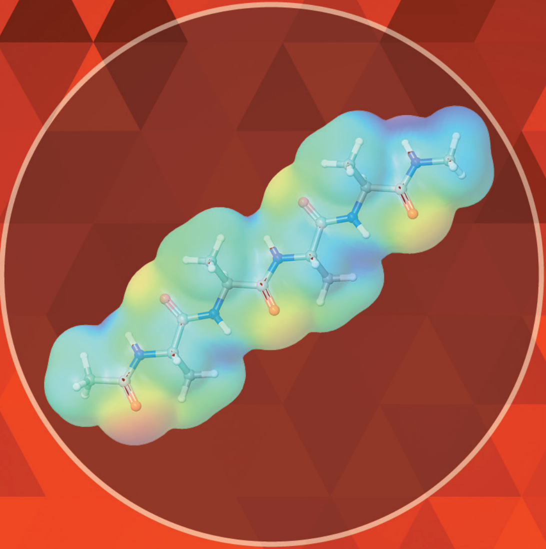
Third Edition

Introduction to
Computational Chemistry



Frank Jensen

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Introduction to Computational Chemistry

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Third Edition

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Preface to the First Edition

Computational chemistry is rapidly emerging as a subfield of theoretical chemistry, where the primary focus is on solving chemically related problems by calculations. For the newcomer to the field, there are three main problems:

(1) Deciphering the code. The language of computational chemistry is littered with acronyms, what do these abbreviations stand for in terms of underlying assumptions and approximations?
(2) Technical problems. How does one actually run the program and what to look for in the output?
(3) Quality assessment. How good is the number that has been calculated?

Point (1) is part of every new field: there is not much to do about it. If you want to live in another country, you have to learn the language. If you want to use computational chemistry methods, you need to learn the acronyms. I have tried in the present book to include a good fraction of the most commonly used abbreviations and standard procedures.

Point (2) is both hardware and software specific. It is not well suited for a textbook, as the information rapidly becomes out of date. The average lifetime of computer hardware is a few years, the time between new versions of software is even less. Problems of type (2) need to be solved "on location". I have made one exception, however, and have included a short discussion of how to make Z-matrices. A Z-matrix is a convenient way of specifying a molecular geometry in terms of internal coordinates, and it is used by many electronic structure programs. Furthermore, geometry optimizations are often performed in Z-matrix variables, and since optimizations in a good set of internal coordinates are significantly faster than in Cartesian coordinates, it is important to have a reasonable understanding of Z-matrix construction.

As computer programs evolve they become easier to use. Modern programs often communicate with the user in terms of a graphical interface, and many methods have become essential "black box" procedures: if you can draw the molecule, you can also do the calculation. This effectively means that you no longer have to be a highly trained theoretician to run even quite sophisticated calculations.

The ease with which calculations can be performed means that point (3) has become the central theme in computational chemistry. It is quite easy to run a series of calculations that produce results that are absolutely meaningless. The program will not tell you whether the chosen method is valid for the problem you are studying. Quality assessment is thus an absolute requirement. This, however, requires much more experience and insight than just running the program. A basic understanding of the theory behind the method is needed, and a knowledge of the performance of the method for other systems. If you are breaking new ground, where there is no previous experience, you need a way of calibrating the results.

The lack of quality assessment is probably one of the reasons why computational chemistry has (had) a somewhat bleak reputation. "If five different computational methods give five widely different results, what has computational chemistry contributed? You just pick the number closest to experiments and claim that you can reproduce experimental data accurately." One commonly sees statements of the type "The theoretical results for property X are in disagreement. Calculation at the CCSD(T)/6-31G(d,p) level predicts that…, while the MINDO/3 method gives opposing results. There is thus no clear consent from theory." This is clearly a lack of understanding of the quality of the calculations. If the results disagree, there is a very high probability that the CCSD(T) results are basically correct, and the MINDO/3 results are wrong. If you want to make predictions, and not merely reproduce known results, you need to be able to judge the quality of your results. This is by far the most difficult task in computational chemistry. I hope the present book will give some idea of the limitations of different methods.

Computers don't solve problems, people do. Computers just generate numbers. Although computational chemistry has evolved to the stage where it often can be competitive with experimental methods for generating a value for a given property of a given molecule, the number of possible molecules (there are an estimated 10^{200} molecules with a molecular weight less than 850) and their associated properties is so huge that only a very tiny fraction will ever be amenable to calculations (or experiments). Furthermore, with the constant increase in computational power, a calculation that barely can be done today will be possible on medium-sized machines in 5–10 years. Prediction of properties with methods that do not provide converged results (with respect to theoretical level) will typically only have a lifetime of a few years before being surpassed by more accurate calculations.

The real strength of computational chemistry is the ability to generate data (e.g. by analyzing the wave function) from which a human may gain *insight*, and thereby rationalize the behavior of a large class of molecules. Such insights and rationalizations are much more likely to be useful over a longer period of time than the raw results themselves. A good example is the concept used by organic chemists with molecules composed of functional groups, and representing reactions by "pushing electrons". This may not be particularly accurate from a quantum mechanical point of view, but it is very effective in rationalizing a large body of experimental results, and has good predictive power.

Just as computers do not solve problems, mathematics by itself does not provide insight. It merely provides formulas, a framework for organizing thoughts. It is in this spirit that I have tried to write this book. Only the necessary (obviously a subjective criterion) mathematical background has been provided, the aim being that the reader should be able to understand the premises and limitations of different methods, and follow the main steps in running a calculation. This means that in many cases I have omitted to tell the reader of some of the finer details, which may annoy the purists. However, I believe the large overview is necessary before embarking on a more stringent and detailed derivation of the mathematics. The goal of this book is to provide an overview of commonly used methods, giving enough theoretical background to understand why, for example, the AMBER force field is used for modeling proteins but MM2 is used for small organic molecules, or why coupled cluster inherently is an iterative method, while perturbation theory and configuration interaction inherently are non-iterative methods, although the CI problem in practice is solved by iterative techniques.

The prime focus of this book is on calculating molecular structures and (relative) energies, and less on molecular properties or dynamical aspects. In my experience, predicting structures and energetics are the main uses of computational chemistry today, although this may well change in the coming years. I have tried to include most methods that are already extensively used, together with some that I expect to become generally available in the near future. How detailed the methods are described depends partly on how practical and commonly used the methods are (both in terms of computational resources and software), and partly reflects my own limitations in terms of understanding. Although simulations (e.g. molecular dynamics) are becoming increasingly powerful tools, only a very rudimentary introduction is provided in Chapter 16. The area is outside my expertise, and several excellent textbooks are already available.

Computational chemistry contains a strong practical element. Theoretical methods must be translated into working computer programs in order to produce results. Different algorithms, however, may have different behaviors in practice, and it becomes necessary to be able to evaluate whether a certain type of calculation can be carried out with the available computers. The book thus contains some guidelines for evaluating what type of resources are necessary for carrying out a given calculation.

The present book grew out of a series of lecture notes that I have used for teaching a course in computational chemistry at Odense University, and the style of the book reflects its origin. It is difficult to master all disciplines in the vast field of computational chemistry. A special thanks to H. J. Aa. Jensen, K. V. Mikkelsen, T. Saue, S. P. A. Sauer, M. Schmidt, P. M. W. Gill, P.-O. Norrby, D. L. Cooper, T. U. Helgaker and H. G. Petersen for having read various parts of the book and providing input. Remaining errors are of course my sole responsibility. A good part of the final transformation from a set of lecture notes to the present book was done during a sabbatical leave spent with Prof. L. Radom at the Research School of Chemistry, Australia National University, Canberra, Australia. A special thanks to him for his hospitality during the stay.

A few comments on the layout of the book. Definitions, acronyms or common phrases are marked in *italic*; these can be found in the index. Underline is used for emphasizing important points. Operators, vectors and matrices are denoted in **bold**, scalars in normal text. Although I have tried to keep the notation as consistent as possible, different branches in computational chemistry often use different symbols for the same quantity. In order to comply with common usage, I have elected sometimes to switch notation between chapters. The second derivative of the energy, for example, is called the force constant k in force field theory; the corresponding matrix is denoted $\mathbf{F}$ when discussing vibrations, and called the Hessian $\mathbf{H}$ for optimization purposes.

I have assumed that the reader has no prior knowledge of concepts specific to computational chemistry, but has a working understanding of introductory quantum mechanics and elementary mathematics, especially linear algebra, vector, differential and integral calculus. The following features specific to chemistry are used in the present book without further introduction. Adequate descriptions may be found in a number of quantum chemistry textbooks (J. P. Lowe, *Quantum Chemistry*, Academic Press, 1993; I. N. Levine, *Quantum Chemistry*, Prentice Hall, 1992; P. W. Atkins, *Molecular Quantum Mechanics*, Oxford University Press, 1983).

(1) The Schrödinger equation, with the consequences of quantized solutions and quantum numbers.
(2) The interpretation of the square of the wave function as a probability distribution, the Heisenberg uncertainty principle and the possibility of tunneling.
(3) The solutions for the hydrogen atom, atomic orbitals.
(4) The solutions for the harmonic oscillator and rigid rotor.
(5) The molecular orbitals for the H_2 molecule generated as a linear combination of two *s*-functions, one on each nuclear centre.
(6) Point group symmetry, notation and representations, and the group theoretical condition for when an integral is zero.

I have elected to include a discussion of the variational principle and perturbational methods, although these are often covered in courses in elementary quantum mechanics. The properties of angular momentum coupling are used at the level of knowing the difference between a singlet and triplet state. I do not believe that it is necessary to understand the details of vector coupling to understand the implications.

Although I have tried to keep each chapter as self-contained as possible, there are unavoidable dependencies. The part in Chapter 3 describing HF methods is a prerequisite for understanding Chapter 4. Both these chapters use terms and concepts for basis sets which are treated in Chapter 5. Chapter 5, in turn, relies on concepts in Chapters 3 and 4, that is these three chapters form the core for understanding modern electronic structure calculations. Many of the concepts in Chapters 3 and 4 are also used in Chapters 6, 7, 9, 11 and 15 without further introduction, although these five chapters probably can be read with some benefits without a detailed understanding of Chapters 3 and 4. Chapter 8, and to a certain extent also Chapter 10, are fairly advanced for an introductory textbook, such as the present, and can be skipped. They do, however, represent areas that are probably going to be more and more important in the coming years. Function optimization, which is described separately in Chapter 14, is part of many areas, but a detailed understanding is not required for following the arguments in the other chapters. Chapters 12 and 13 are fairly self-contained, and form some of the background for the methods in the other chapters. In my own course I normally take Chapters 12, 13 and 14 fairly early in the course, as they provide background for Chapters 3, 4 and 5.

If you would like to make comments, advise me of possible errors, make clarifications, add references, etc., or view the current list of misprints and corrections, please visit the author's website (URL: http://bogense.chem.ou.dk/~icc).

Preface to the Second Edition

The changes relative to the first edition are as follows:

- Numerous misprints and inaccuracies in the first edition have been corrected. Most likely some new ones have been introduced in the process; please check the book website for the most recent correction list and feel free to report possible problems. Since web addresses have a tendency to change regularly, please use your favourite search engine to locate the current URL.
- The methodologies and references in each chapter have been updated with new developments published between 1998 and 2005.
- More extensive referencing. Complete referencing is impossible, given the large breadth of subjects. I have tried to include references that preferably are recent, have a broad scope and include key references. From these the reader can get an entry into the field.
- Many figures and illustrations have been redone. The use of color illustrations has been deferred in favor of keeping the price of the book down.
- Each chapter or section now starts with a short overview of the methods, described without mathematics. This may be useful for getting a feel for the methods, without embarking on all the mathematical details. The overview is followed by a more detailed mathematical description of the method, including some key references that may be consulted for more details. At the end of the chapter or section, some of the pitfalls and the directions of current research are outlined.
- Energy units have been converted from kcal/mol to kJ/mol, based on the general opinion that the scientific world should move towards SI units.
- Furthermore, some chapters have undergone major restructuring:
  - Chapter 16 (Chapter 13 in the first edition) has been greatly expanded to include a summary of the most important mathematical techniques used in the book. The goal is to make the book more self-contained, that is relevant mathematical techniques used in the book are at least rudimentarily discussed in Chapter 16.
  - All the statistical mechanics formalism has been collected in Chapter 13.
  - Chapter 14 has been expanded to cover more of the methodologies used in molecular dynamics.
  - Chapter 12 on optimization techniques has been restructured.
  - Chapter 6 on density functional methods has been rewritten.
  - A new Chapter 1 has been introduced to illustrate the similarities and differences between classical and quantum mechanics, and to provide some fundamental background.
  - A rudimentary treatment of periodic systems has been incorporated in Chapters 3 and 14.
  - A new Chapter 17 has been introduced to describe statistics and QSAR methods.

- I have tried to make the book more modular, that is each chapter is more self-contained. This makes it possible to use only selected chapters, for example for a course, but has the drawback of repeating the same things in several chapters, rather than simply cross-referencing.

Although the modularity has been improved, there are unavoidable interdependencies. Chapters 3, 4 and 5 contain the essentials of electronic structure theory, and most would include Chapter 6 describing density functional methods. Chapter 2 contains a description of empirical force field methods, and this is tightly coupled to the simulation methods in Chapter 14, which of course leans on the statistical mechanics in Chapter 13. Chapter 1 on fundamental issues is of a more philosophical nature, and can be skipped. Chapter 16 on mathematical techniques is mainly for those not already familiar with this, and Chapter 17 on statistical methods may be skipped as well.

Definitions, acronyms and common phrases are marked in *italic*. In a change from the first edition, where underlining was used, *italic* text has also been used for emphasizing important points.

A number of people have offered valuable help and criticisms during the updating process. I would especially like to thank S. P. A. Sauer, H. J. Aa. Jensen, E. J. Baerends and P. L. A. Popelier for having read various parts of the book and provided input. Remaining errors are of course my sole responsibility.

Specific Comments on the Preface to the First Edition

Bohacek *et al.*[1] have estimated the number of possible compounds composed of H, C, N, O and S atoms with 30 non-hydrogen atoms or fewer to be 10^{60}. Although this number is so large that only a very tiny fraction will ever be amenable to investigation, the concept of functional groups means that one does not need to evaluate all compounds in a given class to determine their properties. The number of alkanes meeting the above criteria is $\sim 10^{10}$: clearly these will all have very similar and well-understood properties, and there is no need to investigate all 10^{10} compounds.

Reference

1 R. S. Bohacek, C. McMartin and W. C. Guida, *Medicinal Research Reviews* **16** (1), 3–50 (1996).

Preface to the Third Edition

The changes relative to the second edition are as follows:

Numerous misprints and inaccuracies in the second edition have been corrected. Most likely some new ones have been introduced in the process, please check the book website for the most recent correction list and feel free to report possible problems.

http://www.wiley.com/go/jensen/computationalchemistry3

- Methodologies and references in each chapter have been updated with new developments published between 2005 and 2015.
- Semi-empirical methods have been moved from Chapter 3 to a separate Chapter 7.
- Some specific new topics that have been included:
    1. Polarizable force fields
    2. Tight-binding DFT
    3. More extensive DFT functionals, including range-separated and dispersion corrected functionals
    4. More extensive covering of excited states
    5. More extensive time-dependent molecular properties
    6. Accelerated molecular dynamics methods
    7. Tensor decomposition methods
    8. Cluster analysis
    9. Reduced scaling and reduced prefactor methods.

A reoccuring request over the years for a third edition has been: “It would be very useful to have recommendations on which method to use for a given type of problem.” I agree that this would be useful, but I have refrained from it for two main reasons:

1. Problems range from very narrow ones for a small set of systems, to very broad ones for a wide set of systems, and covering these and all intermediate cases even rudementary is virtually impossible.
2. Making recommendations like “*do not use method XXX because it gives poor results*” will immediately invoke harsh responses from the developers of method XXX, showing that it gives good results for a selected subset of problems and systems.

A vivid example of the above is the pletora of density functional methods where a particular functional often gives good results for a selected subset of systems and properties, but may fail for other subsets of systems and properties, and no current functional provides good results for all systems and properties. I have limited the recommendations to point out well-known deficiencies.

A similar problem is present when selecting references. I have selected references based on three overriding principles:

1. References to work containing reference data, such as experimental structural results, or ground-breaking work, such as the Hohenberg–Koch theorem, are to the original work.
2. Early in each chapter or subsection, I have included review-type papers, where these are available.
3. Lacking review-type papers, I have selected one or a few papers that preferably are recent, but must at the same time also be written in a scholarly style, and should contain a good selection of references.

The process of literature searching has improved tremendously over the years, and having a few entry points usually allows searching both backwards and forwards to find other references within the selected topic.

In relation to the quoted number of compounds possible for a given number of atoms, Ruddigkeit *et al.* have estimated the number of plausible compounds composed of H, C, N, O, S and a halogen with up to 17 non-hydrogen atoms to be 166×10^9.[1]

Reference

1 L. Ruddigkeit, R. van Deursen, L. C. Blum and J.-L. Reymond, *Journal of Chemical Information and Modeling* **52** (11), 2864–2875 (2012).

1

Introduction

Chemistry is the science dealing with construction, transformation and properties of molecules. Theoretical chemistry is the subfield where mathematical methods are combined with fundamental laws of physics to study processes of chemical relevance.$^{1-7}$

Molecules are traditionally considered as "composed" of atoms or, in a more general sense, as a collection of charged particles, positive nuclei and negative electrons. The only important physical force for chemical phenomena is the Coulomb interaction between these charged particles. Molecules differ because they contain different nuclei and numbers of electrons, or because the nuclear centers are at different geometrical positions. The latter may be "chemically different" molecules such as ethanol and dimethyl ether or different "conformations" of, for example, butane.

Given a set of nuclei and electrons, theoretical chemistry can attempt to calculate things such as:

- Which geometrical arrangements of the nuclei correspond to stable molecules?
- What are their relative energies?
- What are their properties (dipole moment, polarizability, NMR coupling constants, etc.)?
- What is the rate at which one stable molecule can transform into another?
- What is the time dependence of molecular structures and properties?
- How do different molecules interact?

The only systems that can be solved exactly are those composed of only one or two particles, where the latter can be separated into two pseudo one-particle problems by introducing a "center of mass" coordinate system. Numerical solutions to a given accuracy (which may be so high that the solutions are essentially "exact") can be generated for many-body systems, by performing a very large number of mathematical operations. Prior to the advent of electronic computers (i.e. before 1950), the number of systems that could be treated with a high accuracy was thus very limited. During the 1960s and 1970s, electronic computers evolved from a few very expensive, difficult to use, machines to become generally available for researchers all over the world. The performance for a given price has been steadily increasing since and the use of computers is now widespread in many branches of science. This has spawned a new field in chemistry, *computational chemistry*, where the computer is used as an "experimental" tool, much like, for example, an NMR (nuclear magnetic resonance) spectrometer.

Computational chemistry is focused on obtaining results relevant to chemical problems, not directly at developing new theoretical methods. There is of course a strong interplay between traditional theoretical chemistry and computational chemistry. Developing new theoretical models may

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Companion Website: http://www.wiley.com/go/jensen/computationalchemistry3

enable new problems to be studied, and results from calculations may reveal limitations and suggest improvements in the underlying theory. Depending on the accuracy wanted, and the nature of the system at hand, one can today obtain useful information for systems containing up to several thousand particles. One of the main problems in computational chemistry is selecting a suitable level of theory for a given problem and to be able to evaluate the quality of the obtained results. The present book will try to put the variety of modern computational methods into perspective, hopefully giving the reader a chance of estimating which types of problems can benefit from calculations.

1.1 Fundamental Issues

Before embarking on a detailed description of the theoretical methods in computational chemistry, it may be useful to take a wider look at the background for the theoretical models and how they relate to methods in other parts of science, such as physics and astronomy.

A very large fraction of the computational resources in chemistry and physics is used in solving the so-called *many-body problem*. The essence of the problem is that two-particle systems can in many cases be solved exactly by mathematical methods, producing solutions in terms of analytical functions. Systems composed of more than two particles cannot be solved by analytical methods. Computational methods can, however, produce approximate solutions, which in principle may be refined to any desired degree of accuracy.

Computers are not smart – at the core level they are in fact very primitive. Smart programmers, however, can make sophisticated computer programs, which may make the computer appear smart, or even intelligent. However, the basics of any computer program consist of doing a few simple tasks such as:

- Performing a mathematical operation (adding, multiplying, square root, cosine, etc.) on one or two numbers.
- Determining the relationship (equal to, greater than, less than or equal to, etc.) between two numbers.
- Branching depending on a decision (add two numbers if $N > 10$, else subtract one number from the other).
- Looping (performing the same operation a number of times, perhaps on a set of data).
- Reading and writing data from and to external files.

These tasks are the essence of any programming language, although the syntax, data handling and efficiency depend on the language. The main reason why computers are so useful is the sheer speed with which they can perform these operations. Even a cheap off-the-shelf personal computer can perform billions (10^9) of operations per second.

Within the scientific world, computers are used for two main tasks: performing numerically intensive calculations and analyzing large amounts of data. The latter can, for example, be pictures generated by astronomical telescopes or gene sequences in the bioinformatics area that need to be compared. The numerically intensive tasks are typically related to simulating the behavior of the real world, by a more or less sophisticated computational model. The main problem in simulations is the multiscale nature of real-world problems, often spanning from subnanometers to millimeters (10^{-10}–10^{-3}) in spatial dimensions and from femtoseconds to milliseconds (10^{-15}–10^{-3}) in the time domain.

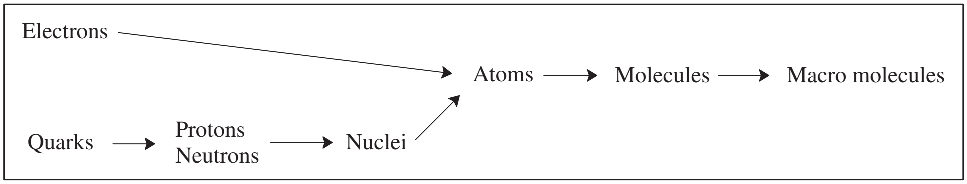

Figure 1.1 Hierarchy of building blocks for describing a chemical system.

1.2 Describing the System

In order to describe a system we need four fundamental features:

- System description. What are the fundamental units or "particles" and how many are there?
- Starting condition. Where are the particles and what are their velocities?
- Interaction. What is the mathematical form for the forces acting between the particles?
- Dynamical equation. What is the mathematical form for evolving the system in time?

The choice of "particles" puts limitations on what we are ultimately able to describe. If we choose atomic nuclei and electrons as our building blocks, we can describe atoms and molecules, but not the internal structure of the atomic nucleus. If we choose atoms as the building blocks, we can describe molecular structures, but not the details of the electron distribution. If we choose amino acids as the building blocks, we may be able to describe the overall structure of a protein, but not the details of atomic movements (see Figure 1.1).

The choice of starting conditions effectively determines what we are trying to describe. The complete phase space (i.e. all possible values of positions and velocities for all particles) is huge and we will only be able to describe a small part of it. Our choice of starting conditions determines which part of the phase space we sample, for example which (structural or conformational) isomer or chemical reaction we can describe. There are many structural isomers with the molecular formula C_6H_6, but if we want to study benzene, we should place the nuclei in a hexagonal pattern and start them with relatively low velocities.

The interaction between particles in combination with the dynamical equation determines how the system evolves in time. At the fundamental level, the only important force at the atomic level is the electromagnetic interaction. Depending on the choice of system description (particles), however, this may result in different effective forces. In force field methods, for example, the interactions are parameterized as stretch, bend, torsional, van der Waals, etc., interactions.

The dynamical equation describes the time evolution of the system. It is given as a differential equation involving both time and space derivatives, with the exact form depending on the particle masses and velocities. By solving the dynamical equation the particles' position and velocity can be predicted at later (or earlier) times relative to the starting conditions, that is how the system evolves in the phase space.

1.3 Fundamental Forces

The interaction between particles can be described in terms of either a force (**F**) or a potential (**V**). These are equivalent, as the force is the derivative of the potential with respect to the position **r**:

$$\mathbf{F}(\mathbf{r}) = -\frac{\partial \mathbf{V}}{\partial \mathbf{r}} \tag{1.1}$$

Table 1.1 Fundamental interactions.

Name	Particles	Range (m)	Relative strength
Strong interaction	Quarks	$<10^{-15}$	100
Weak interaction	Quarks, leptons	$<10^{-15}$	0.001
Electromagnetic	Charged particles	∞	1
Gravitational	Mass particles	∞	10^{-40}

Current knowledge indicates that there are four fundamental interactions, at least under normal conditions, as listed in Table 1.1.

Quarks are the building blocks of protons and neutrons, and lepton is a common name for a group of particles including the electron and the neutrino. The strong interaction is the force holding the atomic nucleus together, despite the repulsion between the positively charged protons. The weak interaction is responsible for radioactive decay of nuclei by conversion of neutrons to protons (β decay). The strong and weak interactions are short-ranged and are only important within the atomic nucleus.

Both the electromagnetic and gravitational interactions depend on the inverse distance between the particles and are therefore of infinite range. The electromagnetic interaction occurs between all charged particles, while the gravitational interaction occurs between all particles with a mass, and they have the same overall functional form:

$$\begin{aligned} \mathbf{V}_{\text{elec}}(\mathbf{r}_{ij}) &= C_{\text{elec}}\frac{q_i q_j}{r_{ij}} \\ \mathbf{V}_{\text{grav}}(\mathbf{r}_{ij}) &= -C_{\text{grav}}\frac{m_i m_j}{r_{ij}} \end{aligned} \tag{1.2}$$

In SI units $C_{\text{elec}} = 9.0 \times 10^9$ N m^2/C^2 and $C_{\text{grav}} = 6.7 \times 10^{-11}$ N m^2/kg^2, while in atomic units $C_{\text{elec}} = 1$ and $C_{\text{grav}} = 2.4 \times 10^{-43}$. On an atomic scale, the gravitational interaction is completely negligible compared with the electromagnetic interaction. For the interaction between a proton and an electron, for example, the ratio between $\mathbf{V}_{\text{elec}}$ and $\mathbf{V}_{\text{grav}}$ is 10^{39}. On a large macroscopic scale, such as planets, the situation is reversed. Here the gravitational interaction completely dominates and the electromagnetic interaction is absent.

On a more fundamental level, it is believed that the four forces are really just different manifestations of a single common interaction, because of the relatively low energy regime we are living in. It has been shown that the weak and electromagnetic forces can be combined into a single unified theory, called *quantum electrodynamics* (QED). Similarly, the strong interaction can be coupled with QED into what is known as the *standard model*. Much effort is being devoted to also include the gravitational interaction into a grand unified theory, and *string theory* is currently believed to hold the greatest promise for such a unification.

Only the electromagnetic interaction is important at the atomic and molecular level, and in the large majority of cases, the simple Coulomb form (in atomic units) is sufficient:

$$\mathbf{V}_{\text{Coulomb}}(\mathbf{r}_{ij}) = \frac{q_i q_j}{r_{ij}} \tag{1.3}$$

Within QED, the Coulomb interaction is only the zeroth-order term and the complete interaction can be written as an expansion in terms of the (inverse) velocity of light, *c*. For systems where relativistic effects are important (i.e. containing elements from the lower part of the periodic table) or when high accuracy is required, the first-order correction (corresponding to an expansion up to $1/c^2$) for the electron–electron interaction may be included:

$$\mathbf{V}_{\text{elec}}(\mathbf{r}_{12}) = \frac{1}{r_{12}}\left[1 - \frac{1}{2}\left(\boldsymbol{\alpha}_1 \cdot \boldsymbol{\alpha}_2 + \frac{(\boldsymbol{\alpha}_1 \cdot \mathbf{r}_{12})(\boldsymbol{\alpha}_2 \cdot \mathbf{r}_{12})}{r_{12}^2}\right)\right] \tag{1.4}$$

The first-order correction is known as the *Breit* term, and $\boldsymbol{\alpha}_1$ and $\boldsymbol{\alpha}_2$ represent velocity operators. The first term in Equation (1.4) can be considered as a magnetic interaction between two electrons, but the whole Breit correction describes a "retardation" effect, since the interaction between distant particles is "delayed" relative to interactions between close particles, owing to the finite value of c (in atomic units, $c \sim 137$).

1.4 The Dynamical Equation

The mathematical form for the dynamical equation depends on the mass and velocity of the particles and can be divided into four regimes (see Figure 1.2).

Newtonian mechanics, exemplified by Newton's second law ($\mathbf{F} = m\mathbf{a}$), applies for "heavy", "slow-moving" particles. Relativistic effects become important when the velocity is comparable to the speed of light, causing an increase in the particle mass m relative to the rest mass m_0. A pragmatic borderline between Newtonian and relativistic (Einstein) mechanics is $\sim{}^1/_3c$, corresponding to a relativistic correction of a few percent.

Light particles display both wave and particle characteristics and must be described by quantum mechanics, with the borderline being approximately the mass of a proton. Electrons are much lighter and can only be described by quantum mechanics, while atoms and molecules, with a few exceptions, behave essentially as classical particles. Hydrogen (protons), being the lightest nucleus, represents a borderline case, which means that quantum corrections in some cases are essential. A prime example is the tunnelling of hydrogen through barriers, allowing reactions involving hydrogen to occur faster than expected from transition state theory.

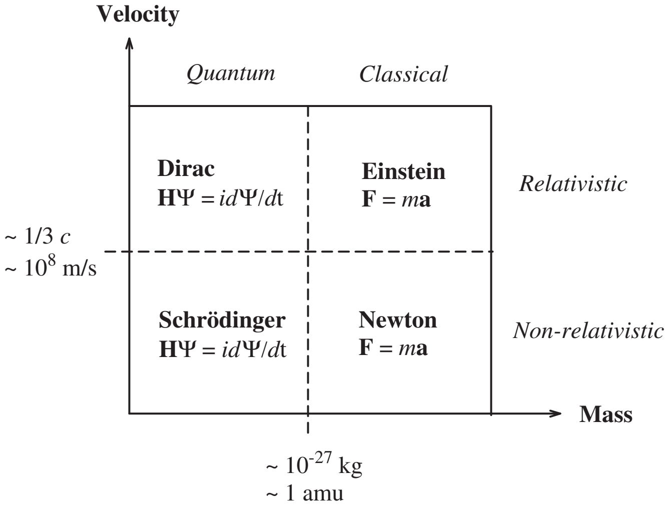

Figure 1.2 Domains of dynamical equations.

A major difference between quantum and classical mechanics is that classical mechanics is *deterministic* while quantum mechanics is *probabilistic* (more correctly, quantum mechanics is also deterministic, but the interpretation is probabilistic). Deterministic means that Newton's equation can be integrated over time (forward or backward) and can predict where the particles are at a certain time. This, for example, allows prediction of where and when solar eclipses will occur many thousands of years in advance, with an accuracy of meters and seconds. Quantum mechanics, on the other hand, only allows calculation of the *probability* of a particle being at a certain place at a certain time. The probability function is given as the square of a wave function, $P(\mathbf{r},t) = \Psi^2(\mathbf{r},t)$, where the wave function Ψ is obtained by solving either the Schrödinger (non-relativistic) or Dirac (relativistic) equation. Although they appear to be the same in Figure 1.2, they differ considerably in the form of the operator **H**.

For classical mechanics at low velocities compared with the speed of light, Newton's second law applies:

$$\mathbf{F} = \frac{\mathrm{d}\mathbf{p}}{\mathrm{d}t} \tag{1.5}$$

If the particle mass is constant, the derivative of the momentum **p** is the mass times the acceleration:

$$\begin{aligned} \mathbf{p} &= m\mathbf{v} \\ \mathbf{F} &= \frac{\mathrm{d}\mathbf{p}}{\mathrm{d}t} = m\frac{\mathrm{d}\mathbf{v}}{\mathrm{d}t} = m\mathbf{a} \end{aligned} \tag{1.6}$$

Since the force is the derivative of the potential (Equation (1.1)) and the acceleration is the second derivative of the position **r** with respect to time, it may also be written in a differential form:

$$-\frac{\partial \mathbf{V}}{\partial \mathbf{r}} = m\frac{\partial^2 \mathbf{r}}{\partial t^2} \tag{1.7}$$

Solving this equation gives the position of each particle as a function of time, that is $\mathbf{r}(t)$.

At velocities comparable to the speed of light, Newton's equation is formally unchanged, but the particle mass becomes a function of the velocity, and the force is therefore not simply a constant (mass) times the acceleration:

$$m = \frac{m_0}{\sqrt{1 - v^2/c^2}} \tag{1.8}$$

For particles with small masses, primarily electrons, quantum mechanics must be employed. At low velocities, the relevant equation is the time-dependent Schrödinger equation:

$$\mathbf{H}\Psi = i\frac{\partial \Psi}{\partial t} \tag{1.9}$$

The Hamiltonian operator is given as a sum of kinetic and potential energy operators:

$$\begin{aligned} \mathbf{H}_{\text{Schrödinger}} &= \mathbf{T} + \mathbf{V} \\ \mathbf{T} &= \frac{\mathbf{p}^2}{2m} = -\frac{1}{2m}\nabla^2 \end{aligned} \tag{1.10}$$

Solving the Schrödinger equation gives the wave function as a function of time, and the probability of observing a particle at a position **r** and time t is given as the square of the wave function:

$$P(\mathbf{r}, t) = \Psi^2(\mathbf{r}, t) \tag{1.11}$$

For light particles moving at a significant fraction of the speed of light, the Schrödinger equation is replaced by the Dirac equation:

$$\mathbf{H}\Psi = i\frac{\partial \Psi}{\partial t} \tag{1.12}$$

Although it is formally identical to the Schrödinger equation, the Hamiltonian operator is significantly more complicated:

$$\mathbf{H}_{\text{Dirac}} = (c\boldsymbol{\alpha} \cdot \mathbf{p} + \boldsymbol{\beta} mc^2) + \mathbf{V} \tag{1.13}$$

The $\boldsymbol{\alpha}$ and $\boldsymbol{\beta}$ are 4×4 matrices and the relativistic wave function consequently has four components. Traditionally, these are labelled the *large* and *small* components, each having an α and β spin function (note the difference between the $\boldsymbol{\alpha}$ and $\boldsymbol{\beta}$ matrices and α and β spin functions). The large component describes the electronic part of the wave function, while the small component describes the positronic (electron antiparticle) part of the wave function, and the $\boldsymbol{\alpha}$ and $\boldsymbol{\beta}$ matrices couple these components. In the limit of $c \to \infty$, the Dirac equation reduces to the Schrödinger equation, and the two large components of the wave function reduce to the α and β spin-orbitals in the Schrödinger picture.

1.5 Solving the Dynamical Equation

Both the Newton/Einstein and Schrödinger/Dirac dynamical equations are differential equations involving the derivative of either the position vector or wave function with respect to time. For two-particle systems with simple interaction potentials $\mathbf{V}$, these can be solved analytically, giving $\mathbf{r}(t)$ or $\Psi(\mathbf{r},t)$ in terms of mathematical functions. For systems with more than two particles, the differential equation must be solved by numerical techniques involving a sequence of small finite time steps.

Consider a set of particles described by a position vector $\mathbf{r}_i$ at a given time t_i. A small time step Δt later, the positions can be calculated from the velocities, acceleration, hyperaccelerations, etc., corresponding to a Taylor expansion with time as the variable

$$\mathbf{r}_{i+1} = \mathbf{r}_i + \mathbf{v}_i(\Delta t) + \tfrac{1}{2}\mathbf{a}_i(\Delta t)^2 + \tfrac{1}{6}\mathbf{b}_i(\Delta t)^3 + \cdots \tag{1.14}$$

The positions a small time step Δt earlier were (replacing Δt with $-\Delta t$)

$$\mathbf{r}_{i-1} = \mathbf{r}_i - \mathbf{v}_i(\Delta t) + \tfrac{1}{2}\mathbf{a}_i(\Delta t)^2 - \tfrac{1}{6}\mathbf{b}_i(\Delta t)^3 + \cdots \tag{1.15}$$

Addition of these two equations gives a recipe for predicting the positions a time step Δt later from the current and previous positions, and the current acceleration, a method known as the *Verlet* algorithm:

$$\mathbf{r}_{i+1} = (2\mathbf{r}_i - \mathbf{r}_{i-1}) + \mathbf{a}_i(\Delta t)^2 + \cdots \tag{1.16}$$

Note that all odd terms in the Verlet algorithm disappear, that is the algorithm is correct to third order in the time step. The acceleration can be calculated from the force or, equivalently, the potential:

$$\mathbf{a} = \frac{\mathbf{F}}{m} = -\frac{1}{m}\frac{\partial \mathbf{V}}{\partial \mathbf{r}} \tag{1.17}$$

The time step Δt is an important control parameter for a simulation. The *largest* value of Δt is determined by the *fastest* process occurring in the system, typically being an order of magnitude smaller than the fastest process. For simulating nuclear motions, the fastest process is the motion of hydrogens, being the lightest particles. Hydrogen vibrations occur with a typical frequency of 3000 cm^{-1}, corresponding to ~10^{14} s^{-1}, and therefore necessitating time steps of the order of one femtosecond (10^{-15} s).

1.6 Separation of Variables

As discussed in the previous section, the central problem is solving a differential equation with respect to either the position (classical) or wave function (quantum) for the particles in the system. The standard method of solving differential equations is to find a set of coordinates where the differential equation can be separated into less complicated equations. The first step is to introduce a *center of mass* coordinate system, defined as the mass-weighted sum of the coordinates of all particles, which allows the translation of the combined system with respect to a fixed coordinate system to be separated from the internal motion. For a two-particle system, the internal motion is then described in terms of a reduced mass moving relative to the center of mass, and this can be further transformed by introducing a coordinate system that reflects the symmetry of the interaction between the two particles. If the interaction only depends on the interparticle distance (e.g. Coulomb or gravitational interaction), the coordinate system of choice is normally a polar (two-dimensional) or spherical polar (three-dimensional) system. In these coordinate systems, the dynamical equation can be transformed into solving one-dimensional differential equations.

For more than two particles, it is still possible to make the transformation to the center of mass system. However, it is no longer possible to find a set of coordinates that allows a separation of the degrees of freedom for the internal motion, thus preventing an analytical solution. For many-body ($N > 2$) systems, the dynamical equation must therefore be solved by computational (numerical) methods. Nevertheless, it is often possible to achieve an approximate separation of variables based on physical properties, for example particles differing considerably in mass (such as nuclei and electrons). A two-particle system consisting of one nucleus and one electron can be solved exactly by introducing a center of mass system, thereby transforming the problem into a pseudo-particle with a reduced mass ($\mu = m_1 m_2/(m_1 + m_2)$) moving relative to the center of mass. In the limit of the nucleus being infinitely heavier than the electron, the center of mass system becomes identical to that of the nucleus. In this limit, the reduced mass becomes equal to that of the electron, which moves relative to the (stationary) nucleus. For large, but finite, mass ratios, the approximation $\mu \approx m_e$ is unnecessary but may be convenient for interpretative purposes. For many-particle systems, an exact separation is not possible, and the *Born–Oppenheimer* approximation corresponds to assuming that the nuclei are infinitely heavier than the electrons. This allows the electronic problem to be solved for a given set of stationary nuclei. Assuming that the electronic problem can be solved for a large set of nuclear coordinates, the electronic energy forms a parametric hypersurface as a function of the nuclear coordinates, and the motion of the nuclei on this surface can then be solved subsequently.

If an approximate separation is not possible, the many-body problem can often be transformed into a pseudo one-particle system by taking the average interaction into account. For quantum mechanics, this corresponds to the Hartree–Fock approximation, where the average electron–electron repulsion is incorporated. Such pseudo one-particle solutions often form the conceptual understanding of the system and provide the basis for more refined computational methods.

Molecules are sufficiently heavy that their motions can be described quite accurately by classical mechanics. In condensed phases (solution or solid state), there is a strong interaction between molecules, and a reasonable description can only be attained by having a large number of individual molecules moving under the influence of each other's repulsive and attractive forces. The forces in this case are complex and cannot be written in a simple form such as the Coulomb or gravitational interaction. No analytical solutions can be found in this case, even for a two-particle (molecular) system. Similarly, no approximate solution corresponding to a Hartree–Fock model can be constructed. The only method in this case is direct simulation of the full dynamical equation.

1.6.1 Separating Space and Time Variables

The time-dependent Schrödinger equation involves differentiation with respect to both time and position, the latter contained in the kinetic energy of the Hamiltonian operator:

$$\begin{aligned} \mathbf{H}(\mathbf{r},t)\Psi(\mathbf{r},t) &= i\frac{\partial\Psi(\mathbf{r},t)}{\partial t} \\ \mathbf{H}(\mathbf{r},t) &= \mathbf{T}(\mathbf{r}) + \mathbf{V}(\mathbf{r},t) \end{aligned} \tag{1.18}$$

For (bound) systems where the potential energy operator is time-independent ($\mathbf{V}(\mathbf{r},t) = \mathbf{V}(\mathbf{r})$), the Hamiltonian operator becomes time-independent and yields the total energy when acting on the wave function. The energy is a constant, independent of time, but depends on the space variables.

$$\begin{aligned} \mathbf{H}(\mathbf{r},t) &= \mathbf{H}(\mathbf{r}) = \mathbf{T}(\mathbf{r}) + \mathbf{V}(\mathbf{r}) \\ \mathbf{H}(\mathbf{r})\Psi(\mathbf{r},t) &= E(\mathbf{r})\Psi(\mathbf{r},t) \end{aligned} \tag{1.19}$$

Inserting this in the time-dependent Schrödinger equation shows that the time and space variables of the wave function can be separated:

$$\begin{aligned} \mathbf{H}(\mathbf{r})\Psi(\mathbf{r},t) = E(\mathbf{r})\Psi(\mathbf{r},t) &= i\frac{\partial\Psi(\mathbf{r},t)}{\partial t} \\ \Psi(\mathbf{r},t) &= \Psi(\mathbf{r})\mathrm{e}^{-iEt} \end{aligned} \tag{1.20}$$

The latter follows from solving the first-order differential equation with respect to time, and shows that the time dependence can be written as a simple phase factor multiplied by the spatial wave function. For time-*in*dependent problems, this phase factor is normally neglected, and the starting point is taken as the time-independent Schrödinger equation:

$$\mathbf{H}(\mathbf{r})\Psi(\mathbf{r}) = E(\mathbf{r})\Psi(\mathbf{r}) \tag{1.21}$$

1.6.2 Separating Nuclear and Electronic Variables

Electrons are very light particles and cannot be described by classical mechanics, while nuclei are sufficiently heavy that they display only small quantum effects. The large mass difference indicates that the nuclear velocities are much smaller than the electron velocities, and the electrons therefore adjust very fast to a change in the nuclear geometry.

For a general N-particle system, the Hamiltonian operator contains kinetic (**T**) and potential (**V**) energy for all particles:

$$\begin{aligned} \mathbf{H} &= \mathbf{T} + \mathbf{V} \\ \mathbf{T} = \sum_{i=1}^{N} \mathbf{T}_i \quad &; \quad \mathbf{V} = \sum_{i>j}^{N} \mathbf{V}_{ij} \end{aligned} \tag{1.22}$$