution of electrons among the bonds. I_{ring} demonstrates a significant value of 0.375, pointing towards a substantial overlap of orbitals along the ring. Moreover, MCI also shows a value of 0.375, this is because there is no across-pattern on triangular molecules. Due to the ring's composition of fewer than six atoms, it is not possible to measure AV_{1245} and $|AV_{min}|$. Lastly, when observing the response to an external magnetic field, the induced ring current exhibits a substantial value of 12.566 nA/T. In Figure 3.4 we see a clear clockwise current.

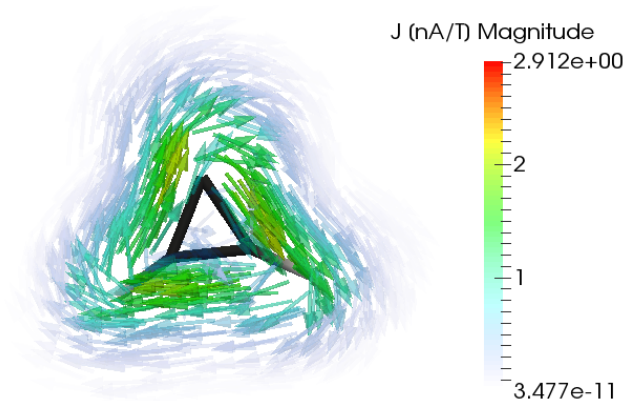


Figure 3.4: Cyclopropenylidene's induced current vector field over the molecule in a parallel plane.

For cyclobutadiene, FLU exhibits a value of 0.100, implying a considerable divergence from the reference electron delocalization. Moreover, BOA and BOA(1) give a result of 0.884, indicating that there is no equalization of the bond order along the molecule. I_{ring} shows a result of 0.005, indicating that orbitals are more localized. In addition, MCI registers a value of 0.010, suggesting that the contribution from distinct delocalization patterns across the ring are significant. Since the ring consists of fewer than six atoms, it is not possible to measure AV1245 and $|AV_{min}|$. Lastly, when examining the response to the external magnetic field, the induced ring current exhibits a substantial magnitude of -81.794 nA/T, the negative sign indicates the paratropic nature of the current which is related with the antiaromatic nature of the molecule. Figure 3.5 shows a very clear counterclockwise current.

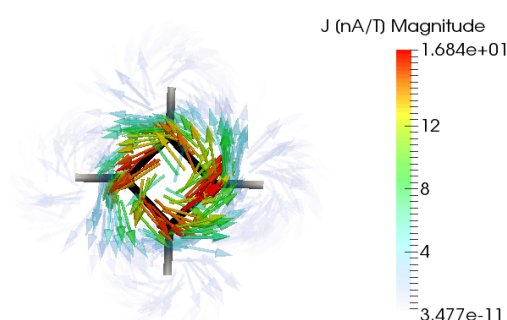


Figure 3.5: Cyclobutadiene's induced current vector over the molecule in a parallel plane.

For 1,3-cyclohexadiene and 1,4-cyclohexadiene, FLU exhibits similar values, respectively, 0.069 and 0.078, indicating a notorious divergence from the reference delocalization in benzene. If we look at BOA, 1,3-cyclohexadiene exhibits a value of 0.446, suggesting the presence of varying bond orders within the molecule. For 1,4-cyclohexadiene, BOA encounters a similar issue as BLA, as it yields a value of zero despite the presence of distinct bond orders in the molecule. In contrast, BOA(1) provides a value of 0.521, which is similar to that of 1,3-cyclohexadiene. Also for both molecules I_{ring} , MCI, AV1245, and $|AV_{min}|$ give similar small values, indicating a negligible delocalization along the ring. Both molecules show a similar response to the external magnetic field, respectively, -0.353 nA/T and -0.336 nA/T. These values are very small so we cannot consider the molecules as antiaromatic, furthermore if we look to Figure 3.6 the orientation of the current is not clear.

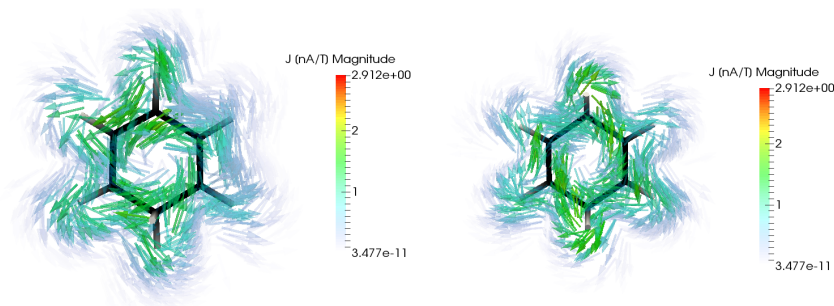


Figure 3.6: 1,3-Cyclohexadiene (left) and 1,4-cyclohexadiene (right) induced current vector field over the molecule in a parallel plane.

For the series of cyclohexatriene, we can see that while the geometry resembles that of the benzene, the values of FLU also tend to zero. BOA also shows a similar behavior. We can also see that while bond lengths tend to equalize, the overlap of the orbitals increases, resulting in large values of I_{ring} , MCI, AV_{1245} , and $|AV_{min}|$. Lastly the induced current does not behave as expected. We observe that 0.8cyclohexatriene yields a lower value of 5.064 nA/T compared to 0.7cyclohexatriene, which has a value of 5.251 nA/T. For 0.9cyclohexatriene, the current increases considerably yielding a value of 8.478 nA/T.

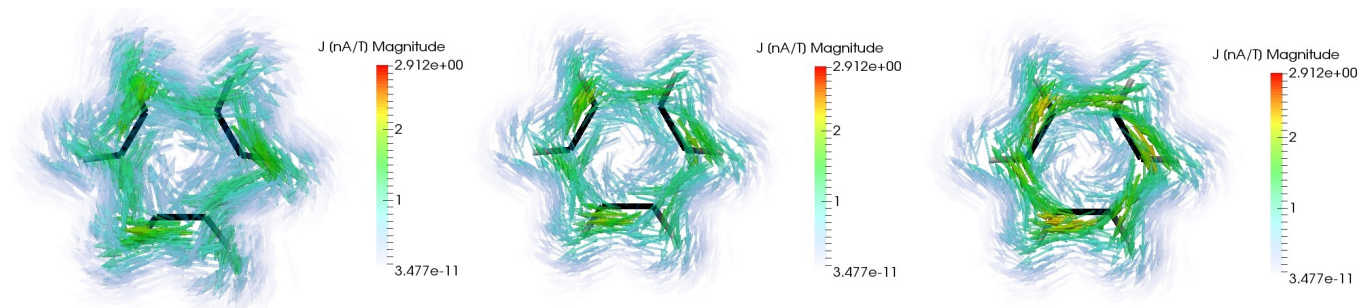


Figure 3.7: (Left) 0.7cyclohexatriene, (middle) 0.8cyclohexatriene, and (right) 0.9cyclohexatriene induced current vector field over the molecule in a parallel plane.

Now we can discuss whether the electronic indices order different molecules in the same way.

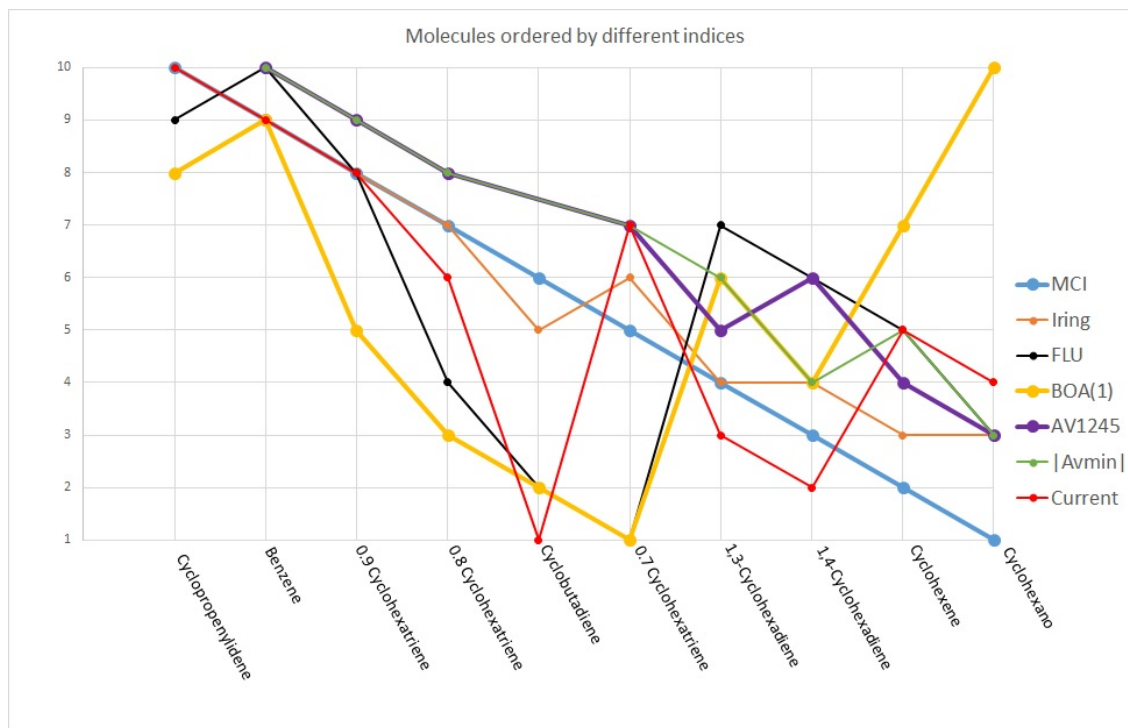


Figure 3.8: Molecules ordered by different electronic indices, from the most aromatic valued with 10 to the less aromatic valued with 1.

Clearly, we observe that different indices order in different ways the same molecules, primarily due to their distinct approaches determining aromaticity. FLU determines aromaticity by comparing values to reference standards. In contrast, BOA(1) assesses the bond order between consecutive bonds, which fails to distinguish cyclohexane as equally aromatic to benzene. On the other hand, I_{ring} , MCI, and AV1245 measure electron delocalization within the ring by evaluating the overlap of various orbitals, leading to a more similar ordering pattern. Additionally, current measures the responsive property of the molecule, allowing it to distinguish aromatic molecules from nonaromatic, but fails in the ordering of the cyclohexatriene series. We see that the current orders similar to I_{ring} in most of the cases.

3.1.3 Analysis of the magnetic index.

Table 3.3: Values of NICS(0) for different carbocyclic molecules.

Molecules	NICS(0)
Benzene	-7.219
Cyclohexane	-1.612
Cyclohexene	0.366
Cyclopropenylidene	-11.625
Cyclobutadiene	28.880
1,3-Cyclohexadiene	2.943
1,4-Cyclohexadiene	3.173
0.7Cyclohexatriene	-5.247
0.8Cyclohexatriene	-3.202
0.9Cyclohexatriene	-4.919

All results can be divided into two groups, the ones with positive signs and the ones with negative signs. The ones with negative values show a response expected from aromatic molecules. This is the case of benzene, cyclopropenylidene, and cyclohexatrienes, these three molecules provide a significant positive response, and can be categorized as aromatic based on this index. Even this said, NICS(0) does not correctly rank the series of cyclohexatrienes. We expected that 0.9cyclohexatriene would yield the most negative value, followed by 0.8cyclohexatriene, and 0.7cyclohexatriene that would produce the less negative value. Contrary to this, NICS(0) indicates that 0.7cyclohexatriene is the most aromatic, followed by 0.9cyclohexatriene, and the least aromatic is 0.8cyclohexatriene.

On the other hand, cyclohexane, due to the minimal response cannot be categorized as aromatic, but rather as very weakly aromatic. The positive sign is related with the response expected in antiaromatic compounds such as cyclobutadiene. This molecule shows a significant response and can be categorized as antiaromatic. On the other hand, molecules such as cyclohexene, 1,3-cyclohexadiene, and 1,4-cyclohexadiene show a small response and cannot be classified as antiaromatic.

3.2 Heterocyclic compounds.

Once seen how different indices work for simple compounds, let's apply them to more complex systems like heterocyclic compounds. In this section, we will discuss the values of different indices obtained for the series of pyridine, pyridazine, pyrimidine, pyrazine, and triazine. All these molecules are similar to benzene but have one or more carbons substituted with nitrogen.

3.2.1 Analysis of geometric indices.

Table 3.4: Values of geometric indices for different heterocyclic compounds.

Molecules	HOMA	BLA	BLA(1)
Benzene	0.992	0.000	0.000
Pyridine	0.998	0.000	0.020
Pyridazine	0.986	0.025	0.029
Pyrimidine	0.997	0.000	0.041
Pyrazine	1.000	0.000	0.019
Triazine	1.000	0.000	0.000

We can see that all molecules show very similar values. For HOMA, the largest deviation is shown by pyridazine, but the difference is not significant. Based on HOMA, all these molecules are categorized as aromatic.

Furthermore, according to BLA and BLA(1), all molecules are classified as aromatic, although certain molecules such as pyridine, pyridazine, pyrimidine, and pyrazine exhibit a slight deviation.

3.2.2 Analysis of electronic indices.

Table 3.5: Values of electronic indices for different heterocyclic compounds.

Molecules	FLU	BOA	BOA(1)	I_{ring}	MCI	AV1245	$ AV_{min} $	Current
Benzene	0.000	0.001	0.001	0.047	0.071	10.415	10.414	12.402
Pyridine	0.004	0.000	0.031	0.044	0.066	9.855	9.570	11.563
Pyridazine	0.007	0.021	0.116	0.045	0.066	9.442	8.641	11.255
Pyrimidine	0.009	0.000	0.010	0.041	0.062	10.881	10.409	11.273
Pyrazine	0.004	0.000	0.036	0.042	0.062	9.143	7.701	10.753
Triazine	0.002	0.000	0.000	0.040	0.059	8.366	8.366	9.984

The index FLU shows very small values for all molecules, indicating that all molecules show similar delocalization values to the reference ones.

On the other hand, for some molecules, BOA and BOA(1) show huge discrepancies. As mentioned earlier, it is more appropriate to utilize BOA(1) for aromatic molecules. For pyridine, pyrimidine, pyrazine, and triazine, BOA(1) gives small values indicating that these molecules are aromatic. But for pyridazine, BOA(1) shows a noteworthy value, pointing out that there are bonds with slightly different bond orders along the ring. However, still they can be considered as aromatic.

For I_{ring} and MCI, all molecules show significant values, indicating that all molecules share a great orbital overlap therefore, pointing out the aromatic nature of the molecules.

For AV1245 and $|AV_{min}|$, all molecules give large values, indicating a considerable delocalization along the ring. If we look at $|AV_{min}|$, we can see that pyridazine and pyrazine show a slight deviation from AV1245, indicating that the delocalization is not completely uniform along the ring. But these deviations are negligible. All values indicate that these molecules are aromatic.

Analyzing the induced current, all molecules exhibit a great positive response to the external magnetic field, indicating their aromatic nature. We can confirm this by looking at Figure 3.9, where all molecules show a clockwise current rotation. It is manifest that the substitution of carbon for nitrogen decreases the response.

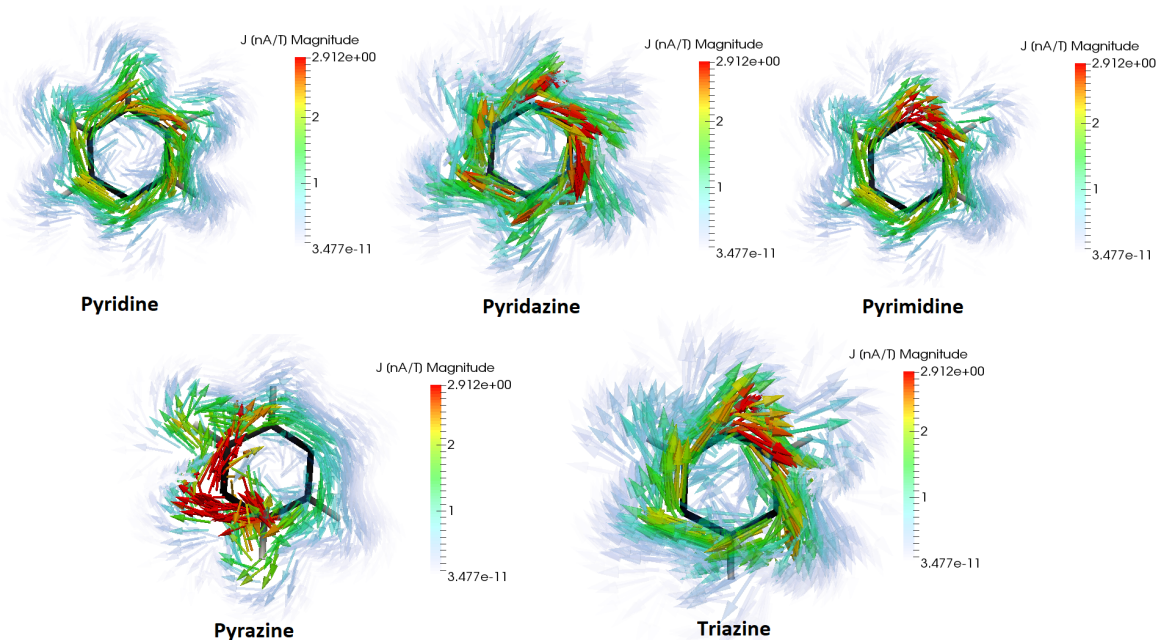


Figure 3.9: Heterocyclic molecules induced current vector field over the molecule in the z plane.

3.2.3 Analysis of the magnetic index.

Table 3.6: Values of NICS(0) for different carbocyclic molecules.

Molecules	NICS(0)
Benzene	-7.219
Pyridine	-6.214
Pyridazine	-4.613
Pyrimidine	-4.571
Pyrazine	-4.570
Triazine	-3.470

We can see that the substitution of nitrogen for carbon decreases significantly the magnetic response. With these response, we can consider molecules as aromatic. For the molecules with two nitrogens, when the distance between two nitrogens increases the magnetic response decreases.

3.3 Annulenes.

In the previous section we have used the same functional, CAM-B3LYP, to obtain the optimized geometry and to evaluate the aromaticity indices. This is because for small molecules the value of the indices is not affected significantly by the functional used. On the other hand, in this section, we will explore diverse index values obtained using different functionals for various annulenes with twelve or more carbon atoms in the ring. This is because the most stable conformation, and its corresponding wavefunction, of annulenes shows an important dependency on the computational method used,[52] which is also reflected in the aromaticity indices values.

3.3.1 Analysis of geometric indices.

Table 3.7: Geometric indices values for different annulenes.

	HOMA	BLA(1)
<u>C₁₂H₁₂ triplet</u>		
UHF	0.238	0.068
UB3LYP	0.854	0.008
UCAM-B3LYP	0.633	0.052
UM06-2X	0.803	0.030
<u>C₁₄H₁₄</u>		
HF	-0.196	0.132
B3LYP	0.917	0.008
CAM-B3LYP	0.477	0.085
M06-2X	0.495	0.082
<u>C₁₄H₁₄ planar</u>		
CAM-B3LYP	0.962	0.007
M06-2X	0.953	0.007
<u>C₁₆H₁₆</u>		
HF	-0.257	0.136
B3LYP	0.338	0.093
CAM-B3LYP	0.162	0.109
M06-2X	0.162	0.108
<u>C₁₆H₁₆ triplet state</u>		
UHF	0.966	0.006
UB3LYP	0.901	0.010
UCAM-B3LYP	0.699	0.054
UM06-2X	0.765	0.044

C₁₂H₁₂ triplet.

We observe that depending on the used functional HOMA and BLA(1) give different values. Regarding HOMA, this variation is significant to determine whether the molecule is aromatic or not. When using UB3LYP and UM06-2X functionals, the molecule exhibits a slight deviation from the reference bond length, but can be classified as aromatic. However, when employing UCAM-B3LYP, HOMA value is clearly reduced, indicating a less aromatic molecule. In the case of UHF, the calculated HOMA value suggests that the molecule is nonaromatic. On the other hand, the variation in values of BLA(1) is not that significant. All values are relatively small, which points to bond length equalization, a signature of aromatic molecules.

C₁₄H₁₄ singlet.

In this case, only B3LYP categorizes C₁₄H₁₄ as aromatic based on HOMA and BLA(1) indices, which presents a C_{2h} symmetry. CAM-B3LYP and M06-2X yield similar values for both indices. For HOMA, both functionals indicate a significant deviation of the bond lengths from the reference values, while for BLA(1), the values obtained are larger than those obtained from B3LYP. However, when HF is used, the values obtained for HOMA indicate a considerable deviation of the bond lengths from the reference values, and for BLA(1), it suggests the presence of significant bond length alternation.

C₁₄H₁₄ Planar geometry.

In this case, CAM-B3LYP and M06-2X functionals give very similar values for both indices. The values yield for HOMA and BLA(1) point out that the geometric properties of the molecule are consistent with the expected ones in aromatic molecules. These conformations correspond to transition states with C_{2h} symmetry, that through a small energy barrier connects the two C_s-symmetry minima.

C₁₆H₁₆ singlet.

For this molecule, the values for HOMA and BLA(1) using the different density functionals indicate that the molecule is not aromatic. With HF, both HOMA and BLA(1) provide the most significant deviations found so far from aromatic molecules. The values obtained with CAM-B3LYP and M06-2X are similar for both indices, pointing out that the geometric properties of the molecules are very different from the expected ones in an aromatic molecule. B3LYP is the one that gives the largest HOMA and the lowest BLA(1), but we cannot consider the molecule aromatic.

C₁₆H₁₆ triplet.

HF and B3LYP give aromatic values for C₁₆H₁₆ according to HOMA and BLA(1). With CAM-B3LYP and M062X the values for HOMA and BLA(1) indicate a reduction in the aromaticity of the molecule.

3.3.2 Analysis of electronic indices.**Table 3.8:** Electronic indices values for different annulenes.

	FLU	BOA(1)	$ AV_{min} $	Current [nA/T]
<u>C₁₂H₁₂ triplet</u>				
UHF	0.023	0.190	0.293	0.768
UB3LYP	0.002	0.018	0.471	16.948
UCAM-B3LYP	0.014	0.174	0.257	7.821
UM06-2X	0.006	0.106	0.601	11.376
<u>C₁₄H₁₄</u>				
HF	0.048	0.613	0.505	3.434
B3LYP	0.001	0.010	4.146	21.019
CAM-B3LYP	0.024	0.426	1.916	9.714
M06-2X	0.022	0.412	2.022	11.777
<u>C₁₄H₁₄ planar</u>				
CAM-B3LYP	0.001	0.007	4.215	21.238
M06-2X	0.001	0.007	4.192	21.223
<u>C₁₆H₁₆</u>				
HF	0.051	0.633	0.245	-1.069
B3LYP	0.028	0.463	0.271	-13.341
CAM-B3LYP	0.038	0.543	0.171	-5.107
M06-2X	0.038	0.539	0.584	-3.806
<u>C₁₆H₁₆ triplet</u>				
UHF	0.003	0.042	1.057	23.067
UB3LYP	0.002	0.035	1.156	22.808
UCAM-B3LYP	0.015	0.184	0.374	7.785
UM06-2X	0.010	0.149	0.810	14.709

C₁₂H₁₂ triplet.

We can see a great variation in the values for all indices. The FLU index gives values expected in an aromatic molecule when the functionals UB3LYP, UCAM-B3LYP, and UM06-2X are use. With UHF, the obtained value is quite larger and we cannot consider it as aromatic. If we analyze the values of BOA(1), only using the functional UB3LYP can be considered as aromatic, with all the other functional BOA(1) categorize C₁₂H₁₂ triplet as nonaromatic . If we look to $|AV_{min}|$ all values are very small, any functional indicates that the molecule is not aromatic.

If we consider the response property, the values of the induced current vary significantly depending on the functional used. The obtained value for the induced current using UHF is very small, which corresponds to response expected in a nonaromatic molecule. On the other hand, when UB3LYP and UM06-2X functionals are used, the value obtained for the induced current resembles to the ones expected in aromatic molecules. When the induced current is measured using UCAM-B3LYP, the obtained value is ambiguous. It is not small enough to consider it nonaromatic, yet it is not large enough to indicate an aromatic response.

C₁₄H₁₄.

For FLU, only B3LYP density functional categorizes the molecule as aromatic, with the other functionals the obtained values for FLU are larger and cannot be considered as aromatic. For BOA(1), only B3LYP gives a value expected in aromatic molecules. All the other molecules present large values to consider them as aromatic. In the case of |AVmin|, only B3LYP presents a significant value to consider it as aromatic, CAM-B3LYP and M06-2X give smaller and inconclusive values; all functionals provide small values of |AVmin| to categorize them as aromatic.

For C₁₄H₁₄ also, the values of the induced current vary a lot depending on the used functional. With B3LYP, CAM-B3LYP, and M06-2X the obtained values are large and similar to the ones expected in aromatic molecules. On the other hand, the obtained current using HF is not large enough to be considered as an aromatic response.

C₁₄H₁₄ planar.

In this case, CAM-B3LYP and M06-2X give identical values for FLU and BOA(1), these values are very small, pointing out the aromatic nature of the molecule, also for |AVmin| both functionals provide similar values. It is important to keep in mind that the conformations correspond to transition states with C_{2h} symmetry, analogous of the geometry obtained using B3LYP.

Looking to the response property, the values of the induced current are very large. In this case all indices point that the molecule is aromatic.

C₁₆H₁₆.

For FLU, all functionals yield large values indicating that the electron delocalization is smaller than the expected one in aromatic molecules. A similar behavior is also observed for BOA(1) and |AVmin|.

Looking to the values of the induced current, all methods give negative values, indicating that the direction of the current is counterclockwise. When HF, CAM-B3LYP, and M062X are used to calculate the current, the response of the molecule is modest, and cannot be considered as antiaromatic. Conversely, when the current is calculated using B3LYP the magnitude of the current is significant and it points out the antiaromatic nature of the molecule.

C₁₆H₁₆ triplet state.

Analyzing FLU, UHF and UB3LYP give very small values, similar to expected ones in aromatic molecules; UM06-2X presents a larger value indicating a lower aromaticity. On the other hand, with UCAM-B3LYP FLU yields a significantly large and inconclusive value. For BOA(1), UHF and UB3LYP show similar values to the expected ones in aromatic molecules. The values for BOA(1) obtained using UCAM-B3LYP and UM06-2X are large and point out that the molecule is not aromatic. Looking to the values of $|AV_{min}|$, it's manifest that the values obtained with different functionals are very small to consider them as aromatic.

The values obtained for the response property vary largely depending on the used functional. The calculated induced current using UHF, B3LYP, and UM06-2X indicate that the response is similar to the one expected in an aromatic molecule. On the other hand, with UCAM-B3LYP the magnitude of the induced current is smaller and points out that the molecule is weakly aromatic.

3.3.3 Analysis of the magnetic index.

Table 3.9: NICS(0) magnetic index value for various annulenes with different density functionals.

singlet molecules	C ₁₄ H ₁₄	C ₁₄ H ₁₄ planar	C ₁₆ H ₁₆
<u>functionals</u>			
HF	-1.318	—	1.622
B3LYP	-12.617	—	10.253
CAM-B3LYP	-5.955	-14.543	4.527
M06-2X	-9.740	-14.580	5.088
triplet molecules	C ₁₂ H ₁₂	C ₁₆ H ₁₆	
<u>functionals</u>			
UHF	-1.486	-13.507	
UB3LYP	-14.359	-13.529	
UCAM-B3LYP	-6.421	-4.283	
UM06-2X	-6.754	-7.516	

C₁₂H₁₂ triplet.

Analyzing the magnetic response of the molecule using different methods, we see that all values are negative, pointing out the diatropic nature of the current a characteristic shared by aromatic molecules. The value for NICS(0) obtained with HF is much smaller than the expected one in aromatic molecule. With CAM-B3LYP and M06-2X the values that NICS(0) yield are similar to the expected ones in aromatic molecules. On the other hand, we see that B3LYP gives a large response.

C₁₄H₁₄.

We observe a comparable pattern to that of the previous molecule, where only UHF is obtained a magnetic response not comparable to a response expected in aromatic molecules, UCAM-B3LYP and UM06-2X give similar values to expected in aromatic molecules and with UB3LYP NICS(0) yields a huge value.

C₁₄H₁₄ transition state.

In this case, with both functionals, we obtained very similar values. We see that the magnetic response is very large, indicating the aromatic nature of the molecule.

C₁₆H₁₆.

In this case, all values are positive, pointing out the paratropic nature of the current a characteristic shared by antiaromatic molecules. With HF the value obtained for NICS(0) is not large enough to consider an antiaromatic response. With CAM-B3LYP and M06-2X the obtained values are unclear. The value obtained for NICS(0) using B3LYP is large, indicating that the magnetic response to the external field is similar to the expected one in an antiaromatic molecule.

C₁₆H₁₆ triplet state.

For this case, UHF and UB3LYP give very similar magnetic response. Both functionals give a very large negative value. The functional UM06-2X shows a smaller response comparable to the expected one in aromatic molecule. On the other hand, with UCAM-B3LYP NICS(0) yields a smaller value but still can be considered as an aromatic response.

3.4 Discussion.

Table 3.10: A summary of the homocyclic molecules and how they are classified by different indices. A (aromatic), NA (nonaromatic), and AA (antiaromatic).

Molecules	HOMA	BLA(1)	FLU	BOA(1)	I_{ring}	MCI	AV1245	AV_{min}	Current	NICS(0)
Benzene	A	A	A	A	A	A	A	A	A	A
Cyclohexane	NA	A	NA	A	NA	NA	NA	NA	NA	NA
Cyclohexene	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Cyclopropenylidene	unclear	NA	unclear	NA	A	A	—	—	A	A
Cyclobutadiene	NA	NA	NA	NA	NA	NA	—	—	AA	AA
1,3-Cyclohexadiene	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
1,4-Cyclohexadiene	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
0,7Cyclohexatriene	NA	NA	NA	NA	NA	NA	NA	unclear	unclear	unclear
0,8Cyclohexatriene	NA	NA	NA	NA	NA	NA	NA	NA	unclear	NA
0,9Cyclohexatriene	NA	NA	unclear	NA	unclear	A	unclear	unclear	unclear	unclear

Table 3.11: A summary of the heterocyclic molecules and how they are classified by different indices. A (aromatic), NA (nonaromatic), and AA (antiaromatic).

Molecules	HOMA	BLA(1)	FLU	BOA(1)	I_{ring}	MCI	AV1245	AV_{min}	Current	NICS(0)
Benzene	A	A	A	A	A	A	A	A	A	A
Pyridine	A	A	A	A	A	A	A	A	A	A
Pyridazine	A	A	A	A	A	A	A	A	A	A
Pyrimidine	A	A	A	A	A	A	A	A	A	A
Pyrazine	A	A	A	A	A	A	A	A	A	A
Triazine	A	A	A	A	A	A	A	A	A	A

Table 3.12: A summary of the annulene molecules and how they are classified by different indices and functionals. A (aromatic), NA (nonaromatic), and AA (antiaromatic).

	HOMA	BLA(1)	FLU	BOA(1)	AV_{min}	Current	NICS(0)
<u>C₁₂H₁₂ triplet</u>							
UHF	NA	NA	NA	NA	NA	NA	NA
UB3LYP	A	A	A	A	NA	A	A
UCAM-B3LYP	NA	NA	A	NA	NA	unclear	A
UM06-2X	A	A	A	NA	NA	A	A
<u>C₁₄H₁₄</u>							
HF	NA	NA	NA	NA	NA	NA	NA
B3LYP	A	A	A	A	A	A	A
CAM-B3LYP	NA	NA	NA	NA	unclear	A	A
M06-2X	NA	NA	NA	NA	unclear	A	A
<u>C₁₄H₁₄ transition state</u>							
CAM-B3LYP	A	A	A	A	NA	A	A
M06-2X	A	A	A	A	NA	A	A
<u>C₁₆H₁₆</u>							
HF	NA	NA	NA	NA	NA	NA	NA
B3LYP	NA	NA	NA	NA	NA	AA	AA
CAM-B3LYP	NA	NA	NA	NA	NA	NA	unclear
M06-2X	NA	NA	NA	NA	NA	NA	unclear
<u>C₁₆H₁₆ triplet state</u>							
UHF	A	A	A	A	NA	A	A
UB3LYP	A	A	A	A	NA	A	A
UCAM-B3LYP	unclear	unclear	unclear	NA	NA	unclear	A
UM06-2X	A	A	A	NA	NA	A	A

3.4.1 Discussion about the functionals.

In the DFT methods, the exchange-correlation energy functional is approximated in various manners. For instance, some functionals introduce more or less HF% exact exchange. This might change for some molecules that are susceptible to the so called delocalization error.

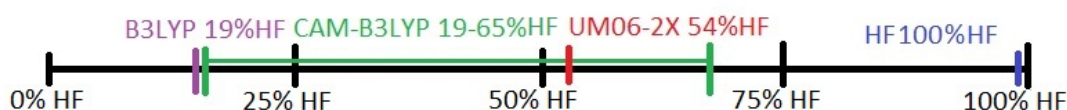


Figure 3.10: How much %HF exchange introduce the different functionals.

It is manifest that HF tends to categorize large annulenes as nonaromatic because it introduces a 100% HF exchange, due to this, it overestimates the electron localization.^[52] On the opposite side, B3LYP tends to categorize annulenes as aromatics, this is because it approximates the exchange-correlation introducing only 19% of HF exchange, overestimating the electron delocalization. The correct description lies somewhere in between HF and the delocalized picture provided by some density functional approximations. CAM-B3LYP and M06-2X show similar values for the different indices, both giving values between HF and B3LYP, because they approximate the exchange-correlation introducing 19-65% HF and 54% HF exchange, respectively. It is worth mentioning that for electron delocalization is more important to introduce HF exchange at long ranges than at short ranges. CAM-B3LYP increases the %HF exchange with increasing ranges, employing 65% at long ranges. For this reason, CAM-B3LYP and M06-2X tend to suffer less from electron delocalization errors than B3LYP. This is the reason why CAM-B3LYP and M06-2X functionals are suggested to study aromaticity in large cycles.

3.5 Intrinsic electronic properties and induced electronic properties.

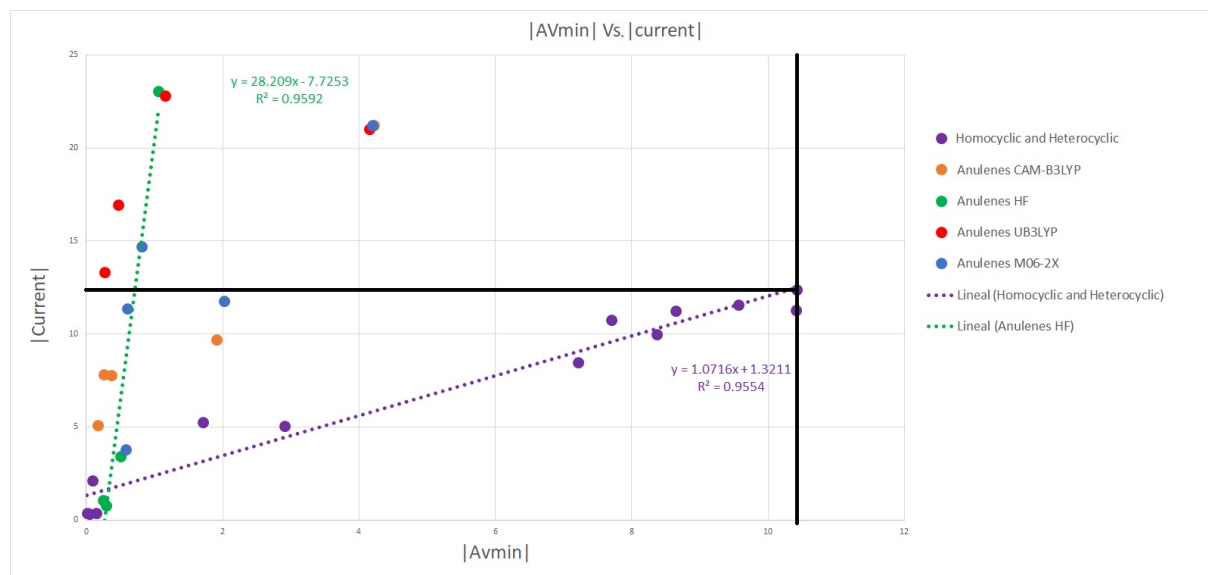


Figure 3.11: Correlation between $|current|$ and $|AV_{min}|$ for different molecules. The black lines indicate the values of benzene for $|AV_{min}|$ and the magnitude of the induced current.

In Figure 3.11, we can see the values of AV_{min} (an index that measures an intrinsic property) and the magnitude of the induced current (a response property) for different molecules.

In purple, we can see the series of homocyclic and heterocyclic molecules. We see that the correlation between both indices is considerable. We can see that molecules that show small values for AV_{min} , indicating a nonaromatic character, also show a small response to the external magnetic field, a behavior expected in a nonaromatic molecule. Conversely, molecules that show large values of AV_{min} , indicating their aromatic character, the shown response also agrees with their aromatic nature.

All the other points correspond to annulenes calculated using various functionals. It is manifest that here we do not see the same behaviour as in the case of homocyclic and heterocyclic molecules. The black lines show the values of AV_{min} and the induced current for benzene. If we look to AV_{min} (intrinsic property) we observe that benzene is depicted as the most aromatic molecule. However, when we examine the response property, we find that certain annulenes exhibit a greater response than benzene. For many cases, even if they show small values of AV_{min} , indicating that in an unperturbed state they exhibit a nonaromatic character, when we look to their response to the external magnetic field, we see that the magnitude of the induced current is similar or even greater than the one expected for aromatic molecules.

Conclusions / Ondorioak

This study provides further support to previous studies,[26, 17, 37] which pointed out the need to employ more than one aromaticity index to ensure the aromatic character of the molecule. This is due to the multidimensional character of aromaticity.[22] This means, that even if a molecule's geometric properties suggest that it is not aromatic, its electronic properties can suggest the opposite. This feature of aromaticity makes the classification of molecules with large rings challenging. The results also show that even the indices that measure the same properties are not consistent when it comes to ranking the molecules according to their aromaticity.

The analysis of the heterocyclic molecules shows that the substitution of a carbon atom by a nitrogen atom affects considerably to the response properties such as NICS(0) and the current decreasing their magnitude.

In large molecules, such as those discussed in section 3.3 on annulenes, the values obtained for different indices are highly dependent on the chosen functional, often resulting in contradictory conclusions regarding the nature of the molecule. We conclude that B3LYP overestimates the aromatic character of the molecule and HF underestimates it.

The main conclusion of this work is that in large molecules the indices that measure intrinsic properties and those that measure induced (response) properties can lead to a contradictory conclusion. This points out that a molecule may not exhibit aromatic properties in the absence of external perturbations, but when an external magnetic field is applied and the response properties are measured, they can be similar to the expected ones in aromatic molecules. This puts in doubt the validity of the NMR methodology to classify molecule as aromatic or not, because it is possible that the applied magnetic field can change the properties of the molecule leading to a conclusion that does not match with the nature of the molecule in the absence of an external perturbation.

The future goal of this project is to modify previously developed indices to study intrinsic properties, such as HOMA, BLA(1), BOA(1), FLU, I_{ring} , MCI, and AV1245 in order to measure the same properties under the perturbation of a magnetic field. This will allow us to get a better

understanding of how do response properties work and will give us a deeper notion of the phenomenon of aromaticity.

Ikerketa honek oinarri sendoagoa ematen die aurretik burututako ikerketei,[26, 17, 37] molekularen izaera aromatikoa ziurtatzeko indize bat baino gehiagoren beharrari. Hau aromatizitateren izaera multidimentsionalaren ondorioa da.[22]. Honek esan nahi duena da, molekularen ezaugarri geometrikoek naiz eta ez erakutsi izaera aromatikoa, bere propietate elektronikoen alderantzizkoa adierazi dezaketela. Aromatizitatearen ezaugarri honek molekulen sailkapena zailtzen du. Emaitzek ere adierazten dute, naiz eta indize ezberdinek propietate bera neurtu ez direla gai modu berean molekulak sailkatzeko beren aromatizitatearen arabera.

Molekula heteroziklikoen azterketak erakusten du karbonoa nitrogenoaz ordezkatzek duen nabarmenezko eragina erantzun propietateetan, adibidez NICS(0) eta korrontearen magnitudea, nabarmen murrizten dela ikusi da.

Molekula handietan, 3.3 atalean agertzen diren bezalakoetan, indize ezberdinekin lortutako baloreak menpekotasun handia erakusten dute, askotan molekulak beren naturaren arabera sailkatzeko orduan aurkako konklusioetara iritxiz. Honetaz gain, B3LYP funtzionalak molekularen izaera aromatikoa exageratzen du eta HF berriz gutxiesten du.

Ikerketaren ondorio nagusia da, molekula handietan propietate intrintsikoak aztertzen dituzten indizeak eta induzitutako (erantzun) propietateak aztertzen dituzten indizeak aurkako konklusioak eman ditzaketela. Honek esan nahi du, nahiz eta molekula batek ez aurkeztu propietate aromatikorik ohiko baldintzetan (kanpo perturbaziorik gabe), posible dela kanpo eremu magnetiko bat ezartzean eta erantzun propietateak neurtzean, hauek bat etortzea izaera aromatikoa duen molekula batekin. Honek zalantzan jartzen du EMN bidez lortutako emaitzak molekulei izaera aromatikoa esleitzerako orduan, izan ere posible bait da EMNan aplikatutako kanpo magnetikoak molekularen propietateak aldatzea, metodo honen bidez esleitutako ezaugarriak eta laborategian erakusten dituen ezaugarriak bat ez etorri.

Proiektu honen hurrengo helburua, propietate intrintsekoak aztertzeo, HOMA, BLA(1), BOA(1), FLU, *I_{ring}*, MCI eta AV1245, garatu diren indizeak eraldatzea da, perturbatutako molekuletan propietate berdinak neurtzeko. Honek ahalbidetuko digu ezagutza hobea izaera erantzun propietateen portaerari buruz eta aromatizitate fenomenoari buruz.

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