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Exploring Chemical Space with Alchemical Derivatives:
Alchemical Transformations of H through Ar and its Ions
as a Proof of Concept.

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Abstract

Alchemical derivatives have been used in recent years to obtain essentially *qualitative* information about the energetics of transformations they describe, e.g., relative stabilities of a series of isomers, following an approach in which the total number of electrons is unchanged during the changes in nuclear charge, the alchemical change. Often the resulting target system bears a different charge than the reference molecule, in this way sometimes deviating the navigation road through chemical compound space. Within the context of Conceptual DFT, in which this ansatz is embedded, we present in this work, the first systematic approach for combining changes in both the number of electrons and the nuclear charge so that for example one can navigate from one neutral atom to another. The case of moving from one neutral atom to its neighbouring neutral atom in the Periodic Table and its extension to include the direct evaluation of its first and second Ionization Energies and Electron Affinities is offered as a proof of concept. A general formalism is presented both for transformations involving both changes in Z or N only or combined Parr's parabolic approach for the N dependence is explicitly considered as a particular case as is the ensemble description at the 0K limit.

Based on our previous work the B3LYP functional in its extended CAMB3LYP version combined with the aug-cc-pCCQZ basis, stressing the importance of tight functions for the core correlation, has been chosen to perform the Coupled Perturbed Kohn Sham calculations of the alchemical derivatives. The analysis of the derivatives (alchemical potential, hardness, stiffness) shows no periodicity as opposed to their N – congeners; the monotonous behaviour of the alchemical potential is scrutinised and is shown to be in line with previous results based on the $1/Z$ expansion. The order of magnitude analysis of the successive derivatives preludes that convergence in the transmutation energy calculations might be reached at third order.

These results are injected in two strategies for obtaining transmutation energies from neutral atoms to a neighbouring neutral atom: one road, the diagonal one, moving along the $Z=N$ diagonal, the other one walking along a pure alchemical road after ionisation of or electron attachment to the reference atom. When comparing exact versus alchemical transmutation energies two conclusions emerge: the anionic road is much less successful than the cationic road, with comparable results for the parabolic approach, the 0K limit and the direct road and within the cationic road a remarkable increase in the quality of the results emerges when passing from the parabolic model to the 0K limit and the indirect road.

The transmutation energy for the cationic pathway even displays chemical accuracy (errors less than 1 kcal/mol for the complete set of atoms from He to Ar) when the procedure is carried at third order in ΔZ for which the perturbation series indeed converges. From the information theory point of view (similarity analysis of the electronic density distributions and information discrimination analysis) no fundamental reason pops up for the difference in quality between the cationic and anionic paths. The difficulties inherent to an accurate description of the anion and its derivatives are responsible for the shortcomings along the anionic paths. The issue of the chemical accuracy versus the treatment within a spin non-polarized version of conceptual DFT is analysed and leads to the conclusion that the main group atoms considered are free from changes in orbital energy sequences leading to different spin states between the intermediate cation or anion and the target atom as opposed to transition metal elements where this issue may lead to significant shortcomings. As a direct application of the formalism, the first (and second) Ionization Energies and Electron Affinities are evaluated showing an almost perfect agreement with the direct evaluation and a difference with

1 experimental values is less than 0.5 eV for the Ionization Energies. For the first Electron Affinity
2 reasonable agreement is obtained with the sometimes hard to evaluate direct and experimental values
3 whereas the second Electron Affinities for atoms with stable mono-anions show a remarkable
4 agreement with the literature data on the resonance states of these unstable systems.

5 Besides proof of concept that with the information content of an atom one can get accurate energetics
6 of its neighbours (proviso this orbital energy sequence issue), the present results are indicative that
7 alchemical derivatives are on the road to yield *quantitative* information when navigating through
8 Chemical Compound Space.

I.Introduction

Chemists continuously try to expand their exploration of Chemical Compound Space (CCS), the space populated by all imaginable chemicals with natural nuclear charges and realistic interatomic distances for which chemical interactions exist¹⁻³ in order to “detect” stable molecules with interesting /optimal properties. Needless to say that, for experimentalists, navigating through Chemical Space is costly to be it alone for the investment of time when facing many synthetic problems. Theoretical and Computational Chemists can be of great help in this endeavour by undertaking a similar journey *in silico*. However, even for them exploring Chemical Space, at a moderate *ab initio* (wavefunction or DFT) level, or even with semi-empirical brute force techniques dramatically increases in computing time and storage requirement with the increasing number of atoms and complexity of the structures characterising the subspace under investigation. Consequently, the search for efficient shortening of the navigation time through CCS is an important challenge for theoretical and computational chemists as they could and should be involved in this journey as computational costs are still way below those of synthetic work. The interplay between theorists and experimentalists is at stake where, ideally the experience of the synthetic chemists should be introduced in the navigation codes, eliminating paths presenting synthetic problems pertaining for example stability issues.

Theoretical and Computational Chemists from their side already presented alternatives to the brute force approach such as simulated annealing,⁴ genetic algorithms,⁵ linear combinations of atomic potentials⁶ and the Inverse Molecular Design approach.^{7,8} These methods have been up-and-coming in the rational design of novel compounds with specific /optimal characteristics.⁹⁻¹¹

A fundamentally different, but also highly promising approach has been von Lilienfeld’s Alchemical Coupling approach.¹²⁻¹⁸ In this ansatz, two iso-electronic molecules in CCS are alchemically coupled through interpolation of their external potentials (i.e. the potential acting on the electrons) in the Hamiltonian. This approach has been used to study reaction energetic,¹⁵ to compute *ab initio* energy gradients, orbital energies¹⁴ and covalent bond potentials,¹⁷ and to explore dissociative water adsorption on iso-electronically BN-doped grapheme.¹⁸ Recently the BN doping of benzene and coronenes was scrutinised unifying coordinate and composition space in terms of Alchemical Normal Modes.¹⁹ Alchemical transformations were used to discuss the variation of the binding energy of oxygen reduction reaction intermediates on alloys of Pd, Pt and Ni.²⁰ In this method, energy derivatives with respect to nuclear charges are playing a fundamental role. These “Alchemical Derivatives”^{21,22} were shown by some of the present authors to find a natural place in the context of Conceptual Density Functional Theory (CDFT)^{23,24} where the $E[N, v]$ functional plays a central role. The energy of an atom, molecule is thereby written as a functional of the number of electrons N and the external potential $v(\mathbf{r})$. Upon perturbation in N and $v(\mathbf{r})$, typically at the onset of a chemical reaction, a perturbation expansion is written wherein each term a derivative of the type appears multiplied by the actual perturbation these derivatives quantify the sensitivity of the system to the considered perturbation, hence their name “response functions” or “sensitivity coefficients”.

A vast literature exists on the evaluation and use of these response functions: responses on dN perturbations are studied in the context of reactions/phenomena involving charge transfer.^{23,24} The most straightforward -first-order- case of a response function for a δv perturbation is the electron density $\rho(\mathbf{r})$ itself, the central quantity of DFT^{23,24} The second order term in the δv perturbation

expansion involves the response function, commonly called the Linear Response Function (LRF).²³⁻²⁶ At first sight tricky to evaluate and interpret, significant progress has been made in recent years in its evaluation and representation, in extracting chemical information (e.g. inductive and mesomeric effects, (anti)aromaticity) from it,^{25,26} in exploring its analogies with macroscopic chemical thermodynamics²⁷ and its connection with molecular conductivity.^{28,29}

The link between LRF and the above-mentioned alchemical derivatives is easily seen. Indeed, second order alchemical derivatives are response functions related to a second order perturbation of a particular type of external potential, namely the change in nuclear charge(s) Z . They proved to be highly valuable in exploring CCS as it was shown by some of the present authors that, on the basis of a simple SCF calculation (HF or DFT) on a given molecule, hereafter referred to as the reference molecule, and its corresponding alchemical derivatives, the CCS of its first neighbours – implying changes in nuclear charges of ± 1 – could be fully explored by simple arithmetic operations at completely negligible supplementary cost to the SCF calculation itself.²² Examples are (in order of increasing complexity): the deprotonation of small molecules and the transmutation of N_2 in its alchemical congeners ($CO, CN^-, C_2^{2-}, ON^+, O_2^{2+}$) with a mean absolute error of transmutation energy of 0.034 a.u., the case of CO (the only neutral transmutant) being excellent (0.63 kcal/mol). In a subsequent study of the iso-electronic substitution of (B,N) units for (C,C) units in carbocyclic systems, the stability sequence of all resulting azaborines was exactly reproduced.³⁰ When passing from “2D” to “3D” benzene, we recently adopted the alchemical approach to study the complete $(CC)_n \rightarrow (BN)_n$ substitution pattern of C_{60} , all the way down to $(BN)_{30}$ ($C_{60} \rightarrow C_{60-2n}(BN)_n$), $n=1,2,\dots,30$ predicting and interpreting the most stable isomers for each n .³¹ This study, based on a *single SCF calculation* on C_{60} and its alchemical derivatives up to second order, revealed that the correct stabilisation sequence for each n is retrieved by adopting an approach in which for each n value, the problem is looked upon without prejudice based on the $n-1$ result (called the “simultaneous” approach). An alternative, simpler, model (in which the n -problem “starts from the best results for the $(n-1)$ -problem (the “successive” approach) was shown to fail already at $n=13$, be it that for some larger n values, e.g. for the belt structure ($n=20$), identical results were obtained. Needless to say that even the successive approach might already be prohibitively demanding in a brute force approach performing standard *ab initio* or DFT calculations on each possible isomer, let it be for the simultaneous method.^{26,31} Very recently the first comprehensive study of atomic first and second alchemical derivatives was published by us³² using both a finite difference approach (*vide infra*) and March and Parr’s combined Z^{-1} and $N^{-1/3}$ expansion^{33,34} for the $E = E[Z, N]$ function in order to gain some first insights into the periodicity of alchemical properties along the Periodic Table.

In retrospect, our work until now has provided evidence that alchemical derivatives (mostly up to second order) might be a valuable tool in exploring CCS in the immediate neighbourhood of a reference molecule $\Delta Z = \pm 1$. However, it should be noticed that all transmutations considered are *iso-electronic*, i.e. the total number of electrons N of the system is unchanged. If we start from a neutral molecule, and no internal compensation occurs in the substitution (e.g. by replacing units (C,C) by (B,N) the total number of electrons is unchanged), the transmutant will be charged (cf. the larger part of the N_2 transmutants mentioned above), in many cases deviating from the Chemical

Subspace under consideration, e.g. neutral molecules. We, therefore, investigate in the present paper transmutations in which both Z and N change, and to the same extent, preserving the charge of the original molecule. As a “proof of concept” we consider neutral atom- neutral atom transmutations. Only at a few places in the literature, namely in the work of Cardenas and co-workers, some examples of such transformations were reported.³⁵ The complexity of this endeavour is that this type of transmutations not only involves the alchemical derivatives, but also “pure” N -derivatives as discussed in Conceptual DFT texts,²⁴ but also mixed derivatives as response functions, the simplest example at second order being at second order.

Cardenas pointed out that this derivative is the negative of the Fukui-potential^{36,37} at the nucleus,^{35,38,39} i.e. the potential due to the Fukui function, $f(\mathbf{r}) = (\partial \rho(\mathbf{r}) / \partial N)_v$,⁴⁰ at the nucleus. They mention in recent work on the predictivity of alchemical derivatives that the analogous third order mixed derivative will be hard to evaluate because of the nodal structure of the dual descriptor $f^{(2)}(\mathbf{r}) = (\partial^2 \rho(\mathbf{r}) / \partial N^2)_v$, the second derivative of $\rho(\mathbf{r})$ with respect to N most probably causing numerical instability. An explicit example of a series of alchemical transformations involving changes in N has recently been presented by the same authors³⁹ transmuting a Al_{13} cluster into $\text{Al}_{13-n}\text{Si}_n$ ($n = 1, 2, 3, 4$). They observe, upon inclusion of N derivatives up to second order, results of varying quantity with increasing n reaching the important conclusion that the perturbation expansion for $E = E[Z, N]$ converges slower in N than in Z .

In the present paper, our ultimate aim to show is that starting from the properties *only* of an initial system ($Z = Z, N = N$) (non-calligraphic letter denotes the value of the variable denoted by a calligraphic letter), the energy of its neighbouring system ($Z = Z + \Delta Z, N = N + \Delta N$) and $\Delta Z, \Delta N \in \{-1, 0, 1\}$ can be predicted. For example, starting from the neutral atom ($Z = Z, N = Z$), the energy of its neighbouring (neutral) atoms ($Z = Z - 1, N = Z - 1$) and ($Z = Z + 1, N = Z + 1$) can be predicted, as well as their Ionization Energies and Electron Affinities. In other words, we investigate if the information content of a reference atom is sufficient to predict with a certain accuracy the energy of a neighbouring atom, including Ionization energy and Electron Affinity. To the best of our knowledge, it is the first time this computational endeavour is set up, and its relationship to information content is explored. A DFT based approach will be followed in the evaluation of energies and its derivatives.

The paper is organised as follows. In Section II the Theoretical Background and the Methodology is explained. In Section III the Results and Discussion are presented: after some benchmarking of Basis set and DFT Functional the results for the alchemical derivatives (up to fourth order) (III.1) and the transmutation energies in the case of neutral to neutral transmutations (III.2) are presented and analysed for the complete series of first and second row atoms (H to Ar) comparing the exact transformation energy (the difference between the exact (at the level of approximation considered) energies of the two neighbouring atoms in the Periodic Table and its alchemical approximation (cases $\Delta Z = \Delta N = \pm 1$). In III.3 we present as a natural by-product of the adopted formalism a road to evaluate first Ionization Energies and atomic Electron Affinities avoiding the sometimes problematic description of the anion, and including also the case of second Electron Affinities avoiding the cumbersome treatment of resonance states of atomic anions. In Section IV some general conclusions are drawn, and an outlook for future research is presented.

II Theoretical Background and Methodology

Limiting the change in the electron number and the nuclear charge to the $\{-1, 0, 1\}$ set, the reference system can be transmuted to eight neighbours. As is sketched in Figure 1 (the neutral Nitrogen atom is used as an illustrative example), the transmutations of the reference systems can be split into four groups. The first group of transmutations involves atom ionisation or electron uptake, and the transmutation vector characterising this transmutation is $(\Delta Z = 0, \Delta N = \pm 1)$ (in general, all transmutations along the vertical lines in Figure 1). The transmutation vector characterising the second group is $(\Delta Z = \pm 1, \Delta N = 0)$ (in general, transmutations along the horizontal lines in Figure 1), the products of this type of transmutation are isoelectronic systems. Starting from the neutral nitrogen atom, this transmutation yields to the carbon anion or the oxygen cation. The next group, these are transmutations from a neutral atom to its preceding or successive neutral atom (from neutral nitrogen to neutral carbon or neutral oxygen), the transmutation vector characterising this transmutation being $(\Delta Z = \pm 1, \Delta N = \Delta Z)$. The last group is characterised by the $(\Delta Z = \pm 1, \Delta N = -\Delta Z)$ vector. Following this vector, the neutral nitrogen is transmuted into the carbon dianion or the oxygen dication.

[FIGURE I]

The energy of the transmutants, limited to the n -order terms, can be approximated as

$$E_{(n)}[Z, \Delta Z, N, \Delta N] = \sum_{i=0}^n \sum_{j=0}^{n-i} \frac{1}{i!j!} \left(\frac{\partial^{i+j} E[Z, N]}{\partial Z^i \partial N^j} \right) \bigg|_{Z=Z, N=N} \Delta Z^i \Delta N^j. \quad (1)$$

It can be rewritten as (for simplicity, non-calligraphic letters denotes the property is calculated at $(Z = Z, N = Z)$ vector

$$E_{(n)}[Z, \Delta Z, N, \Delta N] = E[Z, N] + \sum_{i=1}^n \frac{1}{i!} \left(\frac{\partial^i E[Z, N]}{\partial N^i} \right) \Delta N^i + \sum_{i=1}^{n-1} \sum_{j=1}^{n-i} \frac{1}{i!j!} \left(\frac{\partial^{i+j} E[Z, N]}{\partial Z^i \partial N^j} \right) \Delta Z^i \Delta N^j + \sum_{i=1}^n \frac{1}{i!} \left(\frac{\partial^i E[Z, N]}{\partial Z^i} \right) \Delta Z^i \quad (2)$$

The first summation in Eq.(2), (terms with $j = 0, i > 0$ from Eq.(1)) contains the traditional electronic response functions of Conceptual DFT, $(\partial^i E[Z, N] / \partial N^i)_Z$: the electronic chemical potential ($i = 1$)⁴¹, the chemical hardness ($i = 2$)⁴² and the hyperhardness ($i = 3$)⁴³ where the condition of the constant external potential, $v(\mathbf{r})$, has been cast in a condition for constant Z . In the last summation (terms with $j = i, i > 0$ from Eq.(1)), the alchemical derivatives appear, $(\partial^i E[Z, N] / \partial Z^i)_N$: the alchemical potential ($i = 1$), the alchemical hardness ($i = 2$), the alchemical hyperhardness ($i = 3$)^{21,22}. The remaining terms in Eq.(2) are the energy of the reference system and the summation in which the mixed derivatives with respect to N and Z are involved, $(\partial^i E[Z, N] / \partial Z^j \partial N^{i-j})$. As

1 already mentioned in the Introduction the second order mixed derivative, ($i = 2, j = 1$), is known and
 2 easily seen to be the negative of the Fukui potential $v_f(\mathbf{r})$ (0) at the origin in the atomic case^{35,38}

$$3 \quad \left(\frac{\partial^2 E[Z, N]}{\partial Z \partial N} \right) = - \int \left(\frac{\partial \rho(\mathbf{r}, Z, N)}{\partial N} \right)_Z \frac{d\mathbf{r}}{r} = - \int \frac{f(\mathbf{r}, Z, N)}{r} d\mathbf{r}, \quad (3)$$

4 where $f(\mathbf{r}, Z, N) = (\partial \rho(\mathbf{r}, Z, N) / \partial N)_Z$ is the Fukui function. Numerical problems are expected for
 5 the dual descriptor potential in the corresponding second order N -derivative due to the intricate
 6 nodal structure of the dual descriptor^{38,44}

$$7 \quad \left(\frac{\partial^3 E[Z, N]}{\partial Z \partial N^2} \right) = - \int \left(\frac{\partial^2 \rho(\mathbf{r}, Z, N)}{\partial N^2} \right)_Z \frac{d\mathbf{r}}{r} = - \int \frac{f^{(2)}(\mathbf{r}, Z, N)}{r} d\mathbf{r}. \quad (4)$$

8 The remaining third order derivative, not discussed in the literature hitherto, is easily shown to be an
 9 integral of the Fukui kernel $f(\mathbf{r}, \mathbf{r}')$ weighted by $1/r$ and $1/r'$ if the nucleus is placed at the origin.

$$10 \quad \begin{aligned} \left(\frac{\partial^3 E[Z, N]}{\partial Z^2 \partial N} \right) &= \left(\frac{\partial}{\partial N} \iint \left(\frac{\delta E[Z, N]}{\delta v(\mathbf{r}) \delta v(\mathbf{r}')} \right)_N \left(\frac{\partial v(\mathbf{r})}{\partial Z} \right)_N \left(\frac{\partial v(\mathbf{r}')}{\partial Z} \right)_N d\mathbf{r} d\mathbf{r}' \right)_Z \\ &= \left(\frac{\partial}{\partial N} \iint \left(\frac{\delta \rho(\mathbf{r})}{\delta v(\mathbf{r}')} \right)_N \frac{1}{r} \frac{1}{r'} d\mathbf{r} d\mathbf{r}' \right)_Z = \left(\frac{\partial}{\partial N} \iint \frac{\chi(\mathbf{r}, \mathbf{r}')}{rr'} d\mathbf{r} d\mathbf{r}' \right)_Z \\ &= \iint \frac{f(\mathbf{r}, \mathbf{r}')}{rr'} d\mathbf{r} d\mathbf{r}', \end{aligned} \quad (5)$$

11 where $f(\mathbf{r}, \mathbf{r}') = (\partial \chi(\mathbf{r}, \mathbf{r}') / \partial N)_Z$ is the N derivative of the linear response function. This
 12 expression bears perfect analogy with that of the alchemical hardness

$$13 \quad \begin{aligned} \left(\frac{\partial^2 E[Z, N]}{\partial Z^2} \right)_N &= \iint \left(\frac{\delta E[Z, N]}{\delta v(\mathbf{r}) \delta v(\mathbf{r}')} \right)_N \left(\frac{\partial v(\mathbf{r})}{\partial Z} \right)_N \left(\frac{\partial v(\mathbf{r}')}{\partial Z} \right)_N d\mathbf{r} d\mathbf{r}' \\ &= \iint \left(\frac{\delta \rho(\mathbf{r})}{\delta v(\mathbf{r}')} \right)_N \frac{1}{r} \frac{1}{r'} d\mathbf{r} d\mathbf{r}' = \iint \frac{\chi(\mathbf{r}, \mathbf{r}')}{rr'} d\mathbf{r} d\mathbf{r}', \end{aligned} \quad (6)$$

14 which in the case of an atom reduces to a $1/r$ and $1/r'$ weighted integral of LRF.

15 In the evaluation of the expression from Eq.(2), the N derivatives (pure and mixed) are problematic,
 16 related to the nature of the $E[N, v[Z]]$, with the well-known derivative discontinuity and its
 17 consequences for its differentiability (for a recent account see for example⁴⁵). The properties of a
 18 system with a noninteger electron number (involved in the derivative definition) are traditionally
 19 defined either by interpolating between the property-values for integer electron number(s) or by
 20 adopting the open-system picture, where the system is free to interchange electrons with a
 21 (noninteracting) electron reservoir, and the system's properties are constructed using the grand
 22 canonical ensemble.⁴⁶ In an interpolation model, the energy is expressed as a parameterised function

1 $E_{\lambda}[N, Z, \{E_1, E_2, \dots, E_M\}]$, where the parameters $\lambda = \lambda_1, \lambda_2, \dots, \lambda_M$ are determined by the requirement
2 that the function has the correct energy values for some integer electron numbers,
3 $\tilde{E}_{\lambda}[N = N_m, Z, \{E_1, E_2, \dots, E_M\}] = E[N = N_m, Z] = E_i$. The form of the function to be
4 parameterized is motivated by physical considerations, and several different models (polynomial,
5 rational, exponential, etc.) are prevalent in the literature: from Parr's celebrated parabolic model⁴² to
6 exponential and rational functions.^{43,47,48} In an ensemble model, the system is free to exchange
7 electrons with a "bath" of electrons, but it is not excited or otherwise perturbed by the reservoir of
8 electrons. At 0K limit, the ensemble description of the system is equivalent to the piecewise linear
9 interpolation.^{46,49}

10 Assuming that the interpolation function E_{λ} is differentiable up to k -th order in N and $n \geq k$, Eq.(1)
11 can be rewritten as

$$\begin{aligned} \tilde{E}_{(n,k)}[Z, \Delta Z, N, \Delta N] &= \sum_{i=0}^{n-k} \sum_{j=0}^k \frac{1}{i!j!} \left(\frac{\partial^{i+j} E[Z, N]}{\partial Z^i \partial N^j} \right) \Delta Z^i \Delta N^j \\ &+ \sum_{i=n-k+1}^n \sum_{j=0}^{n-i} \frac{1}{i!j!} \left(\frac{\partial^{i+j} E[Z, N]}{\partial Z^i \partial N^j} \right) \Delta Z^i \Delta N^j. \end{aligned} \quad (7)$$

13 Note that the internal summations in the first component of Eq.(7) includes all possible pure N
14 derivatives and the reference energy whose sum in the interpolation model can be replaced by the
15 correct energy for some integer electron number

$$\begin{aligned} \sum_{i=0}^{n-k} \sum_{j=0}^k \frac{1}{i!j!} \left(\frac{\partial^{i+j} E[Z, N]}{\partial Z^i \partial N^j} \right) \Delta Z^i \Delta N^j &= \sum_{i=0}^{n-k} \frac{1}{i!} \left(\frac{\partial^i}{\partial Z^i} \sum_{j=0}^k \frac{1}{j!} \left(\frac{\partial^j E[Z, N]}{\partial N^j} \right) \Delta N^j \right)_{\text{N}} \Delta Z^i \\ &= \sum_{i=0}^{n-k} \frac{1}{i!} \left(\frac{\partial^i E_m}{\partial Z^i} \right)_{\text{N}} \Delta Z^i \end{aligned} \quad (8)$$

17 where $E_m = E[Z, N_m]$ and $N_m = N + \Delta N$.

18 It can easily be seen using Parr's parabolic approach, ($k=2$), that the equation above can be
19 rewritten for $\Delta N = \pm 1$ as

$$\begin{aligned} \tilde{E}_{(n,2)}[Z, \Delta Z, N, \pm 1] &= E_{+/-}^Z + \sum_{i=1}^{n-2} \frac{1}{i!} \left(\frac{\partial^i E_{+/-}^Z}{\partial Z^i} \right)_{\text{N}} \Delta Z^i \\ &+ \frac{1}{(n-1)!} \left(\frac{\partial^{n-1}}{\partial Z^{n-1}} \left(E_0^Z \pm \frac{1}{2} (E_+^Z - E_-^Z) \right) \right)_{\text{N}} \Delta Z^{(n-1)} + \frac{1}{n!} \left(\frac{\partial^n E_0^Z}{\partial Z^n} \right)_{\text{N}} \Delta Z^n \end{aligned} \quad (9)$$

21 where $E_{+0/-}^Z \equiv E[Z = Z, N = Z + \Delta N]$ and $\Delta N \in \{-1, 0, +1\}$; the $(E_+^Z - E_-^Z)/2$ and $(E_+^Z + E_-^Z - 2E_0^Z)$

22 expressions for electronic potential and hardness, μ_0^Z and η_0^Z were used. The identity from Eq.(8) for

23 this approach for $\Delta N = \pm 1$ has the following form

$$\sum_{j=0}^2 \frac{(\pm 1)^j}{j!} \left(\frac{\partial^j E[Z, N]}{\partial N^j} \right)_N = E_0^Z \pm \mu_0^Z \Delta N + \frac{1}{2} \eta_0^Z \Delta N^2 = E_{+/-}^Z. \quad (10)$$

At 0K limit of the ensemble model, Eq.(7) is simply

$$\tilde{E}_{(n,1)}[Z, dZ, N, \pm 1] = E_{+/-}^Z + \sum_{i=1}^{n-1} \frac{1}{i!} \left(\frac{\partial^i E_{+/-}^Z}{\partial Z^i} \right) \Delta Z^i + \frac{1}{n!} \left(\frac{\partial^n E_0^Z}{\partial Z^n} \right) \Delta Z^n \quad (11)$$

From Eqs.(9) and (11), it becomes clear that the energy of transmutants for the $(\Delta Z = \pm 1, \Delta N = \Delta Z)$ vector, the diagonal road in Figure 1, and for the $(\Delta Z = \pm 1, \Delta N = -\Delta Z)$ vector, the antidiagonal road, can be calculated using pure alchemical derivatives.

These derivatives do not suffer from the discontinuity problem as N and Z are essentially different in the quantum-mechanical description of an atom. Z can be considered as a parameter in the Hamiltonian operator enabling differentiation without the intricacies encountered for N , the latter being an integer denoting the number of electrons and henceforth determining the number of variables in the wavefunction.

As a final comment it should be remarked that simple combinations of alchemical derivatives, in principle, frees us from the evaluation of a double integral of a N -derivative of the linear response function which itself is far from trivial to evaluate.^{25,50}

III Results and Discussion

III.1 Alchemical Derivatives

In order to evaluate the transmutation energies, Eqs.(9)-(11), one should first obtain the alchemical derivatives up to several orders, also permitting to estimate if the third order approach succinctly adopted in the previous formalism is adequate. The first and second order derivatives were obtained analytically by extending the coupled perturbed approach described in Ref. ²² for closed shell systems to open shell systems. The finite difference approach can be used to calculate higher derivatives. The first and second derivative of some quantity $A[Z]$, in this approach, are

$$\left(\frac{\partial A[Z]}{\partial Z} \right) \approx \frac{A[Z + \delta, N] - A[Z - \delta, N]}{2\delta} \equiv \tilde{A}_{(1)}[Z, \delta], \quad (12)$$

$$\left(\frac{\partial^2 A[Z]}{\partial Z^2} \right) \approx \frac{A[Z + \delta, N] + A[Z - \delta, N] - 2A[Z, N]}{\delta^2} \equiv \tilde{A}_{(2)}[Z, \delta]. \quad (13)$$

The third order derivatives, e.g. the alchemical stiffness γ^{al} can be obtained by numerical differentiation as either the first derivative of the alchemical hardness, η^{al} ,

$$\tilde{\gamma}_{(1)}^{\text{al}}[Z, \delta; N] \equiv \frac{\eta^{\text{al}}[Z + \delta, N] - \eta^{\text{al}}[Z - \delta, N]}{2\delta} \approx \left(\frac{\partial^3 E[Z, N]}{\partial Z^3} \right)_N \quad (14)$$

alternatively, the second numerical derivative of the alchemical potential, $\tilde{\gamma}_{(2)}^{\text{al}}$ (not used in this work).

The fourth order derivative, denoted as $\tilde{\kappa}^{\text{al}}$, is evaluated by a double numerical differentiation of the alchemical hardness

$$\tilde{\kappa}_{(2)}^{\text{al}}[Z, \delta; N] \equiv \frac{\eta^{\text{al}}[Z + \delta, N] + \eta^{\text{al}}[Z - \delta, N] - 2\eta^{\text{al}}[Z, N]}{\delta^2} \approx \left(\frac{\partial^4 E[Z, N]}{\partial Z^4} \right)_N. \quad (15)$$

The δ value was chosen as a compromise between the precision (small δ) and too much numerical error. A value of 0.01 turned out to yield this compromise. It was seen that for this δ value, the difference between both results for $\tilde{\gamma}^{\text{al}}$ is in most cases, negligible and will not be mentioned in the tables. Another conclusion is that the fourth order derivative, κ evaluated as a double numerical differentiation of the alchemical hardness, shows strong numerical instabilities. Therefore it will be omitted from our investigations. To illustrate these issues, the data for Nitrogen calculated at CAMB3LYP/aug-cc-pCVQZ level were used in Figure 2.

[Figure 2]

Concerning the level of theory, based on our previous experience,^{22,30} for all atoms considered (H-Ar) the B3LYP functional^{51,52} in its CAMB3LYP version,⁵³ combining the hybrid qualities of B3LYP with a long-range correction was chosen as the DFT functional. Use was made of Dunning's correlation consistent basis-sets including polarisation functions by definition in its "maximalized" aug-cc-pCVQZ⁵⁴ version with functions describing the effect of core correlations. These "tight" functions, denoted as C, were shown to be essential in alchemical transformations for adequately describing the changes in the electronic distribution in the core region upon transmutation.^{22,30} All calculations were performed with a locally modified version of the GAMESS program.⁵⁵

In Table 1, the alchemical derivatives, up to third order, for the neutral atoms H-Ar at B3LYP/aug-cc-pCVTZ level of theory. The corresponding values for the mono-cations and mono- and di-anions calculated at CAMB3LYP/aug-cc-pCVQZ level, to be discussed more succinctly in this contribution, are given in the Supporting Information (SI).

[TABLE I]

The first point is that the CPKS first and second order derivatives correspond in order of magnitude and sequence with the values obtained by numerical differentiation, reported in³². The present values are obviously to be preferred because of their analytical nature and will be the starting point of our discussion and further calculations. It means, however, that the discussion concerning orders of magnitude and evolution along the Periodic Table for second-order derivatives held in³² is still largely valid. For the first order derivatives, no CPKS ansatz is necessary. As shown by Politzer, they can be written as the electrostatic potential at the nucleus (for a detailed account see⁵⁶). They show a monotonous decrease, with a more negative value upon increasing Z . Note their fundamental difference with the N -derivative with the well-known pattern of periodicity showing up in the electronegativity.²³ For a detailed interpretation of the monotonous decrease, we refer to Ref.³²

1 The change in the alchemical potential when passing from one neutral atom to another, implying
 2 $dN = dZ$,

$$3 \quad \left. \frac{d\mu^{\text{al}}}{dZ} \right|_{dN=dZ} = \left(\frac{\partial \mu^{\text{al}}}{\partial Z} \right)_N + \left(\frac{\partial \mu^{\text{al}}}{\partial N} \right)_Z = \iint \chi(\mathbf{r}, \mathbf{r}') \frac{1}{r} \frac{1}{r'} d\mathbf{r} d\mathbf{r}' - \int \frac{(\partial \rho(\mathbf{r}) / \partial N)_Z}{r} d\mathbf{r} \quad (16)$$

4 is negative upon increasing Z . This conclusion based on the fact that the linear response function,
 5 $\chi(\mathbf{r}, \mathbf{r}')$, is a seminegative definite operator due to the concavity in $v(\mathbf{r})$ of the $E[v, N]$
 6 functional,⁵⁰ therefore, the atomic alchemical hardness is a non-positive number. The second term is
 7 the negative Fukui potential at the nuclear position.^{35,37} The electrostatic potential of the Fukui
 8 function does not show negative values: it exhibits a maximum close to the nuclear position and
 9 decays with the distance.^{35,36} There is also shown, using the Z^{-1} expansion,³³ for neutral atoms μ^{al}
 10 decreases as $Z^{-4/3}$ with a proportionality factor of the order of -1.5.³²

11 The second derivative η^{al} is always appreciably smaller than the first one, μ^{al} . For Li-Ne, the
 12 $\mu^{\text{al}} / \eta^{\text{al}}$ ratio is increasing from 2.5 to 7.7, and for the second row typically one order of magnitude or
 13 even more. Again no periodicity is observed, as opposed to the corresponding N -derivative, the
 14 chemical hardness.²³

15 Now, let us discuss, the third order derivatives, γ^{al} . In general, they show positive values, but for
 16 hydrogen, helium, and noble gases, they can be negative depending on the calculation level (e.g., for
 17 Ne, γ^{al} is positive with the “tight” function in basis set and negative without it). In absolute value,
 18 for the first row, and from Be on, they are of the order of 20 à 30 mHartree (see SI), two orders of
 19 magnitude smaller than their second order analogues; for the second row, values of the order of 50
 20 mHartree (with exceptions for Na and Mg showing a value twice as high) are found, also typically
 21 two orders of magnitude smaller than the second order derivatives. The small γ^{al} value can easily be
 22 retraced by inspection of alchemical hardness values for ions as compared to neutral atoms as given
 23 in the SI. Considering, for example, the series of alchemical hardness values of C^{2+} B^{1+} Be^0 Li^- , one
 24 retrieves a close to a linear relationship with values of -2.499, -2.500, -2.505, -2.563 Hartree, the
 25 largest deviation, not unexpectedly, found for the anion. Similar quartets are found for nearly all
 26 atoms (both first and second row) and nearly all triplets excluding the anion show an almost perfect
 27 linear behaviour, all this pointing towards small or very small γ^{al} values. Based on this order of
 28 magnitude analysis and taking into account that the perturbation in Z considered is usually ± 1 (in
 29 Section III.1 a few cases are discussed with $\Delta Z = \pm 2$) we can see that the individual terms in a
 30 perturbation expansion are expected to have converged at third order. The fourth order derivatives,
 31 κ^{al} , mentioned above thus can safely be omitted from our investigations, as moreover, some
 32 exploratory calculations hinted to strong numerical instabilities. Note that the faster-convergence of
 33 the $E[Z, N]$ in Z than in N (the order of magnitude of the electronic chemical potential and the
 34 chemical hardness is the same²³) is in line with the comments by Munoz and Cardenas in their work
 35 on the transmutation of Al clusters.³⁹

36

37 III.2 The Diagonal and Non-Diagonal Road

38

1 Returning now to Figure I, we see that the properties of the chosen system can be predicted basing
 2 ourselves on either the properties of its first nearest neighbours, $\Delta Z = \pm 1$ and $\Delta N = 0$ or $\Delta N = \pm 1$
 3 and $\Delta Z = 0$, (horizontal or vertical lines in Figure 1) or on the properties of its second nearest
 4 neighbours $\Delta Z = \pm 1$ and $\Delta N = \pm \Delta Z$ (diagonal lines). The latter choice will be called the diagonal
 5 road, the former the non-diagonal road.

6 Following the diagonal road in the direction $\Delta Z = \Delta N = \pm 1$ and stopping the Taylor
 7 expansion at third order, Eqs.(9) and (11) becomes

$$8 \quad \tilde{E}_{(3,2)}[Z, \Delta Z = \pm 1, N, \Delta Z] = E_{+/-}^Z \pm \mu_{+/-}^{\text{al},Z} + \frac{1}{4} \left(2\eta_0^{\text{al},Z} \pm (\eta_+^{\text{al},Z} - \eta_-^{\text{al},Z}) \right) \pm \frac{1}{6} \tilde{\gamma}_0^{\text{al},Z} \quad (17)$$

9 for Parr's parabolic approach, and at the 0K limit

$$10 \quad \tilde{E}_{(3,1)}[Z, \Delta Z = \pm 1, N, \Delta Z] = E_{+/-}^Z \pm \mu_{+/-}^{\text{al},Z} + \frac{1}{2} \eta_{+/-}^{\text{al},Z} \pm \frac{1}{6} \tilde{\gamma}_0^{\text{al},Z} \quad (18)$$

11 The difference between alchemical and exact energies for a neutral atom is

$$12 \quad \Delta_{(3,k)}^{+/-}[Z] = \tilde{E}_{(3,k)}[Z - \Delta Z, \Delta Z = \pm 1, N = Z - \Delta Z, \Delta Z] - E[Z, Z] \quad (19)$$

13 where $\Delta Z = \pm 1$. For Parr's parabolic approach it is

$$14 \quad \Delta_{(3,2)}^{+/-}[Z] = E_{+/-}^{Z\mp 1} \pm \mu_{+/-}^{\text{al},Z\mp 1} + \frac{1}{4} \left(2\eta_0^{\text{al},Z\mp 1} \pm (\eta_+^{\text{al},Z\mp 1} - \eta_-^{\text{al},Z\mp 1}) \right) \pm \frac{1}{6} \tilde{\gamma}_0^{\text{al},Z\mp 1} - E_0^Z, \quad (20)$$

15 and at the 0K limit

$$16 \quad \Delta_{(3,1)}^{+/-}[Z] = E_{+/-}^{Z\mp 1} \pm \mu_{+/-}^{\text{al},Z\mp 1} + \frac{1}{2} \eta_{+/-}^{\text{al},Z\mp 1} \pm \frac{1}{6} \tilde{\gamma}_0^{\text{al},Z\mp 1} - E_0^Z. \quad (21)$$

17 Example, the nitrogen energy obtained from the Carbon data, one is

$$18 \quad \Delta_{(3,2)}^{+,N} = E^{C^-} + \mu^{\text{al},C^-} + \frac{1}{4} \left(2\eta^{\text{al},C} + (\eta^{\text{al},C^-} - \eta^{\text{al},C^+}) \right) + \frac{1}{6} \tilde{\gamma}^{\text{al},C} - E^N, \quad (22)$$

$$19 \quad \Delta_{(3,1)}^{+,N} = E^{C^-} + \mu^{\text{al},C^-} + \frac{1}{2} \eta^{\text{al},C^-} + \frac{1}{6} \tilde{\gamma}^{\text{al},C} - E^N \quad (23)$$

20 while from the Oxygen data it is

$$21 \quad \Delta_{(3,2)}^{-,N} = E^{O^+} - \mu^{\text{al},O^+} + \frac{1}{4} \left(2\eta^{\text{al},O} - (\eta^{\text{al},O^-} - \eta^{\text{al},O^+}) \right) - \frac{1}{6} \tilde{\gamma}^{\text{al},O} - E_0^N, \quad (24)$$

$$22 \quad \Delta_{(3,1)}^{-,N} = E^{O^+} - \mu^{\text{al},O^+} + \frac{1}{2} \eta^{\text{al},O^+} - \frac{1}{6} \tilde{\gamma}^{\text{al},O} - E^N. \quad (25)$$

23 Looking at Figure 1, the transmutation of the reference atom into the target atom can be achieved in
 24 the two paths. The first one involves the transmutation of the reference atom into the target atom ion
 25 then into its neutral form, e.g. $C \rightarrow N^+ \rightarrow N$. The second one engages the reference-atom ion, e.g.
 26 $C \rightarrow C^- \rightarrow N$. Because the first way requires information about the target-atom ion, this path will
 27 no longer be considered in this work.

It is easy to see that the second path is equivalent to the transmutation along the non-diagonal road

$$E[Z \pm 1, Z \pm 1] = E[Z, Z] + (E[Z, Z \pm 1] - E[Z, Z]) + (E[Z \pm 1, Z \pm 1] - E[Z, Z \pm 1])$$

$$\approx E_{+/-}^Z \pm \mu_{+/-}^{\text{al},Z} + \frac{1}{2} \eta_{+/-}^{\text{al},Z} \pm \frac{1}{6} \tilde{\gamma}_{+/-}^{\text{al},Z} = E_{(3)}[Z, \pm 1, Z \pm 1, 0]. \quad (26)$$

The difference between alchemical and exact energies for the non-diagonal road is

$$\Delta_{(3)}^{+/-}[Z] = E_{+/-}^{Z \mp 1} \pm \mu_{+/-}^{\text{al},Z \mp 1} + \frac{1}{2} \eta_{+/-}^{\text{al},Z \mp 1} \pm \frac{1}{6} \tilde{\gamma}_{+/-}^{\text{al},Z \mp 1} - E[Z, Z]. \quad (27)$$

which for the illustrative example is

$$\Delta_{(3)}^{+,N} = E^{C^-} + \mu^{\text{al},C^-} + \frac{1}{2} \eta^{\text{al},C^-} + \frac{1}{6} \tilde{\gamma}^{\text{al},C^-} - E_0^N, \quad (28)$$

$$\Delta_{(3)}^{-,N} = E^{O^+} - \mu^{\text{al},O^+} + \frac{1}{2} \eta^{\text{al},O^+} - \frac{1}{6} \tilde{\gamma}^{\text{al},O^+} - E_0^N. \quad (29)$$

[Table 2]

In Table 2, we summarise the results for the diagonal and non-diagonal road, denoted as $T_{+/-}^Z$ and $D_{(Z \pm 1)^\pm \rightarrow Z}$, respectively. These results are based either on the anion of the preceding-atom (e.g. T_+^O , $D_{N^- \rightarrow O}$ in Figure 1) or on the cation of the successive-atom (e.g. T_-^C , $D_{N^+ \rightarrow C}$) which we will call to result from “the anion road” or “the cation road”, respectively. The difference in the between alchemical and exact energies for the $T_{+/-}^Z$ type transmutation can be calculated either in the Parr’s parabolic approach or in the 0K limit of the ensemble approach, Eq.(20) or Eq.(21) respectively. An overall comparison between the cationic road and the anionic road shows that the anionic road is performing less strongly .For this anionic road the results for the indirect (both the parabolic model and the 0K limit) and the indirect road are roughly and on the average comparable . The cationic road however shows a clear- cut tendency of improvement from the parabolic model via the 0K limit to the indirect road displaying by far the overall best results. The comparison of the diagonal road results, $T_{+/-}^Z$, with the results obtained in the non-diagonal road, $D_{(Z \pm 1)^\pm \rightarrow Z}$, (essentially in the cationic road) shows that the availability of the mixed-derivatives calculations in an analytical manner is crucial to achieving high-quality results. In the parabolic approach, the data for neutral and ionic states are engaged. In the 0K limit, this engagement reduces to two states, a neutral and one of the ionic states. The non-diagonal-road results are based only on one ionic state, the anion or the cation.

From the whole of the above discussion, it becomes clear that ,if high quality results are aimed at , non-diagonal route combined with the cationic road yields much more-satisfactory results than the if high quality results are aimed at the diagonal route, and so our further analysis will be limited only to this strategy.

The question arises why the non-diagonal road is less successful in the anionic case . As stated above $\Delta_{(3)}^+$ and $\Delta_{(3)}^-$ reveal a remarkable difference in quality. Starting with the anion-road, the $\Delta_{(3)}^+$ results can be grouped into two groups: the cases with an absolute error less than 10 mHartree and more than 10 mHartree. These disagreements, for Li, B, Na, Al, result from a transmutation process in which

the anion of the atom at their left in the Periodic Table is unstable. Indeed He, Be, Ne, and Mg do have an unstable anion and a negative electron affinity,^{57 [65]} putting question marks on how to handle this quantity in our working formulas (for the issue of handling negative electron affinities in the conceptual DFT see ⁵⁸). Moreover, the alchemical potentials, due to the instability of the anion cannot be expected of the same quality as in case of the stable anion. One should on top of that not forget that, even for stable anions, there is ample evidence in the literature⁵⁹ that the ab initio study of stable atomic and molecular anions involves much more complications than in case of neutral or cationic systems. Even if the EA might be reasonable the other properties associated with that anion, such as in our case the alchemical derivatives, may be of poor(er) quality given shortcomings in its wavefunction.

Nevertheless, disregarding the outliers for the well-founded reasons explained above (and the case of He which in our view suffers from doubling the nuclear charge when starting from H), the results for the first group are quite encouraging within an average unsigned deviation of 5.4 mHartree, i.e. less than 3.5 kcal/mol. It is rewarding to compare this value with the actual transmutation energies: at the level of theory considered, $D_{(Z-1)^- \rightarrow Z}$. For the transmutation to nitrogen from carbon-anion, this value is of the order 16.7 Hartree, increasing up to 67.3 Hartree for the transmutation from chlorine anion to argon (corresponding from 10 500 kcal/mol up to 42 200 kcal/mol).

Passing now to the $\Delta_{(3)}^-$ values, the cation road, one sees that the results even markedly improve. Except for two outliers (Ne and Na which bear the same origin as the Mg case in the $\Delta_{(3)}^+$ values, and which will be discussed hereafter, the convergence is impressive as are the final results. The absolute error in the energy prediction is less than 1.6 mHartree, *meaning that one arrives at the order of 1 kcal/mol⁻¹ i.e. reaching chemical accuracy.*

[Figure 3]

One final problem remains the outliers Mg for $\Delta_{(3)}^-$ and Ne and Na for $\Delta_{(3)}^+$. The derivative-calculation scheme used in this work assumes that atomic basis set functions, which are usually taken as gaussian type orbitals, do not depend on the perturbation in Z . In other words, that the reference-atom basis set will be suitable to describe the target atom, what is not valid for any truncated basis set. The most straightforward way to solve this problem is to introduce basis set functions which are explicitly dependent on the nuclear charge and thus, they will also be-subject to differentiation. This solution is an obstacle. Firstly, Hellmann-Feynman theorem is no longer satisfied since the wave function loses its variational property. Secondly, expressions defining derivatives become more complicated.²² Based on our experience, the conclusion was that the effect of basis set dependence on the perturbation is insignificant and can be omitted when large basis set sets are used. After ample numerical studies, we concluded that the basis set derivatives with respect to Z are essential for quantitative accuracy. In Figure 3, the basis-set dependence of the alchemical hardness is presented. In the case of the oxygen hardness, its value is accurately calculated using the nitrogen, fluorine or neon basis set (the left-top panel in Figure 3). Also, the alchemical hardness for the fluorine cation is well reproduced with the oxygen and neon basis set, but the nitrogen basis set based calculation shows a small deviation. In the case of the fluorine alchemical hardness (the right-top panel), the alchemical hardness at $Z = 9$ is similar for the first-row atom basis set, but the η_0^F value is drastically different if the sodium basis set is used. In the case of the neon hardness (the left-bottom panel), the hardness value is correctly calculated at $Z = 10$ only if the fluorine basis-set is used. Also,

the influence of the basis set on the hardness value for the sodium cation can be noted. Finally, in the sodium case (the right-bottom panel), the dependence of the hardness value on the basis set is observed even for using the basis set of the atoms from the same row. In conclusion, our results can be considered to be conclusive for explaining the outliers Mg for $\Delta_{(3)}^-$ and Ne and Na for $\Delta_{(3)}^+$: their position at the end or the beginning of a row in the Periodic Table with the associated sharp difference in the basis set as compared to their neighbours involved in the alchemical transformation calculus.

The final results prove the intrinsic value of the alchemical derivative approach: given some (energetic) properties of a reference neutral atom, the energy of the neighbouring neutral atom, in this case, the one to the left in the Periodic Table, can be evaluated with remarkable precision. The difference in quality between both approaches can be traced back with the overall better description of the reference states in the cation road than that in the anion road.

We, therefore, conclude that the anion road is less adequate, though, when used with caution (stability condition for anions) is not bad at all but that the cation road is preferable, in the less performant anion road is in our view not due to a fundamental failure of our ansatz, but merely due to computational problems involving anions. Taken together, both the $\Delta_{(3)}^+$ and the $\Delta_{(3)}^-$ values, for sure, offer a “proof of principle” that the alchemical derivative approach can deliver systematically quantitatively good results for transforming one neutral atom into another. Note that these results do not concern relative values as in previous studies where the relative stability of 2 and 3 D BN doped benzenes were studied,^{30,31} but that they are a stringent numerical test on energies of individual systems.

One might be tempted (vide supra) to cast this result in an information-theoretical context, pioneered in chemistry by Sears, Parr and Dinur⁶⁰ in a rather intuitive way. What about the atom to the left? Is there a fundamental difference? Some of the present authors (for reviews see^{61,62}) analysed the similarity between the electron density (the fundamental carrier of information in DFT) of atoms along the Periodic Table. It turned out that similarity is maximal between nearest neighbours, indicating no fundamental difference between left and right side neighbours masking in this way Periodicity. For example Carbo's Quantum Similarity Index⁶³ between P and Si on one hand and P and S on the other hand only differs in the fourth decimal (0.9969 and 0.9974), with similar results for the information discrimination.⁶¹ This brings us to the conclusion that in principle our results for the left and right road should be of similar quality but that the difference is primarily due to the appreciably better description of the cationic than the anionic states. This issue will be further addressed in Section III.3 on the evaluation of ionisation energies and electron affinities.

A final comment in this Section is self-reflective: why are the results for the cation road so (surprisingly?) good although in the whole endeavour spin and associated multiplicity of the target state is not considered, i.e. we were working all the time in the context of spin-independent Conceptual DFT. A spin-polarized version has been launched already some time ago under the impetus of Ghosh and Ghanty⁶⁴ on one side and Galvan, Gazquez and Vela^{65,66} on the other side (for reviews see^{67,68}) and involves the inclusion of S , the difference in number of α and β electrons, in the energy functional. In principle one could rewrite the whole formalism starting from an extended equation (1), obviously leading to several pure S -derivatives and a substantial extra number of mixed derivatives (working up to third order), taking moreover care that the derivatives with respect to Z and/or N are taken at a constant S value. It was, therefore, decided not to embark in this endeavour in order not to further dilute this “proof of principle” paper under further computational

issues. For main row elements, the electronic configuration is “stable “ upon this journey from reference to target atom, and the latter is reached at the correct spin state. It should be noted that when scrutinising the NIST database,⁶⁹ and as widely known in Transition Metal Chemistry, most elements from the Transition Metals, the Lanthanides and the Actinides do show alternations of configuration. For example Ti has a 3d²4s² configuration, Ti⁺ 3d²4s¹ and Sc 3d¹4s². A more detailed analysis most probably in the context of Spin-Polarized CDFT would be at stake in these cases.

III.3 Towards the Evaluation of Ionization Energies and Electron Affinities.

As a direct application of the formalism described in Section II, we present a way for direct evaluation of the ionisation energies and electron affinities of a neighbouring atom starting from the energy of what we called the reference atom. Besides completing our proof of concept (evaluation of atomic energetic properties through those of neighbouring atoms through alchemical derivatives coupled with variations in N) the formalism also offers an elegant way, in the case of electron affinities, to obtain estimates for the first and second electron affinities which are hard to get both experimentally and theoretically (for the first electron affinity) and which always involve unstable dianions in case of the second electron affinity.

Although unstable double anions are involved, which do not exist in a bound state,⁷⁰ some long-lived resonances of doubly negative ions have been observed experimentally.⁵⁷ So the second electron affinity of the atom has been discussed at length in the literature, and different methods have been proposed to evaluate the double anion resonance.⁷⁰ As for most first and second row elements, some literature data is available, summarised by Sergeev. We thought it was a challenge to see where our formalism leads to on the case of these second electron affinities, both in order of magnitude and concerning the sequence, with particular attention to the (relative) values of the most documented cases O and S.^{70,71}

The ionisation energy can be calculated through the anion road as

$$I_{(+)}^Z \equiv E_{(3)}[Z-1, +1, N=Z-1, 0] - E_{(3)}[Z-1, +1, N=Z, 0]$$

$$= E_0^{Z-1} - E_+^{Z-1} + (\mu_0^{\text{al}, Z-1} - \mu_+^{\text{al}, Z-1}) + \frac{1}{2}(\eta_0^{\text{al}, Z-1} - \eta_+^{\text{al}, Z-1}) + \frac{1}{6}(\tilde{\gamma}_0^{\text{al}, Z-1} - \tilde{\gamma}_+^{\text{al}, Z-1}), \quad (30)$$

when the cation road then yields

$$I_{(-)}^Z \equiv E_{(3)}[Z+1, -1, N=Z-2, 0] - E_{(3)}[Z+1, -1, N=Z-1, 0]$$

$$= E_{+2}^{Z+1} - E_+^{Z+1} - (\mu_{+2}^{\text{al}, Z+1} - \mu_+^{\text{al}, Z+1}) + \frac{1}{2}(\eta_{+2}^{\text{al}, Z+1} - \eta_+^{\text{al}, Z+1}) - \frac{1}{6}(\tilde{\gamma}_{+2}^{\text{al}, Z+1} - \tilde{\gamma}_+^{\text{al}, Z+1}), \quad (31)$$

for example in the Nitrogen case

$$I_{(+)}^N = E^C - E^{C^-} + (\mu^{\text{al}, C} - \mu^{\text{al}, C^-}) + \frac{1}{2}(\eta^{\text{al}, C} - \eta^{\text{al}, C^-}) + \frac{1}{6}(\tilde{\gamma}^{\text{al}, C} - \tilde{\gamma}^{\text{al}, C^-}), \quad (32)$$

$$I_{(-)}^N = E^{\text{O}^{+2}} - E^{\text{O}^+} - (\mu^{\text{al}, \text{O}^{+2}} - \mu^{\text{al}, \text{O}^+}) + \frac{1}{2}(\eta^{\text{al}, \text{O}^{+2}} - \eta^{\text{al}, \text{O}^+}) - \frac{1}{6}(\tilde{\gamma}^{\text{al}, \text{O}^{+2}} - \tilde{\gamma}^{\text{al}, \text{O}^+}), \quad (33)$$

[Table III]

It is clear from our discussion in the previous sections that the anion road, Eq.(30), involving properties of the neutral and anion forms of the neighbouring atom, will be less well adapted for evaluation of ionisation energy than the cation road, Eq.(31): where properties of the cation and dication are involved. Therefore in Table III, the cation road results and the direct value obtained at the same level of theory are presented as the difference between these results and the experimental values, e.g. for the nitrogen ionisation energy $\Delta_{(3)}^- I^N = I_{(-)}^N - I_{\text{exp}}^N$ and $\Delta I^N = E_+^N - E_0^N - I_{\text{exp}}^N$ for the cation road and direct calculations respectively. The deviation between the values for the ionisation energies obtained via the direct way and the cation road themselves in most cases is less than 0.01 eV. The agreement between experimental and our alchemical theoretical values, both for first and second row atoms, is striking, with an average deviation of less than 0.5 eV. All this giving even more confidence to our proof of concept.

Coming to the first electron affinity and discarding the anion road from the beginning, the cation road procedure involves only properties of the neutral and cation form of the transmuted atom (see Figure I). The first electron affinity can be approximated as

$$A_{(-)}^Z \equiv E_{(3)}[Z+1, -1, N=Z-1, 0] - E_{(3)}[Z+1, -1, N=Z, 0]$$

$$= E_-^{Z+1} - E_0^{Z+1} - (\mu_-^{\text{al}, Z+1} - \mu_0^{\text{al}, Z+1}) + \frac{1}{2}(\eta_-^{\text{al}, Z+1} - \eta_0^{\text{al}, Z+1}) - \frac{1}{6}(\tilde{\gamma}_-^{\text{al}, Z+1} - \tilde{\gamma}_0^{\text{al}, Z+1}) \quad (34)$$

so in the Nitrogen case, it has a form

$$A_{(-)}^N = E^{O^+} - E^O - (\mu^{\text{al}, O^+} - \mu_0^{\text{al}, O}) + \frac{1}{2}(\eta^{\text{al}, O^+} - \eta^{\text{al}, O}) - \frac{1}{6}(\tilde{\gamma}^{\text{al}, O^+} - \tilde{\gamma}^{\text{al}, O}) \quad (35)$$

The accuracy of this approximation can be examined based on the difference between results from Eq.(34) and the experimental electron affinity, in comparison with the difference between the direct calculation of the electron affinity and the experimental one, e.g., for the nitrogen electron affinity $\Delta_{(3)}^- A^N = A_{(-)}^N - A_{\text{exp}}^N$ and $\Delta A^N = E_0^N - E_-^N - A_{\text{exp}}^N$.

From Table 4, we see that the alchemical approach yields to reasonable electron affinity prediction. The mean absolute error for the entries with a positive value of experimental electron affinity 0.11 eV for the cation road based prediction, in comparing with 0.16 eV for the direct calculations.

The second electron affinity, A_2^Z , can be predicted either based on the neutral and anionic form of the successive atom or based on the neutral and cation form of the second successive atom (e.g., the A_2^Z carbon based on the nitrogen properties or the oxygen properties respectively). Based on the anion road results discussed above, the first one is skipped by analogy. The second one, involving only properties of the neutral and cationic form of the reference system, yields for the second electron affinity

$$A_{2,(-)}^Z \equiv E_{(3)}[Z+2, -2, N=Z-1, 0] - E_{(3)}[Z+2, -2, N=Z, 0], \quad (36)$$

e.g., the second electron affinity for Carbon is calculated based on the properties of neutral Oxygen and its cation (note that here the second neighbour is involved leading to a more significant Z perturbation)

$$A_{2,(-)}^C = E^{O^+} - E^O - 2(\mu^{\text{al},O^+} - \mu^{\text{al},O}) + 2(\eta^{\text{al},O^+} - \eta^{\text{al},O}) - \frac{4}{3}(\tilde{\gamma}^{\text{al},O^+} - \tilde{\gamma}^{\text{al},O}) \quad (37)$$

The method proposed in this work can be compared with the investigation of the existence of a resonance state for doubly charged atomic negative ions from the behaviour of the ground state with decreasing nuclear charge in the paper by Sergeev and Kais mentioned above.⁷⁰ In Table 5 values obtained via Eq.(36) and from Sergeev and Kais work are listed. In their paper, the cases where the monoanion is already unstable were not considered. The results show a remarkable agreement in the sense that the maximal deviation is in general, smaller than 1 eV and mostly appreciably smaller. Once again, the outlier is Mg as the reference system for the Ne value prediction, and as the target system. Coming back to the case most extensively studied in the literature (O) the extensive list of values tabulated by Sergeev obtained via a plethora of different approaches defines a range in which our value perfectly fits. On top of that the sequence within a row (increasing from left to right) is respected in the first row; in the second row only the position of the S value, be it with the correct order of magnitude, is incorrect. On the other hand, the ratio O vs S, both showing closed shell resonances, is reasonably well reproduced (1.40 vs 1.60).

All in all, these results for Electron Affinities are encouraging and inspiring for studies when one is facing unstable systems to obtain educated guesses for first and/or second electron affinities.

IV Conclusions

A strategy for evaluating alchemical transmutations involving both a change in nuclear charge and a change in electron number has been developed. The transmutation to first nearest neighbours, ($\Delta Z = \pm 1$ and $\Delta N = 0$ or $\Delta N = \pm 1$ and) $\Delta Z = 0$, and the second nearest neighbours ($\Delta Z = \pm 1$ and) $\Delta N = \pm \Delta Z$ of the neutral atom, with extension to the direct evaluation of ionization energy and first and second electron affinities is taken as a proof of concept study to investigate if adequate absolute energies can be obtained in the Conceptual DFT context in which this approach is embedded. It was shown that the availability of the mixed-derivatives calculations in an analytical manner is crucial to achieving high-quality results in predictions which are based on the second nearest neighbours, the diagonal road results. An overall comparison between the cationic road and the anionic road shows that the anionic road is performing less strongly. For this anionic road the results for the direct (both the parabolic model and the 0K limit) and the indirect road are roughly and on the average comparable. The cationic road however shows a clear-cut tendency of improvement from the parabolic model via the 0k limit to the indirect road displaying by far the overall best results.

Within the Coupled Perturbed Kohn Sham formalism and a CAMB3LYP/aug-cc-pCCQZ level of theory, the results for the cationic road are of *chemical accuracy* (errors less than 1 kcal /mol for the complete set of atoms from He to Ar) when the procedure is carried at third order in ΔZ for which the perturbation series converges. From the information theory point of view (similarity analysis of the electronic density distributions and information discrimination analysis) no fundamental reason pops for the difference in quality between the cationic and anionic paths. The difficulties inherent to an accurate description of the anion and its derivatives are responsible for the shortcomings along the anion road. The formalism is shown to be easily applicable to the direct evaluation of ionisation energies and first and second electron affinities of the target atom with excellent agreement between the direct and the alchemical route for the ionisation energies. The excursion into first and second

electron Affinities yields very consistent results for stable mono-anions and promising estimation for the second electron affinity, associated to invariably, unstable systems with results comparable with literature data on resonance states of atomic anions.

Besides a proof of concept that with the information content of an atom one can get accurate energies of its neighbours (proviso that orbital energy sequences are not changing leading to different spin states between the charged intermediate and the target atom), the present results are indicative that alchemical derivatives are on the road to give *quantitative* information when navigating through Chemical Compound Space.

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SUPPORTING INFORMATION

TABLE S1 Alchemical derivatives (in eV) up to third order (μ, η, γ) for the mono-cations and mono- and di-anions of the atoms H-Ar. Values for the neutral atoms (Table 1 in Main Text) are included for comparison. (all values refer to CAMB3LYP aug-cc-pCVQZ level of theory- see main text) The evolution of the Alchemical Hardness is given in a separate figure (see main text)

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10

1 **Table 1.** Alchemical derivatives up to third order ($\mu^{\text{al}}, \eta^{\text{al}}, \mu^{\text{al}}, \tilde{\gamma}_{(1)}^{\text{al}}$) for the neutral atoms H -Ar (in
2 a.u.) from CPKS calculation at B3LYP aug-cc-pCVTZ level of theory. The “ Z^{-1} ” results for the first
3 and second alchemical derivatives previously obtained in Ref 32 are given for comparison. All data
4 in Hartree, except $\tilde{\gamma}_{(1)}^{\text{al}}$ values in mHartree.

Z	Alchemical derivatives				
	CP KS			Z^{-1} method	
	μ^{al}	η^{al}	$\tilde{\gamma}_{(1)}^{\text{al}}$	μ^{al}	η^{al}
H	-0.995	-0.990	24.63	-0.625	-1.000
He	-3.371	-1.965	89.93	-3.376	-1.984
Li	-5.717	-2.241	130.40	-5.715	-2.268
Be	-8.419	-2.479	36.68	-8.419	-2.506
B	-11.390	-2.746	40.07	-11.390	-2.769
C	-14.697	-3.001	40.64	-14.698	-3.018
N	-18.337	-3.254	39.57	-18.329	-3.309
O	-22.257	-3.511	49.33	-22.266	-3.503
F	-26.510	-3.766	49.25	-26.487	-3.854
Ne	-31.097	-4.020	48.15	-31.131	-4.005
Na	-35.423	-3.893	364.65	-35.433	-4.181
Mg	-39.923	-4.104	195.88	-39.937	-4.278
Al	-44.498	-4.080	286.09	-44.515	-4.397
Si	-49.242	-4.228	242.65	-49.258	-4.508
P	-54.146	-4.363	209.42	-54.161	-4.614
S	-59.180	-4.490	190.72	-59.200	-4.710
Cl	-64.373	-4.618	170.61	-64.396	-4.816
Ar	-69.723	-4.743	153.68		

1 **Table 2.** Difference between alchemical and exact transmutation energies. The diagonal road results
2 $T_{+/-}^Z$ are calculated using the parabolic and 0K limit approach, $\Delta_{(3,2)}^{+/-}$ from Eq.(20) and $\Delta_{(3,1)}^{+/-}$ from
3 Eq.(21) respectively. The non-diagonal road results, $\Delta_{(3)}^{+/-}$ from Eq.(27). All data in mHartree

4

Z	the anion road			the cation road		
	T_+^Z		$D_{(Z-1)^- \rightarrow Z}$	T_-^Z		$D_{(Z+1)^+ \rightarrow Z}$
	$\Delta_{(3,2)}^+$	$\Delta_{(3,1)}^+$	$\Delta_{(3)}^+$	$\Delta_{(3,2)}^-$	$\Delta_{(3,1)}^-$	$\Delta_{(3)}^-$
H				-243.67	1.00	-0.83
He		37.29	-89.31	3.54	-4.37	0.85
Li	-280.54	-35.87	-55.25	36.09	-0.94	1.49
Be	-1.66	-9.57	-2.49	13.85	-0.98	0.72
B	15.17	-21.86	-218.30	8.24	-0.88	0.78
C	2.51	-12.32	-8.12	10.04	-1.04	0.63
N	3.48	-5.64	-3.78	7.17	-2.31	0.62
O	7.00	-4.09	-8.62	7.12	-2.37	0.46
F	5.84	-3.65	-4.89	-58.50	-2.62	0.37
Ne	5.51	-3.98	-2.26	18.86	-3.09	8.65
Na	-16.19	39.69	43.99	42.81	17.92	22.14
Mg	22.80	0.86	35.69	14.26	-3.46	1.23
Al	66.48	41.59	-91.96	7.80	-2.03	1.43
Si	5.69	-12.03	7.61	8.20	-1.38	1.29
P	5.38	-4.45	7.47	6.14	-1.46	1.19
S	6.07	-3.51	3.94	5.40	-1.14	1.15
Cl	4.62	-2.98	5.06	-26.40	-0.95	1.12
Ar	4.18	-2.36	5.13			

5

6

1 **Table 3.** First ionisation energy: difference between experimental and theoretical values obtained via
2 the alchemical method, $\Delta_{(3)}^{-} I^{\text{N}} = I_{(-)}^{\text{N}} - I_{\text{exp}}^{\text{N}}$, and the direct method, $\Delta I^{\text{N}} = E_{+}^{\text{N}} - E_{0}^{\text{N}} - I_{\text{exp}}^{\text{N}}$. All data in
3 eV.

Z	$\Delta_{(3)}^{-} I^{\text{Z}}$	ΔI^{Z}
He	0.189	0.216
Li	-1.543	-1.524
Be	3.437	3.445
B	0.424	0.426
C	0.307	0.303
N	0.168	0.163
O	0.493	0.486
F	0.317	0.314
Ne	0.118	0.170
Na	0.256	0.255
Mg	0.044	0.055
Al	0.013	0.025
Si	-0.050	-0.043
P	-0.105	-0.101
S	0.178	0.183
Cl	0.098	0.101
M.A.E	0.484	0.488

4
5

1 **Table 4.** First electron affinity: values obtained via the alchemical, $A_{(-)}^Z$, and the direct method,
2 $E_0^Z - E_-^Z$ and the difference between experimental and theoretical values obtained via the alchemical
3 method, $\Delta_{(3)}^- A^Z$ from Eq.(34), the direct method, $E_0^Z - E_-^Z$. The experimental data, A_{exp}^Z from Ref.⁶⁹.
4 All data in eV.

Z	$A_{(-)}^Z$	$\Delta_{(3)}^- A^Z$	$E_0^Z - E_-^Z$	ΔA^Z	A_{exp}^Z
H	0.932	0.178	0.863	0.109	0.755
He	0.057	—	-2.466	—	unstable
Li	2.197	1.579	2.242	1.624	0.618
Be	-0.410	—	-0.170	—	unstable
B	0.280	0.003	0.369	0.092	0.277
C	1.267	-0.328	1.332	-0.263	1.595
N	-0.011	—	0.069	—	unstable
O	1.583	0.122	1.653	0.192	1.461
F	3.475	0.076	3.533	0.134	3.400
Ne	-0.388	—	-4.951	—	unstable
Na	0.426	-0.122	0.522	-0.026	0.547
Mg	-0.438	—	-0.209	—	unstable
Al	0.274	-0.166	0.357	-0.083	0.440
Si	1.228	-0.157	1.275	-0.110	1.385
P	0.844	0.108	0.890	0.154	0.736
S	2.121	0.048	2.157	0.084	2.073
Cl	3.616	-0.001	3.645	0.028	3.617
M.A.E	—	0.241	—	0.241	—

1 **Table 5.** Second electron affinity, the $A_{2,(-)}^Z$ values from Eq.(36), the A_2^Z from Ref.⁷⁰. All data in eV.

2

Z	$A_{2,(-)}^Z$	A_2^Z
H	4.32	
He	-1.10	
Li	-2.12	
Be	-3.58	-3.43
B	-4.71	-4.88
C	-6.18	-6.11
N	-6.75	-7.48
O	-6.90	-7.65
F	-0.15	
Ne	-2.21	0.95
Na	-2.20	
Mg	-3.21	-1.79
Al	-3.80	-3.44
Si	-4.70	-4.76
P	-4.77	-4.95
S	-4.57	-4.91

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1 **Figure 1.** Possible transmutation in the neighborhood of the nitrogen atom.

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1 **Figure 2.** The accuracy of the numerical differentiation for the alchemical derivatives (top panel) and
2 the stability of the alchemical stiffness and the hyper-stiffness versus the nuclear charge perturbation,
3 δ in the case of the N atom μ^{al} and η^{al} .

1 **Figure 3.** The basis-set dependence of the alchemical hardness. Difference between the alchemical
2 hardness calculated using the original basis set for a given atom and using the neighbour's basis set.
3 The differences in meV. See text for discussion. I would add in each panel the N value

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