Basic Knowledge

1. Computers in Chemistry - Computational Chemistry

Research can be carried out by acquiring knowledge in one or more of the following areas.

The course is structured into five parts:
Facts on Computers and their use in Chemistry: history, development, architecture, and functioning of computers; hardware: from microchips and microprocessors to supercomputers; software: elements of machine language; computer languages; on-line use in analytical chemistry and spectroscopy; digitalization of measurements; curve smoothing; resolution enhancement; integration of signals, etc..

The PC World: PC hardware; special software used in chemistry; text editing; analysis of data and data management; drawing of chemical structures; 3d-pictures of molecules; professional drawings; software for referencing; generation of data bases; expert software.

Programming of a computer: elements of FORTRAN 90; FTN 90 is trained by writing 15 programs to solve problems such as calculation of pH values, concentration measurements or simulation of NMR spectra. Each problem is connected with a special mathematical method (integration, eigenvalue problem, etc.) and a summary is given where the same mathematical problem may turn up in chemistry.

Computational Chemistry I: Computer assisted structure elucidation; Chemometrics; Computer assisted synthesis; artificial intelligence; special data bases; CAS-ONLINE.

Computational Chemistry II: From force fields to molecular simulations; molecular modelling; quantum chemistry: from semiempirical to correlation corrected ab initio methods; how to use a supercomputer; strategies for programming of large programs with 100 000 and more statements.

The main part of the practical work consists of working with computers of different type. All parts of the practical work are compulsory:

PC laboratory: 3 problems have to be solved for each of the following topics: text editing, data analysis, data management; drawing of chemical structures, 3d-representation of molecules; generation of figures, creating and using data bases. At the end, a manuscript with figures, schemes, diagrams, tables, and reference list has to be prepared with professional layout.

Programming of computers: ca. 20 FTN 90 programs (from 30 to 300 lines) are written to solve problems from chemistry. Emphasis is laid on a systematic approach to the problem within the following strategy: 1) translation of the chemical problem into mathematical language; 2) flow chart of a FTN program; 3) programming of a test

version; 4) debugging and testing; 5) improving the program; 6) documentation of the program.
Use of Networks: The student learns how to use networks to get access to other computers. In this connection, basic features of CAS-ONLINE are explained and up to three literature searches are performed.

Molecular Mechanics and Molecular Modeling: The desktop molecular modeller (DTMM) program is used to train basic elements of molecular modelling. 5 advanced projects have to be solved using DTMM.

Use of supercomputers: Semiempirical and ab initio programs (MOPAC, GAUSSIAN) are used to carry out about 6 illustrative calculations (determination of geometry, heat of formation, relative energy, ionisation potential, dipole moment, charge distribution, etc.)

Excursion: The supercomputer center is visited and a guided tour of the CRAY YMP is made. A one-day minisymposium on supercomputing is organised by experts of the supercomputer center.

2. Concepts and Models in Chemistry - MO Theory

1. Atomic and Molecular orbitals (basic facts from MO theory; representation of orbitals; energy diagrams; LCAO-MO approach)
2. Theory of the Chemical Bond (MO description of the bond; electron density description; quantum mechanical description; orbital overlap; bonding in diatomic molecules; electronegativity and bond polarity; PE spectroscopy)
3. Structure of Molecules (Principle of maximum overlap; hybridization; bond orbitals; VSEPR model; the direct valence model)
4. Mulliken-Walsh MO model (Walsh diagrams for AHn (n = 2,3,4), HAB, H2AB, HnAAHn (n=1,2,3) molecules)
5. PMO Model (basic formulas; 1,2,3,4-electron cases; first and second order Jahn-Teller effects)
6. Hückel MO model (s-p-separation; Hückel theory; aromaticity concept)
7. Classical Mechanics applied to chemistry (concepts of strain; molecular mechanics; heats of formation from group increments; molecular modelling)
8. Interactions between orbitals (hyperconjugation; anomeric effect; through-space and through-bond interactions; homoconjugation and homoaromaticity; spiroconjugation)
9. Conformation and configuration of molecules (Rotational potential of single rotor molecules; fourier expansion of potential; electronic effects that determine rotational potential; steric repulsion and steric attraction; cis-effect)
10. Theory of Pericyclic reactions (The Woodward-Hoffmann rules: orbital symmetry analysis; cycloadditions; electrocylic reactions; sigmatropic rearrangements; cheletropic reactions)
11. Evans-Dewar-Zimmermann concept (Evans principle; hückel and Möbius systems; Dewar-Zimmermann rules)

12. Hypervalent Molecules (orbitals and bonding; pseudorotation in AH5)
13. Transition metal chemistry: Basic Facts and Important Terms (nomenclature; role of transition metal complexes in chemical industry; generalized MO diagrams and electron counting rules)
14. ML6, ML5 and ML4 Complexes (octahedral ML6 complexes; high spin and low spin complexes; square planar and tetrahedral ML45n complexes in Biochemistry)
15. MLn Fragments (Lego-principle of MO diagrams; ML2, ML3, ML4, and ML5 fragments and their orbitals)
16. MCp and MCp2 Complexes (CpML3 complexes; CpM fragment orbitals; metallocenes)
17. The isolobal Analogy (isolobal fragments; cluster orbitals; capped annulenes; Wade rules).

3. Applied Quantum Chemistry

1. Early Quantum Theory: historical overview; influence of physics on Theoretical Chemistry; blackbody radiation; photoelectric effect; Bohr and the H atom; de Broglie wavelength; Heisenberg uncertainty principle.
2. The wave equation: differential equations; separation of variables
3. The Schrödinger equation and simple applications such as the particle in the box
4. Basic Quantum Mechanics: state of a system; operators and observables; postulates and general principles of quantum mechanics.
5. The Harmonic oscillator: diatomic molecules; solution of the harmonic oscillator problem; quantum mechanical tunnelling
6. From one to three dimensions: particle in the 3-dimensional box; the rigid rotator; the hydrogen atom; quantum numbers; orbitals.
7. Approximated methods: independent particle approximation; variational method; perturbation theory.
8. Calculation of atoms: application of variational method and perturbation theory to the He atom; Hartree-Fock calculation of the He atom; electron spin and Pauli principle; antisymmetric wave functions and slater determinants; singlet and triplet wave functions; atomic term symbols.
9. Calculation of molecules: VB theory of H2; chemical bonding; MO theory of H2+ and H2; improvement of VB theory; GVB; configuration interaction (CI); CID and CISD.
10. Hartree-Fock theory: Fock operator; HF equations; LCAO-ansatz; Roothaan-Hall equations; SCF.
11. Ab initio theory: STF and GTF; basis sets; RHF and UHF; electron correlation; CI, MBPT, CC, MCSCF.
12. Semiempirical methods: p-methods; Valence electron methods: extended Hückel; NDO methods; CNDO, INDO, MINDO, MNDO, AM1, PM3; use of semiempirical methods.

4. Computer Assisted Drug Design and Molecular Modeling

1. DRUG DISCOVERY AND DRUG DESIGN

1.1 What is a drug?
1.2 The role of drugs in the practice of medicine
1.3 The role of Pharmaceutical Chemistry
1.4 The history of Pharmaceutical Chemistry
1.5 Natural substances as drugs,
Opium, Quinine, Glycosides, Aspirin, Alkaloids
1.5.1 Paradigm shifts in medicine
1.6 Modern drug design: What requirements must a drug fulfill?
1.7 Stages and cost of modern drug design
1.8 Tools and teams in modern drug design
1.9 The role of Computational Chemistry in drug design
1.10 Drug Discovery - Filtering out Failures
1.11 Rational Molecular Design in Drug Research
1.12 Advertisements in the area of CADD

2. COMPUTER ASSISTED DRUG DESIGN (CADD)

2.1 What is CADD? - Explanation of some basic terms
2.2 Pharmacophore, Lock-Key principle and induced fit theory
2.2.1 100 years of the Lock-Key Principle
2.2.2 The Lock-key Principle and the Induced Fit Theory
2.2.3 The nature of pharmacophores
2.2.4 Molecular Flexibility
2.2.5 Identification of pharmacophores
2.2.6 Searching for pharmacophores
2.3 Molecular Recognition and Molecular Docking
2.4 What makes a compound bioactive?
2.5 The objects of CADD and Molecular Modeling
2.6 What are the driving forces of Receptor-Drug interactions?
2.7 Solvent modeling - the role of water
2.7.1 Properties of water
2.7.2 Water as a solvent: Aqueous solutions
2.7.3 Hydrophilic compounds
2.7.4 Hydrophobic compounds
2.7.5 Amphiphatic compounds
2.8 The dynamic aspect of modeling
2.9 How did CADD develop?
2.10 What are the techniques and concepts used in CADD and Molecular Modeling?
2.11 Disciplines and fields contributing to CADD and Molecular Modeling

3. MOLECULAR MECHANICS (MM)

3.1 Basic considerations concerning force fields
3.1.1 Spectroscopic force fields
3.1.2 The diatomic case
3.1.3 Vibrations of polyatomic molecules
3.2 The concept of the force field in MM: historical development
3.3 Transferability of force fields
3.4 The energy expression in MM
3.4.1 Bond stretching potential
3.4.2 Angle bending potential
3.4.3 Inversion or out-of-plane bending potential
3.4.4 Torsional interaction potential
3.5 Nonbonded interaction potential
3.5.1 Electrostatic interaction potentials
3.5.2 Interaction between bond dipole moments
3.5.3 Calculation of electrostatic interactions
3.5.4 How to get partial charges?
3.5.4.1 Charges from electronegativities (Sanderson)
3.5.4.2 Gasteiger-Marsili charges
3.5.4.3 Charges from Molecular Dipole moments
3.5.4.4 Charges from quantum chemical calculations
3.5.5 Dispersion and exchange repulsion interactions
3.5.6 Model potentials for van der Waals interactions
3.5.7 Spherical and nonspherical atoms
3.5.8 The van der Waals (vdW) radius
3.5.9 Parametrization of vdW potentials
3.6 H-bonding
3.6.1 H-bonding potentials
3.7 Cross term potentials
3.7.1 Stretch-bend cross term potential
3.7.2 Other cross term potentials
3.8 Parametrization of a Force Field
3.8.1 Parameter optimization
3.9 Force field energies V
3.9.1 Some Basic considerations Concerning Energies
3.9.2 Molecular Mechanics Calculation of heats of formations
3.10 Determination of energy and geometry
3.10.1 Newton-Raphson Method
3.10.2 Quasi-Newton Methods; Davidon-Fletcher-Powell
3.10.3 Steepest descent method
3.10.4 Conjugate gradient method
3.10.5 Univariate Search Method
3.10.6 Overview over Optimization Methods
3.11 Differences between spectroscopic and MM force fields

3.12 Classification of force fields
3.13 List of force fields presently in use
3.14 Generic Force Fields
3.15 Treatment of long range Coulomb Forces
3.16 Applicability and limitations of a MM approach
3.17 Extension of MM; Description of p-conjugated molecules
3.18 QM/MM methods
3.18.1 How does a QM/MM method work?
3.18.2 The junction between the QM and MM regions
3.18.3 Implementation of the QM/MM approach
3.18.4 Applications of QM/MM

4. SIMULATION OF MACROSCOPIC PROPERTIES

4.1 Basic terms from statistical mechanics
4.1.1 Concept of the ensemble
4.1.2 Collection of formulas
4.2 Searching phase-space and generating an ensemble
4.2.1 Overview over methods
4.2.2 Systematic search methods
4.3. Monte Carlo (MC) methods (Random Methods I)
4.3.1 Monte Carlo Integration: Hit and Miss
4.3. 2 Random number generators
4.3.3 Sample mean integration
4.3.4 Importance sampling
4.3.5 Sampling error
4.3.6 Metropolis MC method
4.4 Random methods without V: Distance Geometry and NMR Spectroscopy (Random methods II)
4.4.1 Nuclear Overhauser Effect (NOE)
4.4.2 Karplus Curves and NMR spin-spin coupling constants
4.4.3 Basic considerations concerning DG
4.4.3.1 Distance constraints
4.4.3.2 DG methods: Embedding and metric matrix method
4.4.3.3 The Metric Matrix method
4.4.3.4 Triangle Inequality Bounds Smoothing
4.4.3.5 Metrization
4.4.3.6 Refinement
4.4.3.7 Chiral constraints and the chiral error function
4.4.3.8 Four-dimensional refinement
4.4.3.9 Minimization
4.5 MD simulation methods
4.5.1 Basic considerations
4.5.2 Practical Aspects of a MDS calculation
4.5.2.1 Choosing the initial configuration

4.5.2.2 Choosing the time step
4.5.2.3 Choosing the initial velocities
4.5.2.4 Checking the MDS calculation
4.5.2.5 Checking equilibration
4.5.3 Verlet method
4.5.4 Leapfrog method
4.5.5 Constrained Verlet: SHAKE method
4.5.6 Different types of MDS
4.5.7 Constant-T methods
4.5.7.1 Weak coupling methods
4.5.8 Constant-P methods
4.5.8.1 Weak coupling methods
4.5.9 Stochastic dynamic simulations
4.5.10 Boundary conditions
4.5.10.1 Vacuum boundary conditions
4.5.10.2 Periodic boundary conditions
4.5.10.3 Extended wall region boundary conditions
4.5.11 Quantities calculated
4.5.12 Radial Distribution function
4.5.13 Calculation of time-dependent properties
4.5.14 History of MDS
4.6 Calculation of the Free energy
4.6.1 Why is it difficult to calculate A, G, and S?
4.6.2 The coupling parameter approach
4.6.3 The Thermodynamic perturbation method
4.6.4 The Thermodynamic integration method
4.6.5 The potential of mean force
4.6.6 Free energy differences and the thermodynamic cycle
4.6.7 Beyond the free energy: Entropy and enthalpy
4.6.8 Practical considerations
4.6.9 Recommendations

5. MOLECULAR MODELING AND MOLECULAR GRAPHICS

5.1 Historical overview
5.2 Development of computer graphics
5.3 Graphical representation of molecules: Standard models
5.4 Graphical representation technologies
5.5 Simplified molecular representations
5.6 Molecular surfaces and volumes
5.6.1 Corey-Pauling-Koltun (CPK) or van der Waals surface
5.6.2 The Solvent accessible surface (SAS)
5.6.3 Solvent excluded surface - Conolly surface
5.6.4 Surfaces of macromolecules
5.6.5 The electron density surface

5.6.6 Channel surface and separating surface
5.7 Molecular volume
5.7.1 Packing defects in the protein interior
5.7.2 Voroni Polyhedra (Dirichlet cells): Protein packing density
5.8 Molecular superposition and molecular similarity
5.8.1 Manual approach (Flexible superposition)
5.8.2 Atom based methods (DISCO and SQ)
5.8.3 Molecular similarity: Field based methods
5.9 Molecular skin
5.10 Mapping of information on molecular surfaces
5.10.1 The lipophilicity potential
5.10.2 The electrostatic potential
5.11 Molecular shape descriptors
5.11.1 Surface Topology Index
5.11.2 Flexibility of the surface
5.12 Examples of modern molecular graphics

6. CONFORMATIONAL ANALYSIS

6.1 Conformations of biomacromolucules
6.1.1 Primary, secondary, tertiary, and quaterny structure of proteins
6.1.2 Details of Protein structure (Appendix to 6.1.1)
6.2 Systematic search methods
6.2.1 Tree search methods
6.2.2 Model-building approaches
6.3 Random search methods
6.3.1 Genetic algorithms
6.3.2 Distance geometry
6.3.3 Metropolis Monte Carlo
6.4 MDS-based methods
6.4.1 Simulated annealing (SA)
6.4.2 Structure refinement by simulated annealing
6.4.3 Crystallographic refinement
6.4.3.1 Structure factor and electron density
6.4.4 NMR structure refinements

7. CHEMOMETRICS

7.1 Orgin and current status
7.2 Multivariate Data
7.2.1 Definitions
7.2.2 Organization and classification of data
7.2.3 Preprocessing

7.2.4 Distances between objects
7.2.5 Latent variables
7.3 Linear Methods
7.3.1 Projection of multivariate data
7.3.2 Principal component analysis (PCA)
7.3.3 Multiple linear regression (MLR) and principle component regression (PCR)
7.3.4 Partial least squares method (PLS)
7.4 Non-linear methods
7.4.1 An example for non-linear models
7.5 Modeling methods
7.5.1 SIMCA principle component modeling
7.5.2 Classification methods
7.5.2.1 Probability density classification (Bayes strategy)
7.5.2.2 K nearest-neigbor classification (KNN)
7.5.3 Factor analysis
7.5.4 Cluster analysis
7.5.5 Linear discriminant analysis (LDA)
7.6 Validation tools
7.6.1 Cross-validation
7.6.2 Bootstrapping
7.6.3 Frequently used statistical indices
7.6.4 Cross-validation in PLS
7.6.5 Chance effects and chance correlation

8. ARTIFICIAL NEURAL NETWORKS (ANN)

8.1 Background and basics of ANN
8.2 What can neural networks do?
8,2,1 Artificial neuron
8.2.2 Net input, net and weight
8.2.3 How to get the best weights?
8.2.4 Transfer functions in neurons
8.2.5 Bias
8.2.6 Linking neurons to networks
8.3 Architecture
8.4 The Kohonen network
8.4.1 Special characteristics
8.4.2 Competitive learning
8.4.3 An example: mapping from 3 to 2 dimensions
8.4.4 Sumary
8.5 Counterpropagation
8.5.1 Supervised competitive learning
8.5.2 Summary
8.6 Error-backpropagation learning

8.6.1 Architecture
8.6.2 Learning by back propagation
8.6.3 Learning algorithm
8.6.4 Essentials
8.7 When is the training finished?
8.7.1 Overtraining
8.8 Applications of ANNs in Drug design
8.8.1 ANN in Quantitive structure activity relationships
8.8.2 ANN to determine the secondary structure of proteins
8.8.3 Kohonen maps of the electrostatic potential

9. LIPOPHILICITY

9.1 Factorization of molecular lipophilicity
9.2 1D-approaches for calculating partition coefficients
9.2.1 Substituent constants of Hansch and Fujita
9.3 2D-appraoches for calculating partition coefficients
9.3.1 Methods based on fragmental constants and correction factors
9.3.2 Method of Leo and Hansch (CLOGP)
9.3.3 Klopman's method (CASE)
9.3.4 Methods based on fragmental constants only
9.3.4.1 Method of Suzuki and Kudo (CHEMICALC)
9.3.4.2 Method of Broto, Moreau and Vandycke (ALOGP)
9.3.5 Methods based on global two-dimensional structural properties
9.3.5.1 Calculation of peptide lipophilicity
9.3.5.2 Calculation of lipophilicity using structural parameters
9.4 3D- approaches for calculating partition coefficients
9.4.1 Solvent-accessible surface areas (SASA)
9.4.2 MO calculations and Bodor's method (BLOGP)
9.4.3 Methods based on molecular fields: the lipophilicity potential (MLP)
9.5 4D- approaches for calculating partition coefficients
9.5.1 Methods based on an ensemble of conformers
9.5.2 Methods based on direct computation
9.5.3 Methods based on a continuum solvation model
9.5.4 Methods based on free energy perturbation methods
9.6 Comparison of the accurary of different methods
9.7 Examples from drug design
9.7.1 log P as a tool to unravel intramolecular interactions
9.7.2 log P values in 2D-QSAR
9.8 Summary of computer programs
9.9 Concluding remarks

10. 2D-QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIPS (2D-QSAR)

10.1 Definition
10.2 QSAR methodology
10.2.1 Historical background
10.3 Basic concepts of QSAR
10.3.1 Hansch analysis
10.3.2 Free-Wilson analysis
10.3.3 An example: Adrenergic activities of N,N-di-methyl-a bromopheneythlamines
10.3.4 Summary
10.4 Molecular descriptors
10.4.1 Electronic parameters
10.4.2 Polar interactions
10.4.3 Steric paramters
10.4.4 Topological paramters
10.4.5 Quantum-chemical descriptors
10.5 Biological parameters
10.6 2D-QSAR in drug design
10.6.1 Transport and distribution of drugs in biological systems
10.6.2 Enzyme inhibition
10.6.3 Model system for cysteine protease
10.6.4 Prediction of mutagenic potencies
10.6.5 QSAR for antimalarical compounds
10.6.6 b_1- and b_2- antagonist activities
10.6.7 Activity-activity relationships
10.7 Validation of QSAR models
10.8 Conclusions

11. 3D-QSAR; COMPARATIVE MOLECULAR FIELD ANALYSIS (CoMFA) and - SIMILARITY ANALYSIS (CoMSIA)

11.1 3-QSAR
11.2 Assumptions in 3D-QSAR
11.3 CoMFA methodology
11.4 Steps of a CoMFA analysis
11.4.1 Pharmacophore hypothesis and alignment
11.4.2 Superposition of all molecules
11.4.3 Box, Grid size and 3D field calculations
11.4.5 Derivation of the CoMFA model
11.4.6 CoMFA coefficient maps
11.4.7 Validation of results
11.5 An example: CBG and TBG binding affinities of steriods

11.6 CoMFA application in drug design, overview
11.7 Conclusions on CoMFA
11.8 Comparative molecular similarity analysis (CoMSIA)
11.8.1 Definition of simularity indices
11.8.2 Similarity fields
11.9 An example benzamidine inhibitors binding to trypsin, thrombin, and factor Xa

12. CADD: METHODS and STRATEGIES

12.0.1 The drug development process (target oriented)
12.1 Lead discovery
12.2 Irrational drug design and combinatorial chemistry
12.2.1 The combinatorial explosion of chemistry
12.2.2 What is combinatorial chemistry
12.2.3 Merrifield's synthesis of peptides
12.2.4 CombChem: Mix-and-split libraries
12.2.5 Historical development of CombChem
12.3 Virtual screening
12.3.1 Setting up a virtual library
12.3.2 Practical considerations: Encoding of the library
12.3.3 The virtual screening process
12.3.4 2D-similarity: Tanimoto coefficients
12.3.5 Clustering (=pooling) of structures
12.3.6 Virtual screening: 3D similarity
12.3.7 Reduction and diversity of a virtual library
12.3.8 Data minining
12.4 Structure-based ligand design: Pharmacophore generation
12.4.1 Structure-based ligand design
12.4.2 Determination of a pharmacophore
12.4.3 The active analog approach (AAA)
12.4.4 Ensemble distance geometry
12.4.5 Ensemble molecular dynamics
12.4.6 Pharmacophores by clique detection
12.4.7 Pharmacophore representation
12.5 Molecular recognition
12.6 Molecular docking
12.7 De Novo design of ligands
12.7.1 Analysis of the receptor: Generation of a constraints model
12.7.1.1 The GRID program
12.7.1.2 The Multiple-Copy Simultaneous Search (MCSS) method
12.7.1.3 The Program LUDI
12.7.2 Structure generation methods
12.7.2.1 The outside-in (linking) approach: LUDI
12.7.2.2 The linking part

12.7.2.3 Creating real molecules
12.7.2.4 The inside-out (building) approach: GROW
12.7.2.4 Program LEGEND
12.7.3 Structure evaluation
12.7.4 When does one use de Novo design?
12.7.5 Practical advice on the application of de Novo design methods
12.7.6 De Novo design: Conclusions and future perspectives
12.8 Petides and peptide analogs as drugs: Peptidomimetics
12.8.1 Peptidomimetics
12.8.2 Design of peptidomimetics: the CAVEAT program

13. PROTEIN MODELING

13.1 The Protein Data Bank (PDB)
13.2 Relationship between sequence and 3D structure of a protein
13.3 Alignment of protein sequences
13.3.1 Needleman-Wunsch alignment method
13.3.2 Multiple sequence alignments (MSA)
13.3.2.1 Construction of the core
13.3.2.2 Construction of loops and turns
13.3.2.3 Construction of the Side chains
13.3.2.4 Refinement of the homology model
13.4 Homology modeling of proteins
13.5 Prediction of protein structures by threading
13.6 Comparison of various strategies in homology modeling
13.7 Protein folding
13.7.1 Thermodynamics of protein folding
13.7.2 Levinthal's paradox and the kinetics of protein folding

14. PRESENT and FUTURE PERSPECTIVES OF DRUG DESIGN

14.1 Successes of CADD
14.2 Genetechnology and drug design
14.3 Bioinformatics
14.4 Future developments
14.4.1 Improvements of force fields
14.4.2 Integration of quantum chemcial methods, better QC/MM methods
14.4.3 Better methods for DG calculations
14.4.4 ADME modeling

5. Ab initio Methods I: Hartree-Fock Theory

1. Introduction

Definition of the term *ab initio*, goals; advantages; size-extensivity, approximations involved; limitations, classification; difference between empirical, semiempirical, and nonempirical methods; What is calculated? Comparison with experimental measurements; acronyms; units; conventions; history

1.1 What are ab initio calculations?
1.2 Goals of ab initio quantum chemistry
1.3 Criteria for ab initio methods
1.4 Approximations and limitations
1.5 What is calculated?
1.6 Classification of methods used in Computational Chemistry
1.7 Acronyms, units, symbols
1.8 History of ab initio Quantum Chemistry
1.9 What ab initio programs are available
1.10 Books on ab initio methods

2. The independent particle model

Unitary vector space, Hilbert space, basis vectors; scalar product, operators, dyadic product, projection operator, Hermitian operator, turn-over rule, unitary operator, eigenvalue problem, Hamilton operator; Born-Oppenheimer approximation, single determinant wavefunction, what is an orbital? spin orbitals and space orbitals; Variational principle, Hartree product; antisymmetry principle, Slater determinant; matrix elements for Slater determinants; Slater-Condon rules, exchange and Coulomb operator, Fock operator, Hartree-Fock equations; canonical form, orbital energy, separation of spin, energy for closed-shell system, restricted HF (RHF), LCAO approach; basis functions, metric of a non-orthogonal basis, overlap integrals, Fock matrix, Roothaan-Hall equations, energy expressions, density matrix

2.1 Some useful basics from quantum mechanics
2.2 The independent particle model
2.3 Hartree product versus Slater determinant
2.4 Determination of the normalization constant
2.5 Matrix Elements over Slater determinants - Slater-Condon rules
2.5.1 One electron operators
2.5.2 Two electron operators
2.6 Simplification of the Hamiltonian to an effective One-electron operator
2.6.1 Hartree Fock (HF) energy formula
2.7 Hartree Fock Equations

2.8 LCAO-Ansatz to solve the HF equations - Roothaan-Hall equations
2.9 Calculation of the energy according to Roothaan-Hall

3. What is needed for a Hartree-Fock (HF) calculation?

flow chart for ab initio calculations; input; choice of the coordinates; Cartesian and internal coordinates, geometry optimization and the right choice of coordinates, z-matrix formalism; dummy atoms; puckering coordinates; determination of symmetry, number of independent internal coordinates, molecular framework group, what ab initio programs are available? How to get them; how to use them?

3.1 Flow chart for a HF calculation
3.2 Input for a HF calculation
3.2.1 Specification of the molecule
3.2.2 Molecular geometry
3.2.2.1 Cartesian versus internal coordinates
3.2.2.2 The z-matrix formalism
3.2.2.3 Special coordinates - puckering parameters
3.3 How to find the right number of coordinates?
3.3.1 Determination of molecular point group in an ab initio program
3.3.2 Number of indpendent coordinates for symmetric molecules
3.4 The molecular framework group
3.5 What ab initio programs are available?

4. The basis functions

Building-block principle, H-type functions and H-type orbitals; Slater-type functions and Slater-type orbitals; the exponent zeta; diffuse and compact basis functions, Slater rules; Gaussian-type functions and Gaussian-type orbitals, cusp problem, energy of the H atom; LCGTF, difference between STFs and GTFs, cartesian Gaussians; advantages and disadvantages; first order and second order GTF, the index l, Gaussian lobe functions;

4.1 The building block principle of MO theory
4.2 Hydrogen type functions and Hydrogen type orbitals
4.3 Slater type functions (STF) and Slater type orbitals (STO)
4.4 Slater rules for zeta values
4.5 Gaussian type functions (GTF) and Gaussian type orbitals (GTO)
4.5.2 Energy of the ground state of H
4.5.3 Comparison of HF, Slater, and Gaussian orbitals
4.5.4 Cartesian Gaussian functions
4.5.5 Gaussian lobe functions
4.6 Summary

5. The basis set

notation; minimal zeta basis; double zeta basis; choice of the exponent, split valence basis, extended basis sets; isotropic limit, HF limit, augmented basis sets; hidden variables; floating functions; bond functions; polarisation functions (p, d, f, g, h); radial and angular polarization, notation for augmented basis sets, weigth, size, and position of a basis function, uncontracted and contracted basis sets; construction of contracted basis sets; contraction criteria; segmented and generalized contraction, the scaling theorem; notation; Huzinaga-Dunning basis sets; Pople minimal basis sets; shell constraints; STO-NG; split valence basis sets, augmented split valence basis sets; addition of diffuse functions; even-tempered basis sets, selection of a basis set, Pople's receipe, basis sets for special molecular properties, Dunning basis sets

5.1 How to use basis functions?
5.2 Notation for basis sets
5.3 Minimal basis sets (MBS, SZ)
5.4 Double Zeta basis sets (DZ)
5.5 Split-valence basis sets (VDZ)
5.6 Extended Basis sets: TZ, QZ, PZ
5.7 Augmented basis sets
5.7.1 Floating basis functions
5.7.2 Bond functions
5.7.3 Polarization functions
5.8 Uncontracted and contracted basis sets
5.8.1 Contraction of a (7s3p) basis for N
5.8.2 Notation for contracted basis sets
5.8.3 Rules for getting contracted basis sets
5.8.4 General contraction schemes
5.9 Pople's minimal basis sets
5.9.1 Scaling theorem
5.9.2 STO-NG minimal basis sets
5.10 Pople's split valence and augmented split valence basis sets
5.11 Special Basis sets
5.11.1 Augmented basis sets with diffuse functions
5.11.2 Even-tempered basis sets
5.12 Selection of an appropriate basis set for a given problem
5.12.1 What is available?
5.12.2 How to select a basis set?
5.12.3 Pople's receipe
5.12.4 How to get basis sets for high accuracy calculations?
5.12.5 What basis set is needed for what property?

6. Calculation of integrals

Single bar and double bar integrals, physical and chemical notation of integrals; number of integrals; shell structure; one-electron integrals; overlap integrals, Cartesian Gaussian functions, spherical Gaussians, transformation from cartesian to spherical Gaussians, angular shell, contaminants, Gaussian product theorem, Laplace transform of r12-1, incomplete Gamma functions, shift of angular momentum, differentiation of Gaussian functions, recurrence relationships, Cartesian Hermite Gaussian-type functions, translational invariance, Gaussian Quadrature, overlap integrals, kinetic energy integrals, nucleus-electron attraction integrals, two-electon repulsion integrals (ERIs), [ss|ss] ERI, prescreening of ERIs, McMurchie-Davidson scheme, Dupuis-King-Rys scheme, Rys polynomials, Pople-Hehre scheme, exponent sharing, early contraction, late contraction, axes rotation, PRISM algorithm, contraction and scaling, choice diagrams, Obara-Saika scheme, Resolution of the identity (RI) method, canonical ordering, sequential and random storing, batch processing, packing and unpacking of ERI labels, synchronous/asynchronous IO, buffering of ERIs

6.1 Notation for electron integrals
6.2 Number of integrals
6.3 Properties of GTFs relevant for integral calculations
6.3.1 Basics
6.3.2 Gaussian Product Theorem
6.3.3 The Laplace Transform of r12-1
6.3.4 The Transfer equation
6.3.5 Differentiation and recurrence relationships
6.3.6 Gaussian Quadrature
6.4 Overlap integrals
6.5 Kinetic energy integrals
6.6 Nucleus-electron attraction integrals
6.7 Evaluation of two-electron repulsion integrals (ERIs)
6.7.1 Evaluation of the [ss|ss] ERI
6.7.1.1 Prescreening of ERIs
6.7.2 McMurchie-Davidson scheme
6.7.3 Dupuis-King-Rys scheme
6.7.4 Pople-Hehre calculation of ERIs
6.7.5 The PRISM algorithm
6.8 The Resolution of the identity (RI) method
6.9 Storage of ERIs

7. Solution of the Self-Consistent Field (SCF) problem

Conventional Roothaan-Hall SCF, the trial and error method, iterative solution of the Roothaan-Hall equations, initial guess, diagonalization of the core hamiltonian, extended Hückel type guess, INDO and MNDO guess, guess from atomic densities, basis set expansion, solution of the pseudo-eigenvalue problem, canonical

orthonormalization, spectral form of S, Schmidt orthonormalization, symmetric orthonormalization, density matrices, projector idempotency constraint, Jacobi diagonalization, Givens-Householder diagonalization, stationary state conditions (with regard to orbitals and basis functions), unitary transformation of MOs, mixing of occupied and virtual orbitals, orbital rotation, energy gradient with regard to expansion coefficients, Brillouin theorem, construction of the Fock matrix, permutational symmetry of ERIs, supermatrix formalism, Raffenetti ordering, timings for construction of the F matrix

7. Solution of the SCF Problem
7.1 Conventional Roothaan-Hall SCF
7.2 Initial Guess
7.2.1 Available methods for setting up the initial guess
7.2.2 Improvement of starting orbitals - Basis set expansion
7.2.3 Reuse of other wavefunctions
7.3 Solution of the pseudo-eigenvalue problem
7.4 Orthogonalization procedures
7.4.1 Schmidt procedure - successive orthonormalization
7.4.2 Löwdin procedure
7.4.3 Comparison of orthonormalization procedures
7.4.4 Comparison between nonorthogonal and orthogonal basis set descriptions
7.5 Diagonalization procedures
7.6 Stationary state conditionms for the SCF
7.7 Construction of the Fock matrix
7.7.1 Raffenetti ordering

8. Convergence of SCF calculations

Convergence criteria for SCF, convergence problems, oscillations, state switching, divergence, counteractions, convergence acceleration, state loyalty, univariate search methods, Fock matrix partitioning, pseudocanonical orbitals, l-dependent form of F, mixing coefficient, energy gradient with regard to l, Bessel equation, overlap of spinorbitals, Camp-King method, unitary transformation by an exponential matrix, diagonalization of a rectangular matrix, orbital rotation, extrapolation methods, Hartree damping, dynamic damping, 3-point extrapolation, Aitken d2 method, 4-point extrapolation, level shifting, starting and termination strategies, Pulay's DIIS, linear dependence of changes in F and P, errors in P and stationary state conditions, ADEM-DIOS, QC-SCF, linear convergence, quadratic convergence, orbital mixing expressed by a CI formalism, Newton-Raphson formulation of the SCF problem,

8.1 General aspects: Convergence and convergence problems
8.1.1 What to do in case of convergence problems?
8.2 Univariate search methods and state loyalty
8.2.1 Pople-Seeger method
8.2.2 State loyalty by the Pople-Seeger method

8.2.3 Camp-King method
8.2.4 Implementation of the Camp-King method
8.3 Extrapolation methods
8.3.1 Damping
8.3.2 Dynamic damping
8.3.3 Aitken method
8.3.4 Roothaan-Bagus-Sack method
8.4 Level shifting
8.5 Direct inversion of the iterative subspace (DIIS)
8.5.1 Precursors of DIIS
8.5.2 Practical aspects of DIIS
8.5.3 Extension of DIIS: ADEM-DIOS
8.6 Quadratically convergent SCF (QC-SCF)
8.6.1 Linear and quadratic convergence
8.6.2 QC-SCF method
8.6.3 Comparison with normal SCF
8.6.4 Implementation of QC-SCF in an ab initio program
8.7 Overview of starting and terminating convergence methods

9. SCF for open shell cases

Different open shell cases, generalized Brillouin theorem, generalized HF equations, coupling terms, generalized Roothaan-Hall equations, partitioned HF (PHF); ROHF according to Roothaan; the McWeeny method for ROHF; unrestricted HF (UHF); Pople-Nesbet equations; properties of the UHF energy; dissociation problem by RHF and UHF; UHF wave function; the expectation value of S2; spin contamination; spin projection methods; UHF electron and spin densities;

9.1 Derivation of a minimum condition for restricted open shell cases - generalized Brillouin theorem
9.2 Generalized restricted open shell theory
9.2.1 General derivation and relationship to MCSCF
9.2.2 Derivation of the pseudo-eigenvalue equations
9.2.3 LCAO Ansatz for ROHF - Generalized Roothaan-Hall equations
9.2.4 Coupling coefficients aIJ and bIJ
9.3 Partitioned HF (PHF)
9.4 Roothaan's ROHF
9.5 McWeeny' ROHF
9.6 Unrestricted HF theory (UHF)
9.6.1 Pople-Nesbet equations
9.6.2 Properties of the UHF energy
9.6.3 The dissociation problem
9.6.4 The UHF wavefunction
9.6.5 Spin projection methods
9.6.5.1 Spin constraint UHF (SUHF)
9.6.6 UHF electron density and spin density distribution

9.6.7 Calculation of hyperfine coupling constants

10. General HF Theory

Complex GHF, real GHF, complex UHF, real UHF, complex RHF, real RHF, form of general spinorbitals, possible constraints, internal and external stability, stability test, form of the Hessian, symmetry dilemma of UHF, singlet instability, non-singlet instabilities, complex HF, the O2 molecule and its 1Dg state, complex orbitals vs. real orbitals, complex Fock matrix, complex HF equations, eigenvalues for the complex problem, flow chart diagram,

10.1 Constraints to complex GHF
10.2 Stability tests
10.2.1 Singlet instability
10.2.2 Non-singlet instabilities
10.3 Complex HF (CHF)
10.3.2 Necessity of using complex HF - the O2 example
10.3.1 Form of complex orbitals
10.3.2 Roothaan Hall for CHF

11. Direct SCF methods for large molecules

M4-myth, number of ERIS for large molecules, storage problem, recalculation of ERIS; prescreening of two-electron integrals; batch processing, recurrence formula for the Fock matrix; cost for an ERI in dependence of l, selective storage of integrals; minimization of errors; changes in the number of ERIs per iteration step

11.1 Number of ERIs for large molecules
11.2 Flow chart for a DSCF program
11.3 Prescreeining of ERIs and neglecting of ERIs
11.4 Recursion formula for the Fock matrix
11.5 Selective storage of ERIs -Semidirect SCF
11.6 Error progression in a DSCF
11.7 DSCF calculations for large molecules

6. Ab Initio Methods II: Electron Correlation Methods (CI and Perturbation Theory)

A. Electron Correlation

1. Why do we need correlation corrected methods?
1.1 Shortcomings of the HF approach
1.2 What is correlation?
2. Electron Density Functions: Density Matrices
2.1 Reduced density matrices
2.2 Energy in terms of Gp - N-representability problem

2.3 Pair density distribution
2.4 Fermi hole and Coulomb hole
2.5 Density matrices in HF theory - Fock-Dirac density matrix
2.6 Pictorial display of electron correlation
3. Definition of the Correlation Energy
3.1 Magnitude of the correlation energy
3.2 Correlation energies from experimental data
4. Types of Electron Correlation
4.1 Static and dynamic electron correlation
4.2 Electron Pair correlation
4.3 Left-right, angular, in-out correlation
4.4 Intraatomic and interatomic correlation
4.5 Internal and external correlation
4.6 Higher correlation effects and higher excitations
5. What Correlation methods are available?

B. Configuration Interaction

CI wave function, properties of CI methods, full CI, truncated CI, tape driven and integral driven CI, UGA, SGA

1. General Considerations
1.1 How many terms are in the full CI wave function
1.2 CI matrix
1.3 Calculation of the CI correlation energy
2. Full CI for H2
3. Truncated CI: CID and CISD
4. Conventional CI calculations
4.1 Integral transformation
4.2 Construction of spin-adapted CSF
4.3 Calculation of matrix elements
4.4 Diagonalization methods: Nesbet method, Davidson method
5. Direct CI
5.1 Multipurpose direct CISD
5.2 A CISD program
6. Correlation Orbitals - Natural Orbitals
6.1 Correlation orbitals
6.2 Natural orbitals
6.3 Calculation of natural orbitals
6.4 Natural orbitals of H_2O
6.5 Iterative natural orbital method
7. Basis sets for correlation calculations
7.1 Repetition of some basic terms
7.2 Pople's basis sets
7.3 Dunning's correlation consistent basis sets
7.4 ANO basis sets

7.5 Dual basis sets
8. Error consistency
8.1 Basis set error consistency: truncation error and BSSE
8.2 BSSE (counterpoise method; inter- and intramolecular BSSE)
8.3 Method error consistency: correlation error and size-extensivity error
8.4 Size-extensivity
Size-extensivity versus size-consistency
8.5 Size-extensivity error of CI
8.6 Size-extensivity corrections: Davidson correction, Pople correction

C. Many-Body Perturbation Theory

1. Rayleigh-Schrödinger Perturbation Theory
general perturbation theory formulas, intermediate normalization, E(0) representation, second order, third order, fourth order corrections
2. Møller-Plesset Perturbation Theory
2.1 First order correction to the energy Eorb
2.2 Second order correction to the energy
2.3 First order correction to the wave function
2.4 Third order correction to the energy
2.5 The original MP perturbation operator
3. Epstein-Nesbet Perturbation Theory
3.1 The EN perturbation operator
3.2 Second order correction to the energy
3.3 Advantages and disadvantages of EN perturbation theory
4. Diagrammatic Perturbation Theory
4.1 Introduction to diagrams
4.2 Hugenholtz diagrams
4.3 Goldstone diagrams
rules, calculation of second order and third order energy
4.4 Brandow diagrams
4.5 How many diagrams exist at MBPTn?
5. General Perturbation Theory
model space and orthogonal space, projection operators
5.1 Feshbach operator
5.2 Brillouin-Wigner Perturbation Theory
5.3 Resolvent expansion of energy and wave function
5.4 General Rayleigh-Schrödinger Perturbation Theory
5.5 Fourth order MP Theory (derivation of the energy formula)
5.6 General MPn Theory (MP5, MP6, etc.)
6. Dependence on the number of particles
6.1 Investigation of first, second, and third order energy
6.2 Size-extensivity of MP energies
6.3 Linked diagram expansion
first order wave operator and first order wave function
second order wave operator and second order wave function

combination of wave operator and perturbation operator diagrams
derivation of the fourth order energy, factorization theorem
6.4 Linked Diagram Theorem
6.5 Characterization of diagrams

7. Convergence of the MPn series

7.1 Convergence behavior (oscillations, divergence)
7.2 Convergence radius and intruder states
7.3 Higher MP order from FCI
7.4 Extrapolation procedures: Pade approximants
7.5 Extrapolation formulas
7.6 Extrapolation procedures: First order and higher order Feenberg scaling

8. Projected MP Theory

8.1 Annihilation versus projection methods
8.2 Calculation of <S2> corrections
8.3 PUHF, PMP2 and PMP3
8.4 Practical considerations

9. Application of MP Theory

9.1 Cost considerations and feasibility
9.2 Programming considerations
9.3 Electron density analysis of MP response densities
9.4 MP geometries
9.5 MP energies
9.6 MP dipole moments and other first order properties
9.7 MP frequencies and IR intensities
9.8 Advantages and disadvantages of MP theory

10. Greens Functions

10.1 One-particle Green's functions
10.2 One-particle Green's functions for an N-electron system
10.3 Calculation of ionization potentials and electron affinities
10.4 How to solve the Dyson equation?
10.5 Relationship between the Green's function method and perturbation theory
10.6 Application of Green's functions

7. Ab initio Methods III: Electron Correlation Methods (From Single to Multi Configuration methods)

1. Basic Concepts - A repetition

1.1 Time-dependent Schrödinger Equation
1.2 Born-Oppenheimer Approximation
1.3 Variational Methods for ground and excited states
1.4 Size consistence and size-extensiveness

2. Single reference - multi determinant problems

2.1 Reference, Configuration, and Determinant

2.2 General ROHF
2.2.1 Generalized Brillouin Theorem
2.2.2 Generalized HF Equations
2.2.3 Generalized Roothaan Hall Equations
2.3 The Low-Spin Open Shell Problem
2.3.1 ROSS
2.3.2 ROHF-MP
2.4 From ROHF to MCSCF

3. Two-Configuration Descriptions
3.1 GVB

4. MCSCF
4.1 Energy Expression in MCSCF
4.2 CI Equations and Generalized Brillouin Theorem
4.3 Methods to determine the MCSCF wave function
4.3.1 Super CI Technique
4.3.2 Quadratically Convergent MCSCF Methods: Newton Raphson Method
4.4 The H2 molecule

5. CASSCF

8. Ab Initio Methods V: Calculation of Molecular Properties

1. Overview over Molecular Properties
1.1 Classification of Molecular Properties
(1- and 2-electron properties; first order, second order and higher order properties; operational classifications; properties derived from the PES, from the wave function; response properties; properties that involve more than one electronic state, properties that are beyond the Born-Oppenheimer approximation)
1.2 Properties derived from the PES
(Energy derivatives: forces, harmonic, cubic, quartic force constants; infrared and Raman intensities; dipole moment, dipole polarizability, dipole hyperpolarizability, magnetic moment, magnetic susceptibility, magnetic hypersusceptibility; electrical anharmonicity; nuclear magnetic shieldings, NMR spin-spin coupling constants)

2. Ab initio Energies
2.1 From ab initio Energies to heats of formation
2.1.1 Correction of heats of formation from T to 0 K
2.1.2 Calculation of experimental molecular energies
2.1.3 Calculation of theoretical energies within the Born-Oppenheimer approximation
2.1.4 Estimation of relativistic effects

2.1.5 Estimation of correlation energies
2.16 How to get to HF limit energies
2.2 Practical considerations
2.3 Direct Calculation of Thermodynamic Properties
(Partition functions; translational, rotational, vibrational corrections; calculation of ZPE and entropy; calculation of enthalpy and free enthalpy; how to read the thermochemistry output of an ab initio program)
2.4 Heats of formation from ab initio Energies: The G Theoretical Model Chemistry
2.4.1 Basis set additivity
2.4.2 Use of isogyric reactions
2.4.3 Gaussian1 (G1) Theory
2.4.4 G2 Theory
2.4.5 Modifications: G2(MP2) and G2M
2.4.6 G3 Theory
2.5 Other ways of calculating heats of formation
2.5.1 Dewar's approach
2.5.2 Bond Additivity Corrections (BAC) method
2.5.3 Transition metal chemistry: PCI80
2.6 The CBS Theoretical Model Chemistry
2.6.1 Determination of the SCF limit
2.6.2 Determination of PNOs
2.6.3 CBS Pair energies
2.6.4 CBS-QCI/APNO model
2.7 Heats of Formation from Formal Reactions
2.7.1 Bond separation energies and isodesmic reactions
2.7.2 Homodesmotic reactions and super-homodesmotic reactions
2.7.3 Resonance and strain energies from homodesmotic reactions

3. Interpretation of the wave function
3.1 Properties of the molecular wave function
3.1.1 The Hellmann-Feynman theorem
3.1.2 The virial theorem
3.1.3 Methods with and without a wave function
3.2 Orbital energies
3.2.1 Koopmans theorem
3.2.2 When does Koopmans theorem apply?
3.2.3 Excitation energies from orbital energies (Singlet and triplet states)
3.2.4 Orbital energies and total energy
3.3 Population analysis
3.3.1 Mulliken population analysis
3.3.2 Shortcomings of the Mullkien population analysis
3.3.3 Improvements of the Mulliken population analysis
3.3.4 Modified atomic orbitals (MAOs)
3.3.5 Charges from the electrostatic potential
3.3.6 Weinhold's natural population analysis: NAOs and NBOs
3.4 The shape of canonical Molecular Orbitals

3.4.1 How to read the coefficients of MOs?
3.4.2 Delocalized and localized MOs
3.4.3 Graphical representations of MOs
3.5 Localization of MOs
3.5.1 Localization criteria
3.5.2 Boys localization
3.5.3 Edminston-Ruedenberg localization
3.5.4 Magnasco-Perico localization
3.5.5 Pipek-Mezey localization

4. Analysis of the electron density distribution
4.1 Properties of the electron density distribution
4.2 Difference density distribution
4.3 Measurement of the electron density distribution
4.4 Ways of analyzing the electron density distribution
4.5 Topological analysis
4.6 Theory of virial subspaces
4.6.1 Open and closed systems
4.6.2 Zero-flux surfaces
4.6.3 Bader's atoms in molecules theory
4.6.4 atomic properties
4.7 The Laplacian of the electron density distribution
4.7.1 The local virial theorem
4.7.2 Bond and lone pair concentrations
4.7.3 The shell structure of the atoms
4.8 Description of the chemical bond
4.8.1 The electrostatic description of the chemical bond
4.8.2 Ruedenberg's description of the chemical bond
4.8.3 Bader's description of the chemical bond
4.8.4 Bond order, bond ellipcity, and bond polarity
4.8.5 A general model of covalent bonds (Cremer-Kraka criteria)
4.8.6 Bond energies and bond dissociation energies
4.8.7 Bond strength as related to intrinsic properties of the bond
4.8.8 Overlap and electronegativity

5. Molecular properties from analytical energy derivatives
5.1 Analytical derivatives in HF theory
5.1.1 HF first derivatives
5.1.2 HF second derivatives
5.1.2 Coupled Perturbed Hartee-Focck (CPHF) theory
5.1.3 Implementation according to Pople
5.1.2 The z-vector formalism of Handy and Schaefer
5.1.5 Overview over RHF and GROHF derivatives
5.2 MPn derivatives
5.3 MCSCF and CASSCF derivatives
5.4 CI derivatives

5.5 Implementation of derivatives in an ab initio program
5.6 General response theory
5.6.1 Expectation value versus response property

6. Molecular Geometries and Geometry Optimizations
6.1 Basic definitions and overview
6.2 Optimization methods - Coordinate systems
6.2.1 Coordinates used for optimization (redundant, nonredundant)
6.2.2 Relationship between internal and Cartesian coordinates: B matrix
6.2.3 Relationships for redundant coordinates: G and K matrices
6.2.4 Gradient and forces for non-redundant and redundant coordinates
6.2.5 Optimization in redundant internal coordinates
6.2.6 Conversion from redundant internal to Cartesian coordinates
6.2.7 Advantages of redundant coordinates
6.2.8 Natural internal coordinates of Pulaty and Boggs
6.2.9 Delocalized internal coordinates of Baker
6.2.10 Use of Cartesian coordinates in optimizations
6.3 Optimization methods - general features
6.3.1 Use of the Hessian for optimizations
6.3.2 Convergence criteria
6.3.3 Stepsize and search direction
6.3.4 Search for a local minimum
6.3.5 Search for a transition state
6.4 Optimization methods
6.4.1 Nonderivative methods
(Univariate search, Simplex method)
6.4.2 Gradient methods
(Steepesct descent, Conjugate gradient methods)
6.4.3 Quasi-Newton methods
(Davidon-Fletcher-Powell, Murtagh-Sargent)
6.4.4 Newton-Raphson methods
6.5 Special search techniques
6.5.1 Minimum search - Schlegel's method
6.5.2 Transition state searches
6.5.3 Mode following method of Baker
6.5.4 Up-hill searches
6.5.5 Rational functional methods
6.6 Definition of the molecular geometry
6.6.1 What is the difference between re, rg, ra, r0, rv, rz?
6.6.2 Quality of HF geometries
6.6.3 MP and CC geometries
6.6.4 DFT geometries

7. Conformational processes
7.1 Basic terms: Conformations and conformers
7.2 Internal rotation

7.2.1 Rigid and flexible rotors
7.2.2 Fourier expansion of the rotational potential
7.2.3 Rotational barriers and their electronic nature
7.2.4 Coupled rotors: Fourier expansion and chemical relevance
7.3 Inversion of molecular conformations
7.3.1 Inversion barriers and electronic nature
7.4 Ring puckering and pseudorotation
7.4.1 The ring puckering coordinates: ring inversion and ring pseudorotation
7.4.2 Conformational space: Dimension and basis conformations
7.4.3 The cyclohexane globe and its extensions
7.4.4 Relationship between acyclic rotors and cyclic pseudorotors
7.5 Acyclic pseudorotors
7.5.1 Berry pseudorotation
7.6 Bond pseudorotation

8. Vibrational frequencies and force constants

8.1 Vibration of the diatomic molecule - a short repetition
8.1.1 The vibrational energy levels in the harmonic approximation
8.1.2 Anharmonic vibration and More potential
8.1.3 Vibrational selection rules
8.1.4 Vibration-rotation spectrum
8.1.5 Raman vibrational spectrum
8.2 Classical calculation of the normal modes of a polyatomic molecule
8.2.1 Cartesian vs. internal coordinates: Wilson B matrix
8.2.2 Mass-weighted coordinates and Wilson G matrix
8.2.3 The harmonic approximation
8.2.4 Derivation of the Euler-Lagrange equations
8.2.5 Generalized force constants and force constant matrix
8.2.6 Calculation of normal modes in terms of Cartesian and internal coordinates
8.3 Infrared and Raman spectra
8.3.1 Vibrational selection rules
8.3.2 Theory of infrared intensities (harmonic approximation)
8.3.3 Calculation of IR intensities with HF and correlated methods
8.3.4 Absolute and relative IR intensities, intensities of isotopomers
8.3.5 Calculation of the Raman spectrum
8.4 Determination of local modes
8.4.1 Isolated stretching modes
8.4.2 Local modes from overtone spectroscopy
8.4.3 Adiabatic internal modes (AIMs)
8.4.4 The properties of AIMs
8.5 Analysis of vibrational spectra
8.5.1 Normal mode analysis
8.5.2 Potential energy analysis
8.5.3 Characterization of normal modes in terms of AIMs
8.5.4 Spectra of isotopomers and their calculation

8.5.5 Correlation of vibrational spectra
8.5.6 Charges from vibrational intensities
8.6 Vibrational-rotational coupling
8.6.1 Coriolis forces
8.7 The effects of anharmonicity
8.7.1 Overtones and combination bands
8.7.2 Fermi resonances
8.7.3 Calculation of cubic and quartic force constants
8.7.4 Vibrational corrections of measured geometries
8.8 The role of force constants for describing bond strength
8.8.1 Badger rule
8.8.2 Force constants from experimental spectra
8.8.3 Force constants and the intrinsic bond dissociation energy

9. Ionization potentials

9.1 Koopmans theorem and its applicability
9.2 PE and ESCA spectroscopy
9.2 Explicit calculation of ionization potentals
9.3 Ionization potentials from Green function methods

10. Electric properties

10.1 The response to electric fields
10.1.1 Molecular response parameters
10.1.2 General theory of response properties in an external electric field
10.1.3 One- and two-electron properties
10.2 Electric multipole moments
10.2.1 Dipole moments
10.2.2 Quadrupole moments
10.2.3 Higher moments
10.2.4 Use of multipole moments: Distributed multipole expansion
10.3 Electric field gradient and nuclear quadrupole coupling constant
10.4 Electrostatic potential
10.5 The molecular polarizability
10.5.1 The static electric polarizability
10.5.2 Polarizability and molecular properties
10.5.3 Hyperpolarizabilities
10.6 Bulk electrical properties
10.6.1 The relative permittivity and the electric susceptibility
10.6.2 Polar molecules
10.6.3 Refractive index and dynamic polarizability
10.7 Optical activity
10.7.1 Circular birefringence and optical rotation
10.7.2 Magnetically induced polarization
10.7.3 Rotational strength

11. Magnetic properties

- 11.1 Interactions of magnetic fields with molecules: response properties
- 11.2 Diamagnetism and paramagnetism
  - 11.2.1 Diamagnetism
  - 11.2.2 Magnetic dipole moment, magnetizability, and magnetic susceptibility
  - 11.2.3 Paramagnetism
- 11.3 Vector functions and their derivatives - a repetition
  - 11.3.1 Derivatives of vector functions
  - 11.3.2 The vector potential
- 11.4 Description of magnetic properties by perturbation theory
  - 11.4.1 The perturbed Hamiltonian
  - 11.4.2 Calculation of diamagnetic and paramagnetic susceptibility
  - 11.4.3 Diamagnetic and paramagnetic current density
- 11.5 Calculation of NMR chemical shifts
  - 11.5.1 Shielding constants
  - 11.5.2 Diamagnetic contribution to shielding
  - 11.5.3 Paramagnetic contribution to shielding
  - 11.5.4 The GIAO method
  - 11.5.5 The IGLO method
  - 11.5.6 The LORG method
  - 11.5.7 GIAO-MP and other methods
  - 11.5.8 The IGLO-DFT method
  - 11.5.9 Results of NMR chemical shift calculations
  - 11.5.10 Choice of the reference
  - 11.5.11 The NMR-ab initio-IGLO method
  - 11.5.12 IGLO-PISA method
  - 11.5.13 State-of-the-art theory: Relativistic corrections
- 11.6 Spin-spin coupling in ESR (Electron Spin Resonance)
  - 11.6.1 Hamiltonian for electron spin coupling
  - 11.6.2 Hyperfine splitting constants
  - 11.6.3 Calculation of the Fermic contact term
  - 11.6.4 Results of unrestricted versus restricted theory
  - 11.6.5 Interpretation of ESR spectra
- 11.7 NMR spin-spin coupling constants
  - 11.7.1 Mechanism of spin-spin coupling between nuclei
  - 11.7.2 The spin-spin coupling Hamiltonian
  - 11.7.3 Ab initio methods for calculating NMR coupling constants
  - 11.7.4 DFT methods for calculating NMR coupling constants
  - 11.7.5 Results obtained with the EOM-CC method
  - 11.7.6 Karplus curves and determination of molecular conformations
  - 11.7.7 Longe range coupling constants
  - 11.7.8 Relationships between coupling constants and other molecular quantities

12. Excited states of molecules

- 12.1 Excited states of a diatomic molecule - a repetition

12.1.1 Coupling of angular momentum: Hund coupling
12.1.2 Selection rules
12.1.3 Vibronic transitions: Franck-Condon principle
12.2 Electronic spectra of polyatomic molecules
12.2.1 Chromophores
12.2.2 Vibronically allowed transitions
12.2.3 Singlet-triplet transitions
12.2.4 Non-radiative decay
12.2.5 Radiative decay: Fluorescence and phosphorescence
12.2.6 Intersystem crossing
12.3 Ab initio methods for calculating excited states
12.3.1 General problems of calculating excited states
12.3.2 The CIS method and its extensions
12.3.3 CASSCF and CAS-PT2
12.3.4 EOM-CC methods
12.3.5 DFT for excited states

13. Molecular interactions and molecular solvation

13.1 Weak molecular interactions: van der Waals complexes
13.2 Forces acting in van der Waals complexes
13.2.1 Electrostatic interactions between molecules
13.2.2 Induced electrostatic interactions
13.2.3 Polarizability and dispersion forces
13.2.4 Overlap or exchange repulsion
13.3 Binding energies and geometries of van der Waals complexes
13.3.1 Basis set and method requirements
13.3.2 Basis set superposition error and counterpoise method
13.3.3 Failure of DFT
13.3.4 Typical binding energies and geometries
13.4 Perturbation theory for intermolecular forces
13.4.1 Short-range perturbation theory
13.4.2 Symmetry-adapted perturbation theories
13.4.3 First order and second order terms
13.5 Electron density description of van der Waals complexes
13.5.1 Difference densities and Laplace concentrations
13.6 Solvation of soluted molecules
13.6.1 Difference between gas phase and solution properties
13.6.2 The supermolecule approach
13.6.3 Continuum models for describing solvation
13.6.4 Cavitation models
13.6.7 Monte Carlo calculations
13.6.8 Methods of molecular dynamics
13.7 Practical Models for intermolecular potentials

9. Density Functional Theory

1. Introduction to DFT
1.1 History of DFT (Thomas-Fermi model)
1.2 Present and future impact of DFT on Chemistry

2. Properties of the exact electron density distribution
2.1 Why to use a density-based theory?

3. Hohenberg-Kohn Theorems
3.1 Searching for the ground-state energy
3.2 The first Hohenberg-Kohn Theorem
3.3 The second Hohenberg-Kohn Theorem
3.4 Spin Polarization
3.5 Scheme for calculations based on the Hohenberg-Kohn theorems

4. Kohn-Sham Equations
4.1 Partitioning of the Hohenberg-Kohn functional F[n]
4.2 The decomposition of the kinetic energy T[n]
4.3 The decomposition of the potential energy V[n]
4.4 The Kohn-Sham equations
4.5 The adiabatic connection scheme
4.6 Partitioning into exchange and correlation contributions

5. Uniform Electron Gas: The Local Density Approximation (LDA)
5.1 The main idea
5.2 Exchange in LDA
5.3 Correlation in LDA
5.4 Advantages and disadvantages of LDA

6. Gradient Corrected DFT
6.1 Gradient expansion
6.2 Generalized Gradient Approximation (GGA)
6.3 Exchange in GGA
6.4 Correlation in GGA

7. Overview over Density Functionals
7.1 Exchange Functionals (Slater exchange, Xa approximation, Becke exchange correction, Becke-Roussel)
7.2 Correlation Functionals (VWN, Perdew-Wang, Lee-Yang-Parr)
7.3 Hybrid methods

8. Improvement of Density Functionals
8.1 Asymptotic behavior
8.2 Limiting cases: homogenous systems, one-electron systems

8.3 The Becke 95 correlation functional
8.4 Exact KS potentials and their application
8.5 Model KS potentials

9. Implementation of DFT
9.1 Programming of the Kohn-Sham Equations
9.2 Numerical Quadrature (Gauss quadrature schemes, accuracy)
9.3 Use of auxiliary bases for densities and potentials
9.4 Available DFT programs
9.5 DFT in Gaussian94

10. DFT methods with Linear scaling
10.1 Fast multipole method
10.2 KWIK
10.3 Integration of functionals using PYS balls
10.4 Use of plane waves
10.5 Use of wavelets

11. Application of DFT methods
11.1 Basis sets for DFT
11.2 Energy derivatives
11.3 Energies and geometries
11.4 Vibrational frequencies and IR intensities

12. Calculation of magnetic properties with DFT methods
12.1 Uncoupled DFT methods
12.2 SOS-DFPT methods
12.3 Current-DFT - An unsolved problem

13. DFT and Excited States
13.1 Hohenberg-Kohn theorems and excited states
13.2 Approaches to treat excited states
13.3 ROSS-DFT and MCSCF-DFT

14. Transition states and van der Waals complexes
14.1 Basic Failures when describing transition states
14.2 Description of H bonding
14.3 Description of van der Waals complexes
14.4 Improvement of DFT

15. DFT and Chemical Concepts
12.1 Chemical potential and electronegativity
12.2 Hardness and softness: HSAB concept
12.3 Fukui function

Possible are also the following fields:

10. Mathematics for Quantum Chemists

1. Vector algebra

1.1 Scalar product
1.2 Vector product
1.3 Triple product

2. Infinite series

2.1 Fundamental concepts
2.1.1 Geometrical series
2.1.2 Harmonic series
2.1.3 Alternating series
2.2 Convergence criteria
2.2.1 Cauchy criterion
2.2.2 d'Almbert criterion
2.3 Series expansion of functions
2.3.1 Taylor series (MacLaurin's series)
2.3.2 Power series
2.4 Complex numbers
2.4.1 Elementary operations
2.4.2 Euler representation

3. Vector analysis

3.1 Scalar and vector fields
3.2 Vector calculus
3.2.1 Curves
3.2.2 Arclength
3.2.2 Tangent, curvature and torsion
3.3 Gradient, Ñ
3.4 Divergence, Ñ•
3.5 Curl, Ñx
3.6 Successive application of Ñ operator, the Laplacian
3.8 Integral relations (Gauss, Stokes)

4. Coordinate systems

4.1 Curvilinear coordinates
4.1.1 Metric
4.1.2 Gradient
4.1.3 Divergence
4.1.4 Laplacian

4.1.5 Curl
4.2 Rectangular Cartesian coordinates
4.3 Circular cylindrical coordinates
4.4 Spherical polar coordinates

5. Tensors

5.1 Linear mapping of vectors, second-rank tensors
5.2 Basis, tensor coordinates and components
5.3 Tensors of arbitrary rank
5.4 Elementary operations with tensors
5.5 Special tensors
5.6 Principal axes and values
5.7 Vector and tensor fields, tensor analysis
5.8 Multipole moments, irreducible tensors
5.9 Behavior of tensors under coordinate rotations

6. Ordinary Differential Equations (ODE's)

6.1 General
6.2 Order of ODE's, explicit and implicit ODE's
6.3. Initial problems, several kinds of problems
6.4 ODE's of first order
6.4.1 Some types of exactly solvable ODE's
6.4.2 Linear first-order ODE's
6.4.3 Existence and uniqueness of solutions, the initial-value problem for the 1st-order ODE
6.5 ODE's of higher order, systems of ODE's
6.5.1 Linear ODE of order ≥ 2
6.5.2 Linear ODE of second order with constant coefficients
6.5.3 Systems of linear ODE of second order with constant coefficients
6.5.4 Initial value, boundary value, and eigenvalue problems
6.5.5 Sturm-Liouville theory and special function systems
6.5.5.1 Sturm-Liouville problems
6.5.5.2 Some important systems of special functions

7. Partial differential equations (PDE's)

7.1 Linear PDE of second order (LPDE2)
7.1.1 The hyperbolic differential equation
7.1.2 The parabolic differential equation
7.1.3 The elliptic differential equation
7.2 Some remarks on non-linear PDE's
7.3 Appendix A1: Spherical harmonics
7.4 Appendix A2: Dirac's d -function

8. Variational calculus

8.1 Functionals and functional derivatives
8.2 Variational problems without constraints
8.3 Variational problem with constraints
8.4 Variational problems with local constraints
8.5 Addendum**:** Ritz method for the Schrödinger equation

9. Vector Spaces

9.1 Vector Algebra: A short repetition
9.2 Vector space
9.2.1 Cartesian vector space R3
9.2.2 Covariant and contravariant components of a vector
9.3 Linear vector space
9.3.1 Definition of linear space L
9.3.2 Linear dependence and linear independence
9.4 Unitary vector space
9.4.1 Function space
9.5 Norm of an element
9.6 Cauchy-Schwarz Inequality
9.7 Triangle Inequality
9.8 Angle between two elements
9.9 Distance between two elements
9.10 Hilbert Space
9.10.1 Cauchy Criterion
9.10.2 Hilbert Space of the square-integrable functions
9.11 Overview over Spaces

10. Operators in Quantum Mechanics (DC)

10.1 Linear Operators
10.2 Eigenfunctions of linear operators
10.3 Matrix elements
10.4 Adjoint operators (Hermitian conjugate)
10.5 Hermitian operators
10.5.1 Properties of Hermitian Operators
10.5.2 Examples of Hermitian operators
10.6 Unitary operators and unitary transformations
10.6.1 Unitary transformation
10.6.2 Unitary transformation of an Hermitian operator
10.6.3 The infinitesimal unitary operator
10.7 Normal operators
10.8 Projection operators
10.9 Functions of operators
10.9.1 Differentiation of an operator

10.10 Commutator of operators
10.11 Overview over operators used in Quantum Mechanics

11. **Matrices and Determinants**

11.1 Linear equation systems
11.2 Some basic definitions
11.3 Matrix addition and matirx multiplication
11.3.1 Addition
11.3.2 Multiplication
11.3.3 Falk diagrams
11.3.4 Commutating matrices
11.4 Special matrices with real numbers
11.4.1 Transposed Matrix
11.4.2 Symmetric and anti(skew)-symmetric matrices
11.4.3 Triangular matrix
11.5 Determinants
11.6 Rank of a matrix and singular matrix
11.7 The inverse of a matrix
11.8 Special matrices with complex numbers
11.8.1 Complex and conjugate-complex matrices
11.8.2 The adjoint (hermitian conjugate) matrix
11.8.3 Hermitian and anti(skew)-Hermitian matrix
11.8.4 Orthogonal and unitary matrices
11.8.5 Normal matrices
11.9 Overview over matrices

12. Eigenvalue problems

12.1 Solving linear equation systems
12.1.1 Gauss elimination
12.1.2 Existence and general properties of solutions
12.2 Eigenvalue equations
12.3 Eigenvalues of Hermitian and other matrices
12.3.1 Similarity transformations and Invariants
12.3.2 Invariants of an unitary transformation
12.3.3 Estimates of the eigenvalues of Hermitian matrices
12.3.4 The Raleigh quotient
12.4 Eigenvalues of a complex matrix
12.5 Diagonalization of matrices
12.5.1 Jacobi diagonalization
12.5.1.1 Algorithm for a Jacobi diagonalization
12.5.2 Givens-Householder diagonalization
12.5.2.1 Givens diagonalization
12.5.2.2 Householder diagonalization
12.5.3 Diagonalization of large matrices

12.5.4 Lanczos method
12.5.5 Nesbet method (see CI course)
12.5.6 Davidson method (see CI course)
12.6 Quadratic forms
12.6.1 Differentiation of a quadratic form
12.6.2 Definiteness of matrices
12.6.3 Characterization of rectangular matrices
12.6.4 Diagonalization of rectangular matrices
12.7 Matrix Factorization
12.7.1 LU Factorization and the Gaussian Elimination revisited
12.7.2 The LDLT and Cholesky factorizations
12.7.3 QR and QL (LQ) factorizations
12.7.4 Spectral decomposition of a matrix
12.8 A non-unit metric: Orthogonalization procedures
12.8.1 Gram-Schmidt Orthonormalization
12.8.2 Löwdin procedures
12.8.2.1 Symmetric orthonormalization
12.8.2.2 Canonical orthonormalization
12.8.3 Comparison and application of orthonormalization procedures
12.9 Overview over eigenvalue problems

13. Optimization

13.1 Definition of optimization problems
13.2 Elements of multivariate analysis
13.2.1 Continuity
13.2.2 Differentiability, gradient, hessian
13.2.3 Taylor's theorem
13.2.3.1 Finite difference approximations to derivatives
13.2.4 Contour plots
13.3 Stationary points of multivariate functions
13.3.1 Minima, global and local
13.3.2 Local versus global methods
13.3.3 Convergence characterization
13.4 Optimization methods used in Quantum Chemistry
13.4.1 Energy-only methods
13.4.1.1 Univariate search
13.4.1.2 Simplex method
13.4.2 Gradient methods
13.4.2.1 Steepest descent methods
13.4.2.2 Conjugate gradient methods
13.4.2.3 Nonlinear conjugate gradient methods
13.4.3 Newton methods
13.4.3.1 Discrete Newton
13.4.3.2 Quasi Newton methods

13.4.3.3 Rank 1 methods, (Broyden's method)
13.4.3.4 Rank 2 methods

14. Probability and Statistics

14.1 Probability, definitions and theorems, Venn diagrams
14.1.1 Counting sample points
14.1.2 Probability of an event
14.1.2.1 Additive rules
14.1.2.2 Multiplicative rules
14.1.2.3 Bayes' rule
14.2 Random variables and probability distributions
14.2.1 Discrete probability distributions
14.2.2 Continuous probability distributions
14.2.3 Empirical distributions
14.2.3.1 Stem and leaf plot
14.2.3.2 Frequency distribution
14.2.4 Joint probability distributions
14.2.4.1 Marginal distributions
14.2.4.2 Conditional probability distributions
14.2.4.3 Statistical independence
14.3 Mathematical expectation
14.3.1 Mean of a random variable
14.3.2 Variance and covariance, standard derivation
14.3.3 Correlation coefficient
14.3.4 Chebyshev's theorm
14.4 Some discrete probability distributions
14.4.1 Discrete uniform distribution
14.4.2 Binomial and multinomial distributions
14.4.2.1 The Bernulli Process
14.4.3 Hypergeometric distribution
14.4.4 Poisson distribution and the Poisson process
14.5 Some continuous probability distributions
14.5.1 Continuous uniform distribution
14.5.2 Normal distribution
14.5.3 Areas under the normal curve
14.5.4 Normal approximation to the binomial
14.5.5 Gamma and exponential distributions
14.5.6 Relationship between Gamma, exponential and Poisson distribution
14.5.7 Other continuous distributions
14.5.7.1 Chi-square distribution
14.5.7.2 Logonormal distribution
14.5.7.3 Weibull distribution
14.6 Fundamental sampling distributions
14.6.1 Central tendency in the sample
14.6.2 Variability in the sample

14.6.3 T-distribution
14.6.4 F-distribution

15. Catastrophe Theory

15.1 The cusp catastrophe
15.2 The dynamic that causes catastrophes
15.3 The mechanism of aggression
15.4 Divergence
15.5 Thom's classification theorem
15.6 Thom's seven elementary catastrophes
15.7 The butterfly catastrophe
15.8 Structural changes and molecular graphs
15.9 Description of reaction mechanism: $H_2 + O(^3P)$

11. Presentation Techniques in Chemistry – How to write a paper? How to give a seminar?

1. Scientific Research and Scientific Writing

1.1 The ultimate result of scientific research is publication
1.2 Scientific communication is a 2-way process
1.3 Thinking and Writing
1.4 There is a well-defined path from thinking to writing
1.5 From thinking to writing in TC
1.6 List of questions to be answered before writing

2. What is a "Scientific Paper"

2.1 Types of scientific communications
2.2 Definition of a scientific paper: primary publication
2.3 Organization of a scientific paper
2.4 Drafting a scientific paper
2.4.1 The writing process
2.4.2 Transitions
2.4.3 The Role of tangible details
2.4.4 Keeping the speed of writing.
2.5 Perception of a paper
2.6 Order of writing up the paper
2.7 Preparing the actual write-up: Notes for authors

3**. The various parts of a Journal Article**

3.1 The Result part
3.2 The Method part
3.3 The Discussion part
3.4 The Introduction part
3.5 The Conclusion

3.6 The Abstract
3.7 The Title
3.8 Authors
3.9 Acknowledgement
3.10 References
3.11 Supporting Information
3.12 Appendix

4. General Rules and Use of Language

4.1 Basic rules
4.2 Scientific language
4.3 Choice of the correct word or phrase
4.4 Articles
4.5 Comparisons
4.6 Parallelism