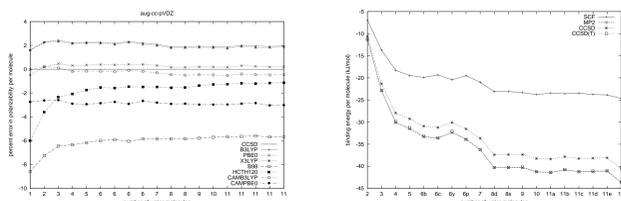


## Water clusters

- (1) Understand which DFT methods reproduce accurate polarizabilities.
- (2) Build polarizable water models from quantum chemical data.
- (3) Simulate condensed phase phenomena accurately by including nuclear quantum effects.

## Results

PBE0 provides the most accurate description of polarizabilities and binding energies of DFT methods tested. MP2 reproduces CCSD(T) binding energies almost perfectly.



## Calibration of coupled-cluster

Basis set effects were evaluated for smaller clusters:

| $\alpha$ | CCSD      |             | aug-cc-pVDZ |             | aug-cc-pVTZ |             | aug-cc-pVQZ |             |
|----------|-----------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
|          | Isotropic | Anisotropic | Isotropic   | Anisotropic | Isotropic   | Anisotropic | Isotropic   | Anisotropic |
| 1        | 9.26      | 1.03        | 9.54        | 0.71        | 9.56        | 0.61        |             |             |
| 2        | 19.11     | 3.47        | 19.36       | 3.24        | 19.31       | 2.83        |             |             |
| 3        | 28.94     | 5.28        | 29.02       | 5.21        | 28.94       | 4.87        |             |             |
| 4        | 39.06     | 7.46        | 38.96       | 7.51        | -           | -           |             |             |

The role of correlation beyond CCSD is nominal:

| Basis       | HF    | MP2   | CCSD  | CC3   | CCSDT |
|-------------|-------|-------|-------|-------|-------|
| aug-cc-pVDZ | 8.163 | 9.190 | 9.225 | 9.158 | 9.160 |
| aug-cc-pVTZ | 8.465 | 9.556 | 9.484 | 9.477 | 9.474 |
| aug-cc-pVQZ | 8.523 | -     | 9.531 | -     | 9.540 |
| aug-cc-pV5Z | 8.530 | -     | 9.538 | -     | 9.554 |
| aug-cc-pV6Z | 8.534 | -     | 9.541 | -     | -     |

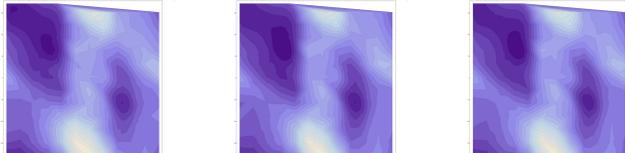
## Peptide torsional potential

The OPLS-AA force field was fit to LMP2/cc-pVTZ(-f) energies of structures determined with Hartree-Fock. That this potential was fit to such a rudimentary method is a severe limitation on its capability.

To better understand which methods are capable of producing accurate energetics for the peptide torsional potential, we are evaluating numerous quantum chemical methods against CCSD(T) for the alanine dipeptide.

## Results for standard methods

SCF/6-311++G\*\* min=(-88,73,-492.9927)      MP2/6-311++G\*\* min=(-78,63,-494.6187)      CCSD(T)/6-311++G\*\* min=(-78,63,-494.7503)



## Drug targets

Small-molecular polarizable force fields rely upon quantum chemistry since the necessary experimental data are not available. Previously, we showed that DFT struggles with polarizabilities of aromatic rings — which are frequently found in drug targets — so an in-depth benchmarking of such molecules is necessary.

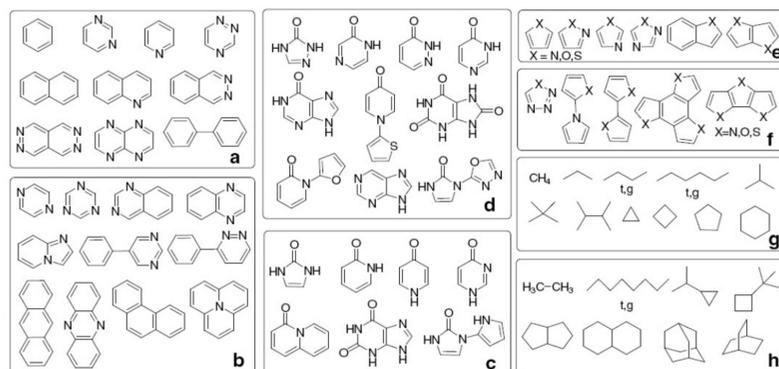
## Density functional theory

There are many levels of approximation within DFT:

$$\begin{aligned} \text{GGA: } & V_{XC}[\rho_\sigma, \nabla\rho_\sigma] \\ \text{Hybrid GGA: } & \alpha V_{XC}[\rho_\sigma, \nabla\rho_\sigma] + \beta V_{HF} \\ \text{AC Hybrid GGA: } & \alpha(r_{ee})V_{XC}[\rho_\sigma, \nabla\rho_\sigma] + \beta(r_{ee})V_{HF} \\ \text{Meta GGA: } & V_{XC}[\rho_\sigma, \nabla\rho_\sigma, \tau\{\{\nabla\phi_{i\sigma}\}\}] \\ \text{Fifth-rung: } & V_{XC}[\rho_\sigma, \nabla\rho_\sigma, \tau\{\{\nabla\phi_{i\sigma}\}\}, \{\epsilon_{i\sigma}\}] \end{aligned}$$

We focus on the most commonly used Hybrid GGAs in chemistry (B3LYP and PBE0) and their asymptotically-corrected (AC) counterparts, since DFT without exact exchange produces polarizabilities of poor quality. AC-DFT fixes the well-known problem with the exponential decay of the exchange potential, which affects the accuracy of polarizabilities.

## The EPIC test set



J.-F. Truchon, A. Nicholls, R. I. Itimie, B. Roux and C. I. Bayly, *J. Chem. Th. Comp.* **4**, 1480 (2008).

## Results

Average errors are computed with respect to the CCSD-LR polarizabilities using the aug-cc-pVDZ basis set.

| Method  | Signed    |             | Unsigned  |             |
|---|-----------|-------------|-----------|-------------|
|   | Isotropic | Anisotropic | Isotropic | Anisotropic |
| B3LYP   | 0.93      | 2.67        | 1.23      | 2.82        |
| PBE0  | 0.00      | 2.00        | 0.99      | 2.41        |
| CAM-B3LYP ( $\mu=0.33, \alpha=0.19, \beta=0.46$ ) | -1.43     | 0.19        | 1.71      | 1.91        |
| CAM-PBE0 ( $\mu=0.30, \alpha=0.25, \beta=0.75$ )  | -2.52     | -1.03       | 2.52      | 1.30        |

Over 50% of the error in B3LYP and PBE0 comes from polyaromatic systems (for example, bisfurane has 17% relative error in the anisotropy).

## Summary

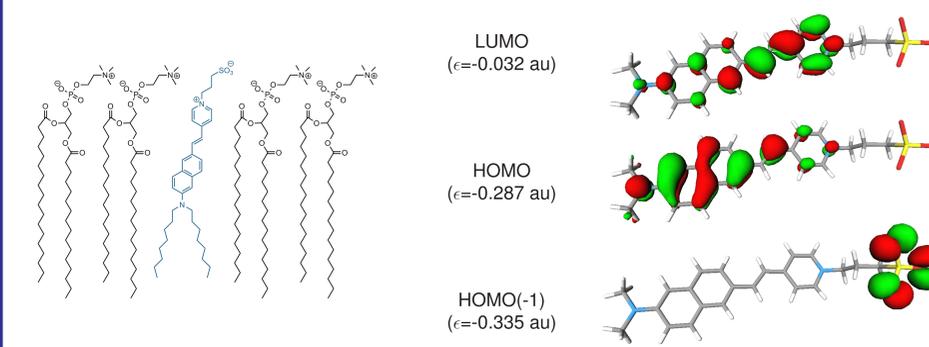
- (1) B3LYP is not an optimal functional for computing polarizabilities.
- (2) PBE0 provides excellent isotropic polarizabilities and is widely available.
- (3) CAMB3LYP is the best overall functional for polarizabilities.
- (4) The asymptotic 100% exact exchange of CAMPBE0 is not well-suited for polarizabilities, although it is necessary for other properties.

## Membranes probes

Fluorescence probes provide insight into many biological systems. The di-8-ANEPPS probe is particularly special due to its sensitivity to local electric-field perturbations. Unfortunately, ANEPPS (the aliphatic tails are not relevant to the electronic spectrum) defies physical description using popular quantum chemical methods.

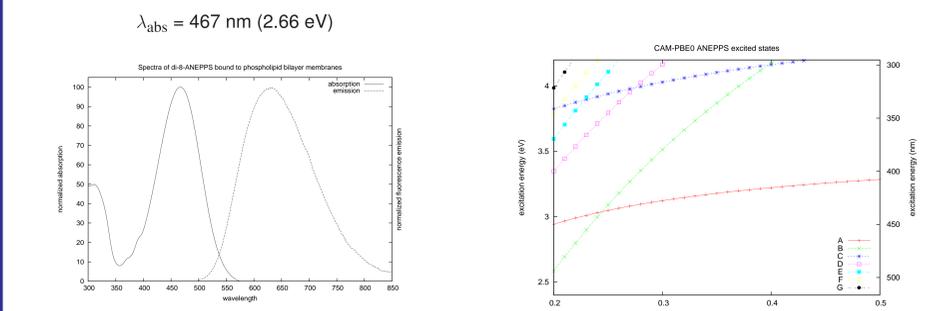
Despite thousands of applications of di-8-ANEPPS in the literature, there have been only a handful of papers characterizing its spectroscopic properties using precise experimental or theoretical techniques.

## ANEPPS fluorescence and the orbital picture



## Failure of TDDFT

Common exchange functionals cannot describe charge-transfer excited states and or the asymptotic potential. To correct for this, approximate exchange is attenuated and replaced with exact exchange.



The failure of DFT is due to the inability to properly describe the zwitterionic ground state and first excited state. Excitations corresponding to annihilation of the zwitterion are unphysical, yet DFT favors them due to problems with approximate exchange.

Inadequate basis sets exaggerate the instability of the zwitterion with DFT, but SCF does not have such issues to the strong localization provided by complete exact exchange.

## Coupled-cluster benchmarks

Coupled-cluster benchmarks including perturbative triples agree well with experiment and establish a baseline for calibrating density-functional-theory.

Based upon CCSD calculations, we estimate the Stokes shift to be 50% from intramolecular relaxation and 50% from environmental relaxation.

The effect of correlation on the excited-state energy is significant: 3.61 eV for CIS versus 2.98 eV for CCSD and 2.81 when triples are included.

| Active space      | CCSD | CR(T) |
|-------------------|------|-------|
| (-1.5, $\infty$ ) | 2.97 | -     |
| (-1.5, 1.5)       | 2.98 | 2.81  |
| (-0.7, 0.7)       | 3.23 | 3.15  |

## Role of benchmarking

- (1) For many systems, including water clusters and dialanine, high-level benchmarking confirms the utility of less expensive methods (particularly MP2).
- (2) Charge-transfer excited states defy description by conventional DFT approaches and suitable functionals were only discovered after high-level benchmarks provided a target.
- (3) Other types of problems, such as nonlinear optical properties, require more extensive benchmark studies due to critical role of solvent. A systematic protocol for benchmarking multiscale methods does not yet exist.

## Challenges for petascale computing

Existing computational chemistry codes are not suited for petascale architectures due to their large memory demands. Most packages are designed to run on “sledgehammer” clusters rather than tightly-coupled, balanced machines.

MP2 and CC algorithms must be integral-direct, be aware of data-locality and possess multiple layers of parallelism which map to multi-core and heterogenous architectures. Existing platforms — MPI and GA — do not adequately allow the programmer to express multi-level parallelism.

Portable performance requires automatic code generation for new procedures, specifically tensor contractions (in progress) and two-electron integrals.

## NWChem implementation and performance references

- (1) JRH, M. Valiev, W. A. de Jong and K. Kowalski, *J. Phys. Chem. A* **111**, 5492 (2007). *Calculations of properties using a hybrid coupled-cluster and molecular mechanics approach.*
- (2) JRH, W. A. de Jong and K. Kowalski, *J. Chem. Phys.* **127**, 144105 (2007). *Dynamic polarizabilities of polyaromatic hydrocarbons using coupled-cluster linear response theory.*
- (3) JRH, W. A. de Jong and K. Kowalski, *J. Chem. Phys.* **128**, 224102 (2008). *Coupled cluster dynamic polarizabilities including triple excitations.*
- (4) K. Kowalski, JRH, W. A. de Jong and A. J. Sadlej, *J. Chem. Phys.* **129**, 226101 (2008). *Coupled cluster calculations for static and dynamic polarizabilities of C<sub>60</sub>.*
- (5) JRH and K. Kowalski, *J. Chem. Phys.* **130**, 194108 (2009). *Parallel computation of coupled-cluster hyperpolarizabilities.*

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