Where is the electron pair?
A QMC detective story

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Vallico Soto, Italy
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Talk overview
What we will cover for sure and maybe cover...

**Electrophilic amination: A QMC study**
- The chemistry
- Electron-pair localization functions (original and modified)
- Sketch current and future work


**Electronic structure by quantum computation**
- Polynomial algorithm for the *exact* solution of the Schrödinger equation on a quantum computer
- Recent results
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Electronic structure by quantum computation
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- Recent results
Making proteins: Synthesis of peptide bonds
Nucleophilic vs. electrophilic substitution

- Carbon-nitrogen bonds are usually formed by the nucleophilic attack of a nitrogen to an electrophilic carbon ($S_{N2}$)
- Reverse process: a nucleophilic carbon replaces a leaving group previously attached to an electrophilic nitrogen

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X-C + HNRR' → C-NRR' ← RR'N-X + C
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- Some reagents have been found and tested

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H N-Cl  H N-SO_3H  RO_2C-N=N-CO_2R
```

Where is the electron pair?
Exploration using QMC

The mission

- Is it possible to rationalize the electronic properties of the already known reagents so as to be able to direct the search for even more effective ones?

- Approach the answer by:
  - Use DMC to calculate energetics
  - Calculate the electron-pair localization function (EPLF) rationalize values, find trends, explain differences, make predictions

Representative molecules

- Typical nucleophilic behavior: \( \text{NH}_3, \text{NH}_2-\text{CH}_3 \) (MA), \( \text{NH}-(\text{CH}_3)_2 \) (DMA), \( \text{N}-(\text{CH}_3)_3 \) (TMA)

- Possible electrophilic behavior: \( \text{NH}_2\text{F}, \text{NH}_2\text{CF}_3 \)
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- Possible electrophilic behavior:
  \( \text{NH}_2\text{F, NH}_2\text{CF}_3 \)
DMC calculations
Calculation parameters

- geometries optimized with GAMESS at MP2//631G* level
- cc-pVTZ basis set
- fourth order SMBH correlation function, absolute deviation minimization
- collection of $10^6$ walkers for EPLF
- $\approx 1\,\text{week}$ computational time on 8 cores.
- All calculations carried out with the Zori code (http://www.zori-code.com)
### Atomization enthalpy differences

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<tr>
<th>Method</th>
<th>Molecule</th>
<th>NH$_3$</th>
<th>MA</th>
<th>DMA</th>
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Numbers are differences with the experimental value at 298.15 K.
Total energies are corrected by zero point energy (ZPE).
Electron Pair Localization Function

\[ d_{\sigma\sigma}(\vec{r}) = \sum_{i=1}^{N} \langle\langle \delta(\vec{r} - \vec{r}_i) \min_{j;\sigma_j=\sigma_i} |\vec{r} - \vec{r}_j| \rangle\rangle, \]

\[ d_{\sigma\bar{\sigma}}(\vec{r}) = \sum_{i=1}^{N} \langle\langle \delta(\vec{r} - \vec{r}_i) \min_{j;\sigma_j\neq\sigma_i} |\vec{r} - \vec{r}_j| \rangle\rangle. \]

EPLF

In terms of these average distances, the EPLF is defined as

\[ \text{EPLF}(\vec{r}) = \frac{d_{\sigma\sigma}(\vec{r}) - d_{\sigma\bar{\sigma}}(\vec{r})}{d_{\sigma\sigma}(\vec{r}) + d_{\sigma\bar{\sigma}}(\vec{r})}. \]

EPLF range

(-1) unpaired (0) long-distance (1) Paired

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EPLF range

(-1) unpaired (0) long-distance (1) Paired

Dimethylamine
A nucleophilic amine

iso-EPLF surface for dimethylamine
Fluoroamine
An electrophilic amine

iso-EPLF surface for fluoroamine
Trimethylamine
A nucleophilic amine

iso-EPLF surface for tri-methylamine
Ammonia
EPLF projected on the electron density

iso-density surface with projected color coded EPLF for ammonia
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A conclusion

EPLF seems to be a very good hydrogen locator!

Let’s go back to definition...

\[
EPLF(\vec{r}) = \frac{d_{\sigma\sigma}(\vec{r}) - d_{\sigma\bar{\sigma}}(\vec{r})}{d_{\sigma\sigma}(\vec{r}) + d_{\sigma\bar{\sigma}}(\vec{r})}.
\]

If the \( \sigma\sigma \) and \( \sigma\bar{\sigma} \) distances are proportional to each other, EPLF is insensitive to the inter-electronic distance.

Assume \( d_{\sigma\bar{\sigma}}(\vec{r}) = xd_{\sigma\sigma}(\vec{r}) \)

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EPLF(\vec{r}) = \frac{1 - x}{1 + x}
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EPLFN
A distance-dependent variant of EPLF

For characterizing an **electro-nucleophilicity** scale, we are interested in measuring how *paired* and *localized* are electrons. We introduce the EPLFN family of functions. In particular EPLF3, the EPLF density

\[
EPLFN(\vec{r}) = \frac{d_{\sigma\sigma}(\vec{r}) - d_{\sigma\bar{\sigma}}(\vec{r})}{(d_{\sigma\sigma}(\vec{r}) + d_{\sigma\bar{\sigma}}(\vec{r}))^{N+1}}
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But... where is the electron pair region?
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\]

But... where is the electron pair region?
Electron Localization Function (ELF)
Conditional pair probability for same spin —spherical average—,

\[ P_{\text{cond}}^{\sigma\sigma}(r, s) = \frac{1}{3} \left[ \sum_j \left| \nabla \phi_j \right|^2 - \frac{1}{4} \frac{\left| \nabla \rho_\sigma \right|^2}{\rho_\sigma} \right] s^2 + \ldots \]

(smaller probability, more localization)
Define

\[ D_\sigma(r) = \sum_j \left| \nabla \phi_j \right|^2 - \frac{1}{4} \frac{\left| \nabla \rho_\sigma \right|^2}{\rho_\sigma} ; \]

and the corresponding quantity for the uniform electron gas

\[ D^0_\sigma(r) = \frac{3}{5} \left( 6\pi^2 \right)^{2/3} \rho_\sigma^{5/3} . \]
Electron Localization Function

Definition

Thus, ELF is defined as

$$\text{ELF}(r) = \frac{1}{1 + (D_{\sigma}/D_{\sigma}^0)^2}.$$ 

Interpretation

- ELF equals one when $D_{\sigma}$ is zero —highest localization.
- ELF equals one half when the localization corresponds to that of the uniform electron gas.
- ELF is smaller for even smaller localization.

EPLF in the ELF basin
Effect of electron correlation on the electron pair region density

For our purposes, the most important property of ELF is that defines a well-defined basin around the lone pair, i.e. defines the pair’s volume.

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Integral LDA</th>
<th>Integral QMC</th>
<th>Distance</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMA</td>
<td>2.295</td>
<td>2.382</td>
<td>0.94</td>
<td>354</td>
</tr>
<tr>
<td>DMA</td>
<td>2.251</td>
<td>2.324</td>
<td>0.95</td>
<td>775</td>
</tr>
<tr>
<td>MA</td>
<td>2.215</td>
<td>2.232</td>
<td>0.95</td>
<td>1488</td>
</tr>
<tr>
<td>NH$_3$</td>
<td>2.167</td>
<td>2.211</td>
<td>0.95</td>
<td>2294</td>
</tr>
<tr>
<td>NH$_2$CF$_3$</td>
<td>2.060</td>
<td>2.144</td>
<td>0.97</td>
<td>1656</td>
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<tr>
<td>NH$_2$F</td>
<td>2.386</td>
<td>2.386</td>
<td>0.86</td>
<td>1852</td>
</tr>
</tbody>
</table>
Alternative localization ideas
Can break down when orbitals are delocalized

But it is also possible to study the electron pair without information from ELF, by projecting the EPLF$^N$ onto the orbital corresponding to the lone pair

$$
\epsilon_N = \frac{\langle \phi_{lp} | EPLF^N | \phi_{lp} \rangle}{\langle \phi_{lp} | \phi_{lp} \rangle}
$$

<table>
<thead>
<tr>
<th>Molecule</th>
<th>$\epsilon_0 \times 10^2$</th>
<th>$\epsilon_3 \times 10^6$</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMA</td>
<td>8.28</td>
<td>1.21</td>
<td>557</td>
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<tr>
<td>DMA</td>
<td>8.34</td>
<td>1.21</td>
<td>514</td>
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<td>MA</td>
<td>8.48</td>
<td>1.96</td>
<td>659</td>
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<td>8.36</td>
<td>7.11</td>
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<tr>
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<td>7.19</td>
<td>1000</td>
</tr>
<tr>
<td>NH$_2$F</td>
<td>8.95</td>
<td>5.41</td>
<td>1452</td>
</tr>
</tbody>
</table>
Finally, the proposed descriptors from EPLFN, integrated over the basin defined by ELF, are presented.

<table>
<thead>
<tr>
<th>Molecule</th>
<th>$\epsilon_0$</th>
<th>$d_0^c$</th>
<th>$\epsilon_3 \times 10^3$</th>
<th>$d_3^c$</th>
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</thead>
<tbody>
<tr>
<td>TMA</td>
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<td>2.35</td>
<td>2.89</td>
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<tr>
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<tr>
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<td>6.20</td>
<td>2.28</td>
<td>4.78</td>
<td>3.01</td>
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<tr>
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<td>2.05</td>
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<td>2.48</td>
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<tr>
<td>NH$_2$CF$_3$</td>
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<td>2.07</td>
<td>6.15</td>
<td>2.70</td>
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<tr>
<td>NH$_2$F</td>
<td>5.10</td>
<td>1.93</td>
<td>7.02</td>
<td>2.43</td>
</tr>
</tbody>
</table>
Summary

- $\epsilon_3$ and $d_3^c$ are proposed as descriptors of the lone pair availability
- EPLF may not be the ultimate tool for analyzing electron pair localization
- EPLFN together with ELF provides a reliable, unambiguous description of the lone pair
Outlook

- Study the effect of more sophisticated trial wave functions $\psi_T$
- Use forward-walking or reptation MC to obtain pure EPLFN estimator
- Currently applying to a set of 15 experimentally relevant molecules of 100 – 200 electrons.
- Explore EPLFN for the description of chemical bonds, radicals, and other kinds of lone pairs.
Thanks!

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