NOVEL FUNCTIONAL FORMS AND PARAMETERIZATION METHODS FOR AB INITIO FORCE FIELD DEVELOPMENT

by

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Soli Deo gloria.

ACKNOWLEDGMENTS

It is customary for authors of academic books to include in their prefaces statements such as this: "I am indebted to ... for their invaluable help; however, any errors which remain are my sole responsibility." Occasionally an author will go further. Rather than say that if there are any mistakes then he is responsible for them, he will say that there will inevitably be some mistakes and he is responsible for them....

Although the shouldering of all responsibility is usually a social ritual, the admission that errors exist is not — it is often a sincere avowal of belief. But this appears to present a living and everyday example of a situation which philosophers have commonly dismissed as absurd; that it is sometimes rational to hold logically incompatible beliefs.

— David C. Makinson (1965)

Above is the famous "preface paradox," which illustrates how to use the `wbepi` environment for epigraphs at the beginning of chapters. You probably also want to thank the Academy.

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NOVEL FUNCTIONAL FORMS AND PARAMETERIZATION METHODS FOR AB INITIO FORCE FIELD DEVELOPMENT

Mary J. Van Vleet

Under the supervision of Professor J.R. Schmidt
At the University of Wisconsin-Madison

FIXME: basically a placeholder; do not believe

I did some research, read a bunch of papers, published a couple myself, (pick one):

1. ran some experiments and made some graphs,
2. proved some theorems

and now I have a job. I've assembled this document in the last couple of months so you will let me leave. Thanks!

J.R. Schmidt

ABSTRACT

FIXME: basically a placeholder; do not believe

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2. proved some theorems

and now I have a job. I've assembled this document in the last couple of months so you will let me leave. Thanks!

PUBLISHED WORK AND WORK IN PREPARATION

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[62] Van Vleet, M. J.; Misquitta, A. J.; Stone, A. J.; Schmidt, J. R. *J. Chem. Theory Comput*. **2016**, *12*, 3851–3870.

Part I

Introduction

1 INTRODUCTION

What are the functions of proteins in the body? How can we identify new and better drugs for improved disease treatment, or optimal materials for designing efficient solar cells? What are the microscopic mechanisms by which chemicals interact, undergo phase transitions, or react to form entirely new species? Increasingly, these and other essential chemical questions can be addressed with the aid of computer simulation,[2–8] recently enabling us to (as a small subset of examples) peer into the detailed mechanisms of enzyme catalysis,[9] watch proteins fold,[10–13] virtually screen for novel drug candidates,[14] and directly simulate hard-to-understand nucleation processes at an atomistic level.[15] The question, of course, is: how?

Beginning in the 1950s and 60s,

==

The aim of computer simulations of molecular systems is to compute macroscopic behavior from microscopic interactions. The main contributions a microscopic consideration can offer are (1) the understanding and (2) interpretation of experimental results, (3) semiquantitative estimates of experimental re- sults, and (4) the capability to interpolate or extrapolate experimental data into regions that are only difficultly accessible in the laboratory.[2]

The design of materials guided by computation is expected to lead to the discovery of new materials, reduction of materials development time and cost, and the rapid evolution of new materials into products.1[4]

Simulations can provide the ultimate detail concerning individ- ual particle motions as a function of time. Thus, they can be used to address specific questions about the properties of a model sys- tem, often more easily than experiments on the actual system. For many aspects of biomolecular function, it is these details that are of interest (for example, by what pathways does oxygen enter into and exit from the heme pocket in myoglobin?). Of course, experiments play an essential role in validating the simulation methodology: comparisons of simulation and experimental data serve to test the accuracy of the calculated results and to provide criteria for improving the methodology. This is particularly important because theoretical estimates of systematic errors inherent in simulations have not been possible âŁ” that is, the errors introduced by the use of empirical potentials are difficult to quantify ... There are three types of applications of simulation methods in the macromolecular area, as well as in other areas involving mesoscopic systems. The first uses simulation simply as a means of sampling configuration space. This is involved in the utiliza- tion of molecular dynamics, often with simulated annealing pro- tocols, to determine or refine structures with data obtained from experiments, as mentioned above. The second uses simulations to obtain a description of the system at equilibrium, including structural and motional properties (for example, atomic mean- square fluctuation amplitudes) and the values of thermodynamic parameters. For such applications, it is necessary that the simula- tions adequately sample configuration space, as in the first appli- cation, with the additional condition that each point be weighted by the appropriate Boltzmann factor. The third area uses simula- tions to examine the actual dynamics. Here not only is adequate sampling of configuration space with appropriate Boltzmann weighting required, but it must be done so as to correctly repre- sent the development of the system over time. For the first two areas, Monte Carlo simulations can be used, as well as molecular dynamics. By contrast, in the third area where the motions and their development with time are of primary interest, only molec- ular dynamics can provide the necessary information. The three sets of applications make increasing demands on simulation methods as to their required accuracy and precision.[7]

1.1 The Importance of Molecular Simulation

This ref[16] is super cool!

What is molecular simulation? What types of problems can it solve? How does molecular simulation work? (Be sure to include solving Newton's EQs of motion and relevant details on the partition function and interaction energies!)

2 BACKGROUND

2.1 Molecular Mechanics and the Theory of Intermolecular Forces

What is a force field? What are the important components of a force field, and how do we model them?

2.1.1 The Many-Body Expansion

How do we break apart a force field into manageable pieces? Why does it make sense to break a force field into 2- and many-body components?

2.1.2 Energy Decomposition Schemes

Intramolecular Interactions

Brief commentary on the non-intermolecular portions of a force field

Electrostatics

Conceptual description of electrostatics: long-range multipoles and charge penetration

Exchange

Quantum-mechanically-based Pauli Exclusion. Theoretical grounds for exponential behavior

Induction

Charge transfer. Polarization. Polarization Damping.

Dispersion

Theoretical Formulation. Damping.

2.2 Ab-Initio Force Field Development

2.2.1 Electronic Structure Benchmarks

SAPT

General SAPT methodology. DFT-SAPT.

Coupled-Cluster Methods

CCSD(T). CCSD(T)-f12.

2.3 ISA-based methods for force field development

What is ISA? How can ISA be used to generate parameters for intermolecular force field development? What progress has been made from this approach?

Part II

Published Work

Part III

Unpublished Work

Part IV

Practical Matters

Part V

Conclusions and Future Work

Part VI

Codes

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ACRONYMS

C | D | I | M | P | S

C

CUS Coordinatively-Unsaturated. iv

D

DMA Distributed Multipole Analysis. v, viii

I

isa Iterated Stockholder Atoms. v, viii, *Glossary:* ISA

M

MOF Metal-Organic Framework. iv

P

PES potential energy surface. ix, 113

POInter **P**arameter **O**ptimizer for **Inter**-molecular Force Fields. vi, vii

S

SAPT Symmetry-Adapted Perturbation Theory. v, ix, *Glossary:* SAPT

GLOSSARY

C | I | L | P | S

C

CCSD(T) Coupled Cluster methods including singles, doubles, and perturbative triples excitations. CCSD(T). Given a sufficiently large (aVQZ or better) basis set, can be used as a 'gold-standard' estimate of the exact potential energy surface. v

I

ISA Iterated Stockholder Atoms,FILL . v

L

LMO-EDA FILL . iv, ix

P

POInter FILL . vi

S

SAPT Symmetry-Adapted Perturbation Theory, a perturbative treatment of intermolecular interactions which is pretty cool. v