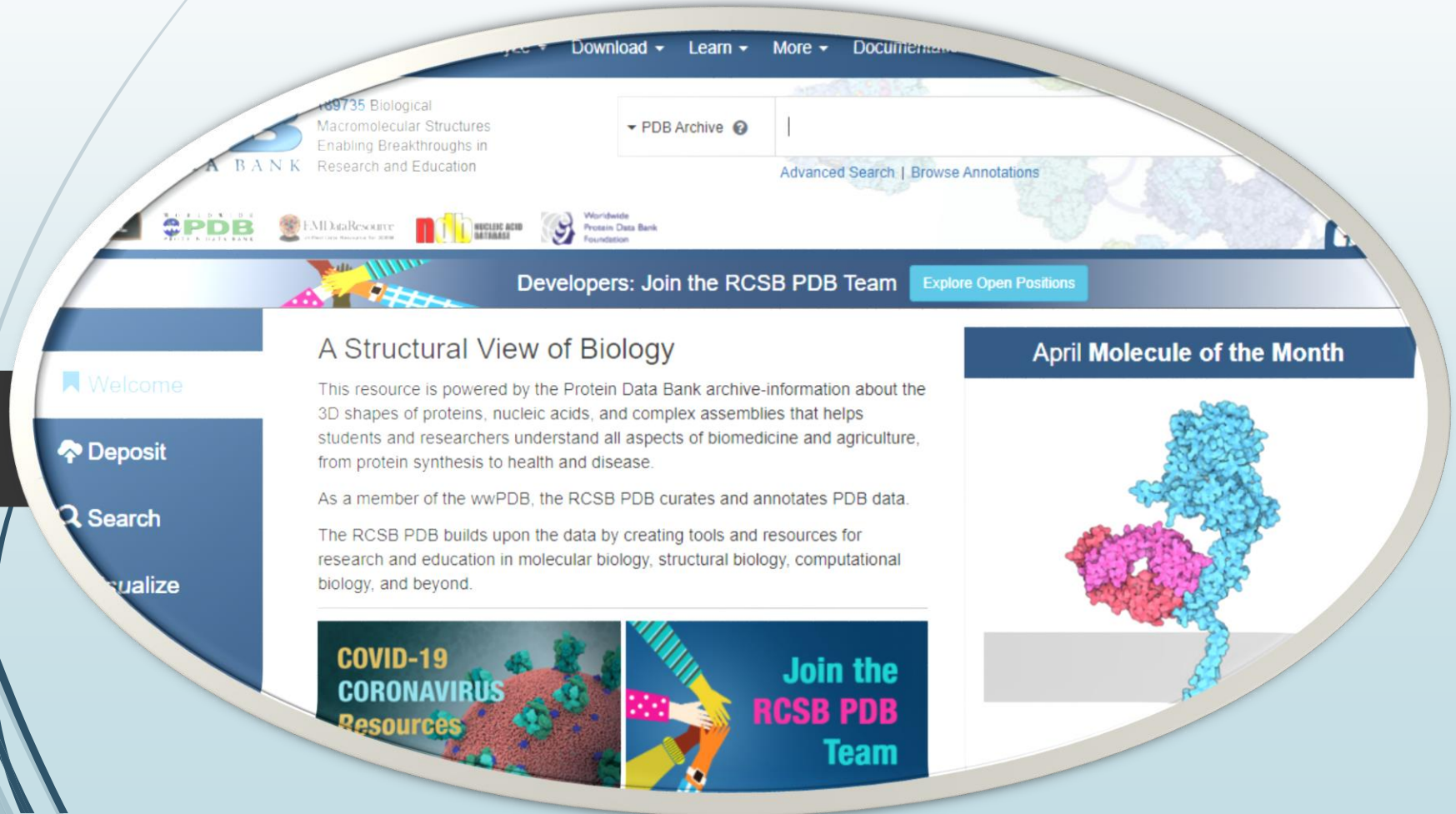
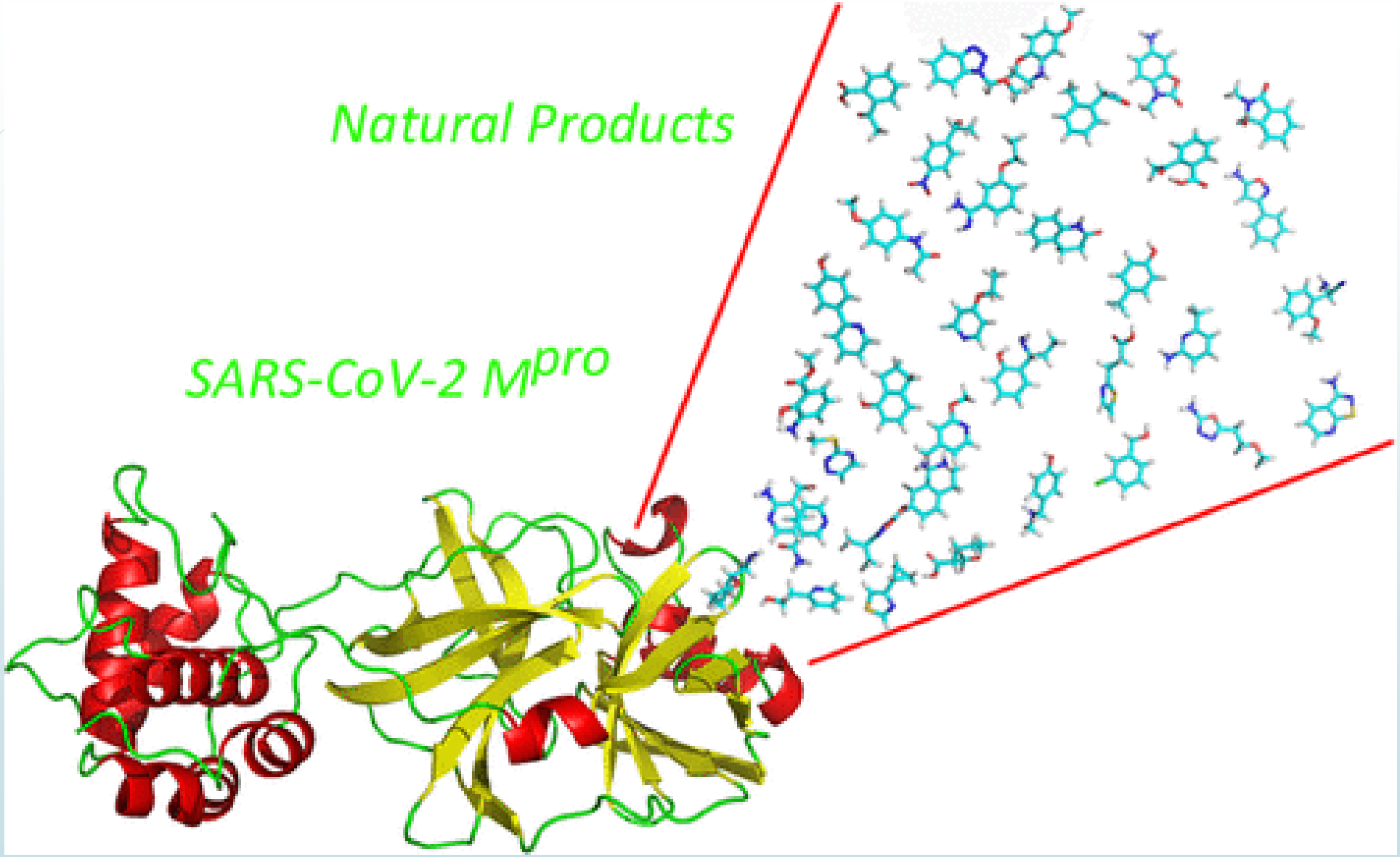
TREND PENELITIAN KIMIA KOMPUTASI



SUWARDI

FMIPA UNY


Natural Products
SARS-CoV-2 M^pro

Computational chemistry

Computational chemistry is

- **a branch of chemistry that uses computer simulation to assist in solving chemical problems**.
- It uses methods of theoretical chemistry, incorporated into computer programs, to calculate the structures and properties of molecules, groups of molecules, and solids.

Kimia komputasi adalah

Cabang kimia yang menggunakan hasil kimia teori yang diterjemahkan ke dalam program komputer melalui *simulasi* komputer untuk menghitung *sifat-sifat* molekul dan perubahannya maupun melakukan *simulasi* terhadap sistem-sistem besar. (Wikipedia)

.

Contoh sifat-sifat molekul yang dihitung antara lain

1. Struktur (yaitu letak atom-atom penyusunnya),
2. Energi dan selisih energi,
3. Muatan,
4. Momen_dipol,
5. Kerapatan_elektronik,
6. Kereaktifan,
7. Frekuensi getaran dan besaran spektroskopi lainnya.

Simulasi terhadap makromolekul (seperti protein dan asam_nukleat) dan sistem yang besar bisa mencakup:

1. Kajian konformasi_molekul dan perubahannya (mis. proses denaturasi protein),
2. Perubahan fase,
3. Peramalan sifat-sifat makroskopik (seperti panas jenis) berdasarkan perilaku di tingkat atom dan molekul.

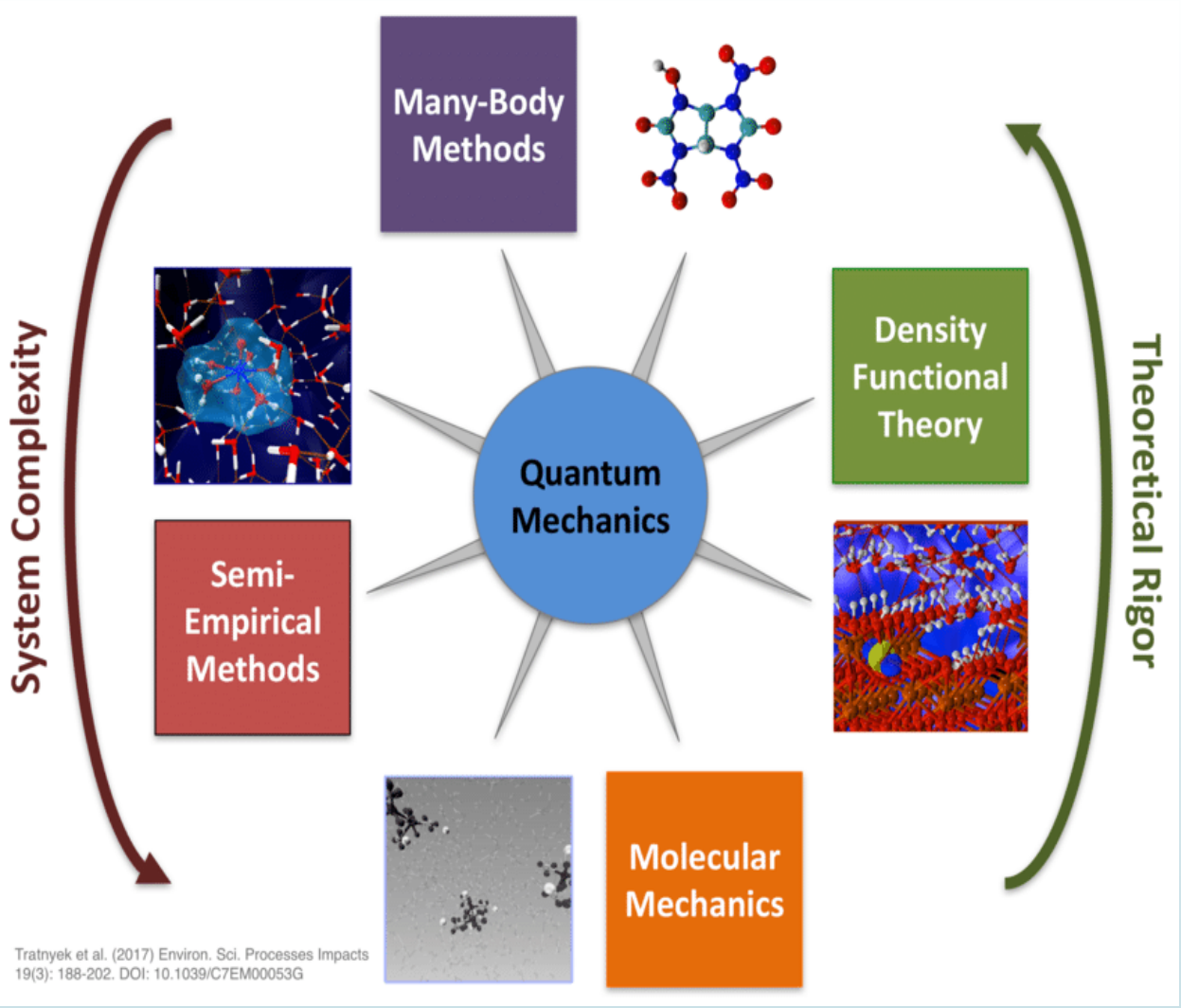
Sistem

1. Makromolekul seperti protein (molecular docking dan molecular dynamics)

2. Banyak molekul seperti gas, cairan (ion logam dalam air, amoniak, campuran amoniak-air, padatan, dan kristal cair

TOOL KIMIA KOMPUTASI

1. Mekanika Molekul
2. Semiempirik
3. Ab Initio
4. DFT
5. Dinamika Molekul

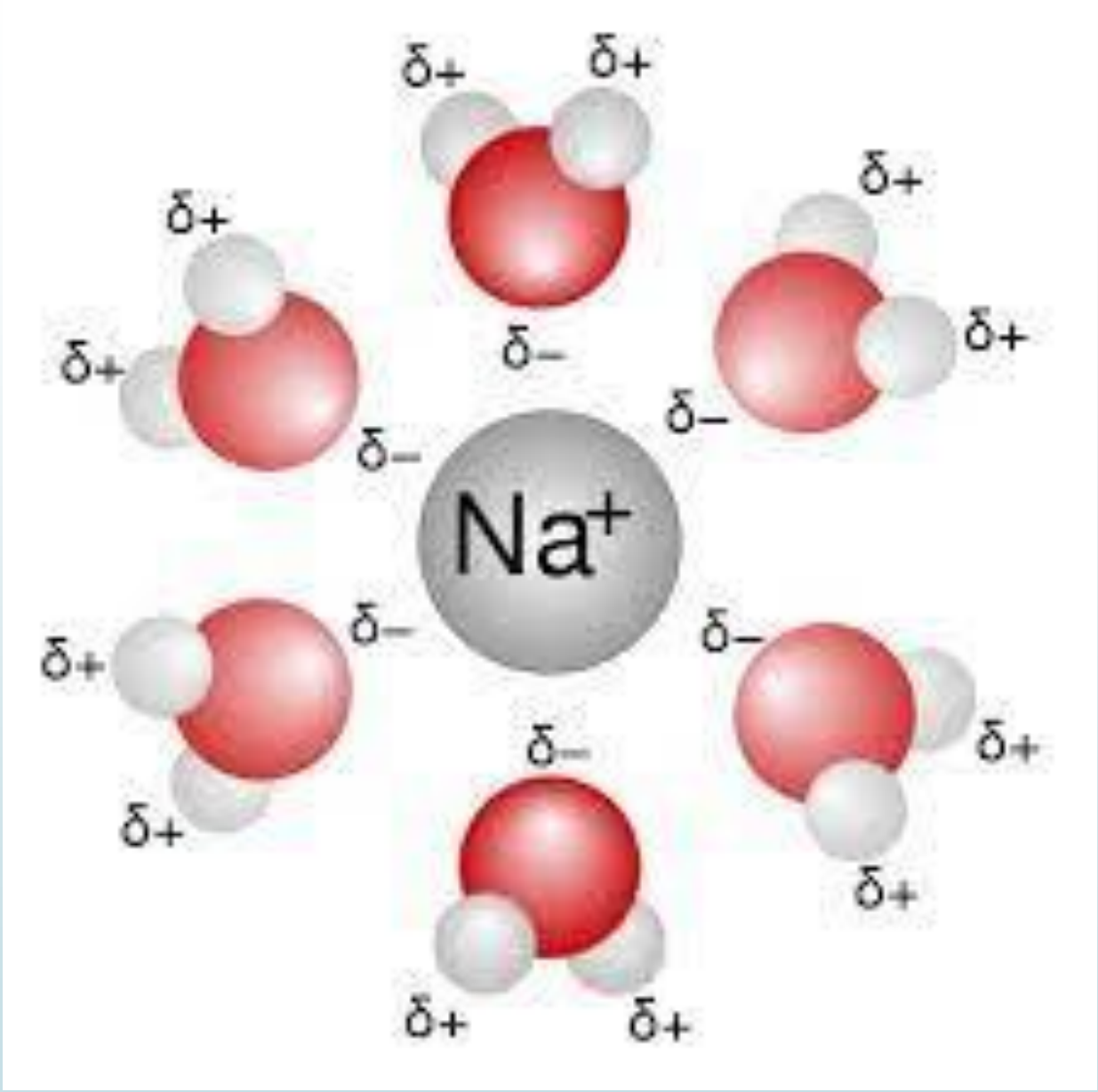


Riset Dalam Kimia Komputasi

1. *Kajian pKa suatu Molekul yang didasarkan pada Teori Kerapatan Fungsional (DFT)*
2. *Desain in silico suatu inhibitor pada target (protein)→ Molecular Docking*
3. *Desain material Photoactive untuk sel surya*

Riset Dalam Kimia Komputasi

4. *Kajian ion logam dalam air, amoniak cair, dan campuran amoniak-air (18,6%)[**SOLVASI**]→ Simulasi Dinamika Molekul QM/MM*
5. *Kajian Solvasi Protein-Ligand dalam bidang Computer Aided Drug Design (CADD) → Simulasi Dinamika Molekul*


δ+
δ+
δ+
δ+
δ−
δ+
δ+
δ−
δ+
Na+
δ−
δ−
δ+
δ+
δ−
δ+
δ+
δ+

Metodologi

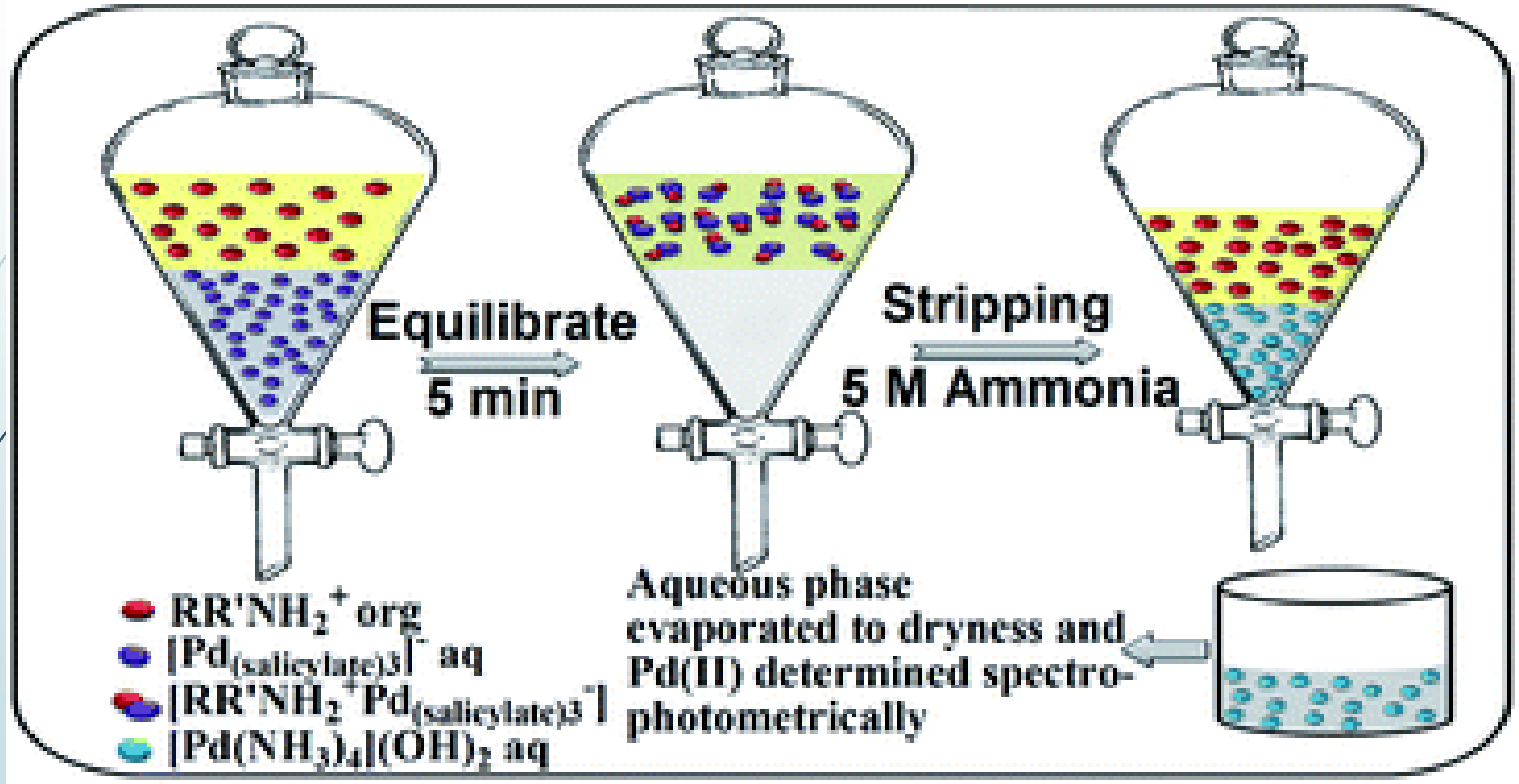
1 Kajian ion logam dalam Air, amoniak cair dan Campuran amoniak-air

Piranti keras

Komputer : Laptop atau PC

Piranti lunak

Gaussian, Gaussview, Turbomole, QM/MM, VMD, XMGRACE dll


Equilibrate
5 min
Stripping
5 M Ammonia
$RR'NH_2^+$ org
$[Pd_{(salicylate)3}]^-$ aq
$[RR'NH_2^+Pd_{(salicylate)3}^-]$
$[Pd(NH_3)_4](OH)_2$ aq
Aqueous phase
evaporated to dryness and
Pd(II) determined spectro-
photometrically

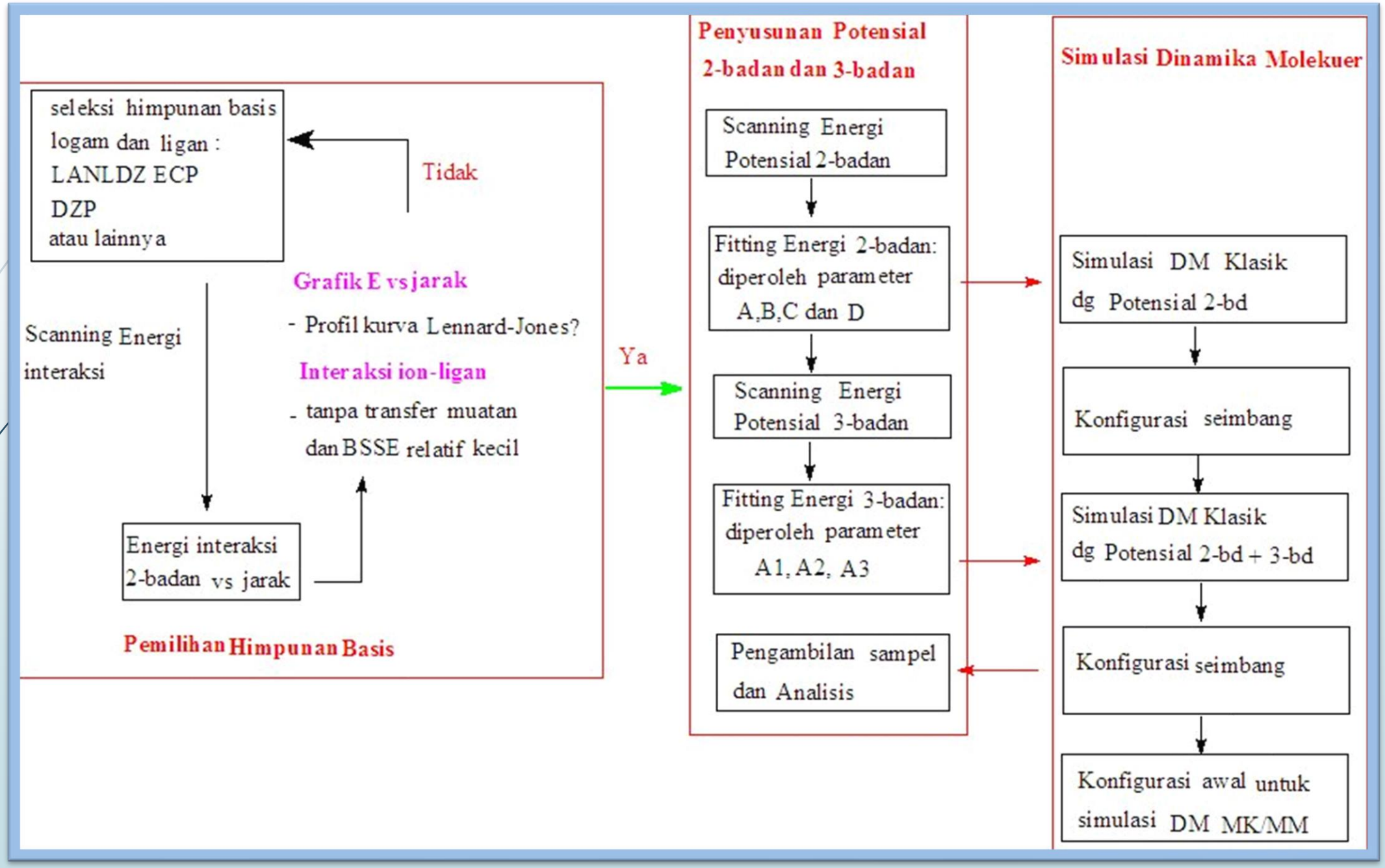
Bahan kajian (Contoh)

1 Zr(IV) + 499 H_2O

1 Zr(IV) + 215 NH_3

1 Zr(IV) + 407 H_2O + 92 NH_3

Metode Penelitian



Simulasi DM Zr(IV) dalam larutan amoniak 18,6% hanya menggunakan potensial pasangan (2-bd)

Potensial 2-bd

1. Zr(IV) atau Zn(II)- NH_3,
2. Zr(IV) atau Zn(II)–H_2O

Simulasi Dinamika Molekuler Klasik

1 **Zr(IV) atau Zn(II)** dalam
407 H_2O dan 92 **NH_3**
T = 298,16 K, p=1 atm,
ρ = 0.927 g cm^{-3},
r_{cut} = 12,0 Å

Fungsi distribusi radial (FDR)

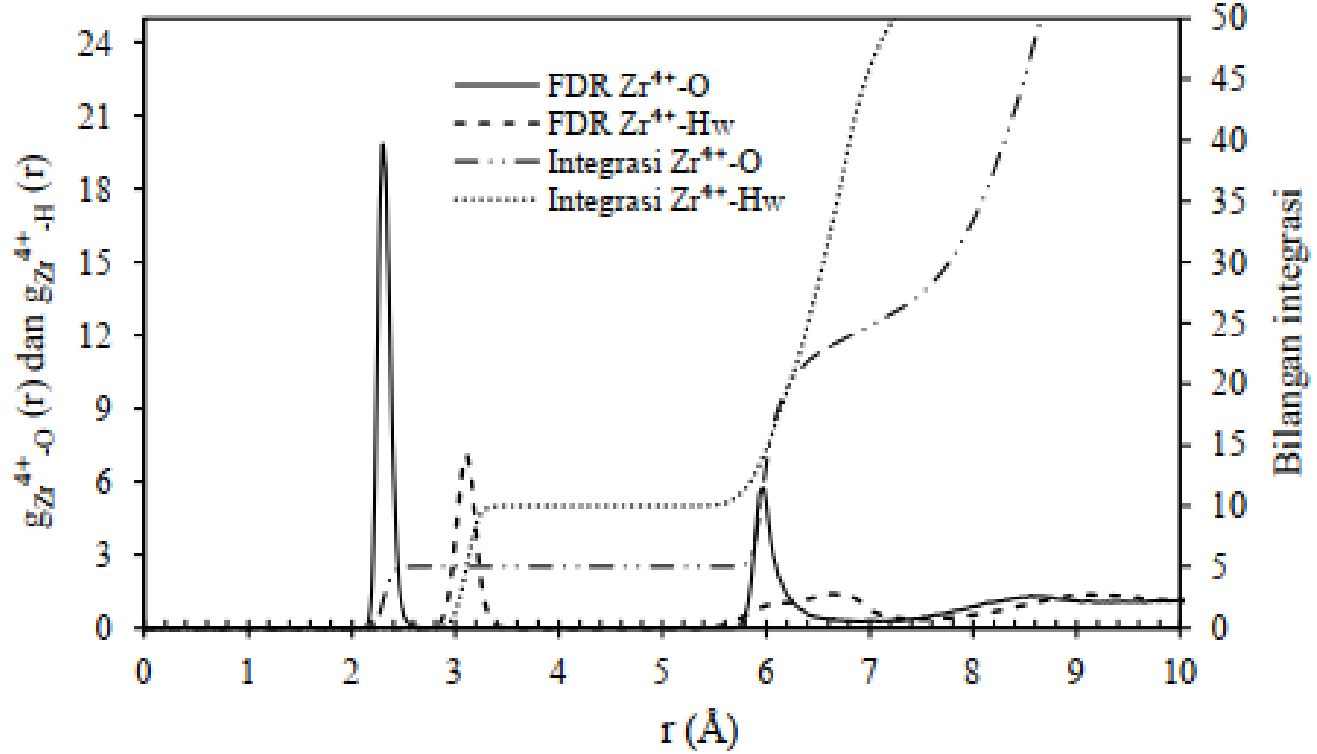
MRT

Distribusi bilangan koordinasi (DBK)

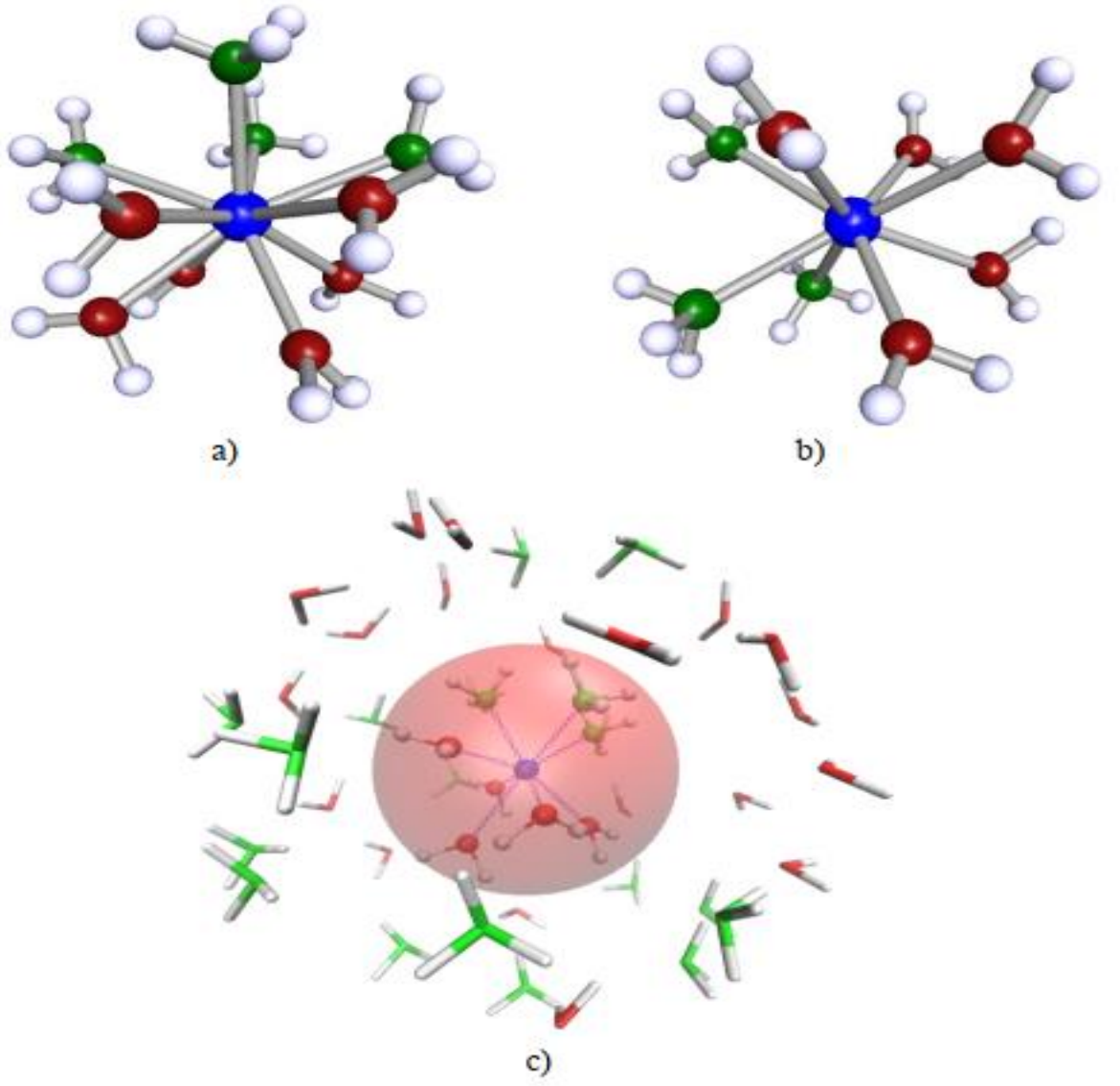
Migrasi ligan

Fungsi distribusi sudut (FDS)

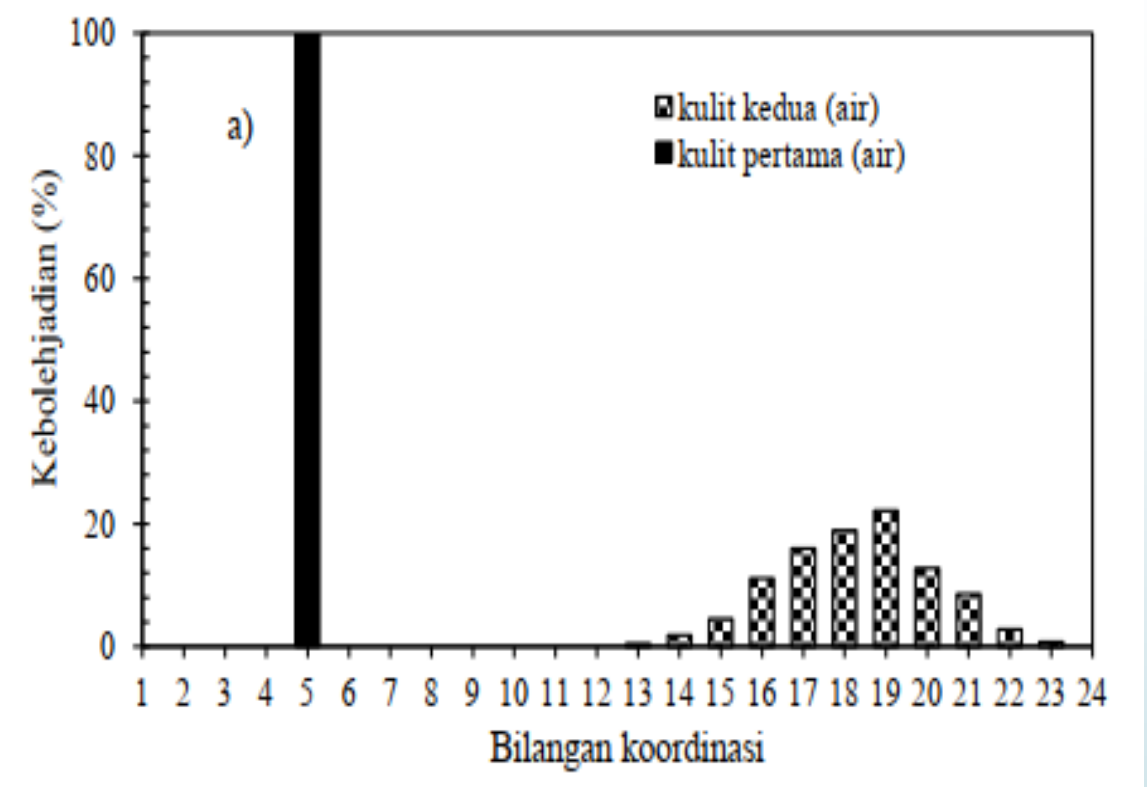
Hasil Simulasi DM QM/MM

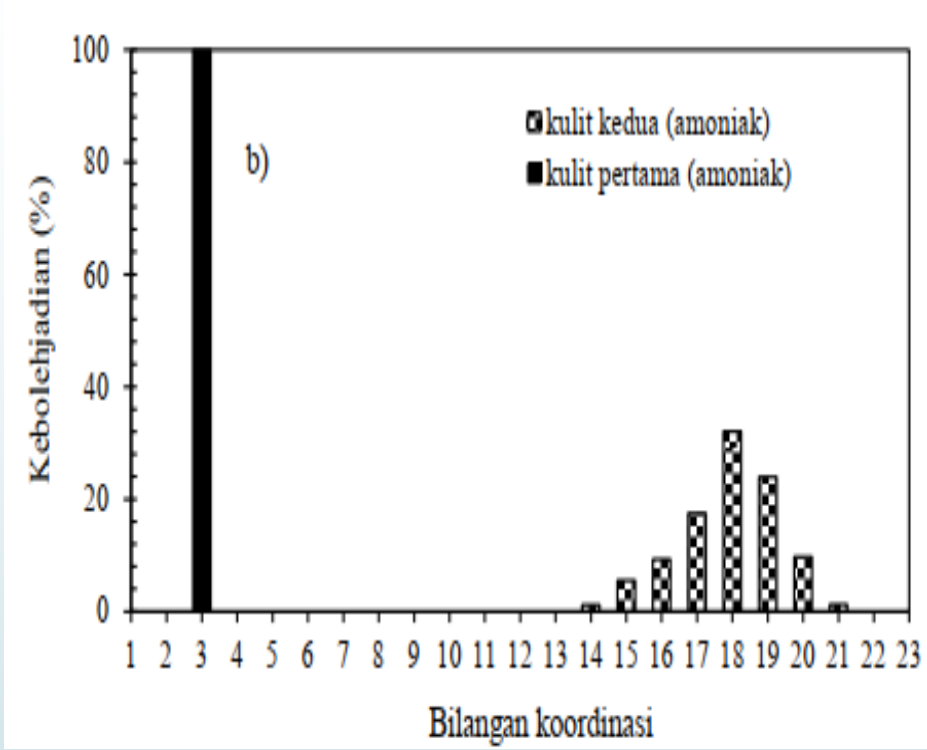


Gambar 5.44 FDR Zr^{4+}-O dan Zr^{4+}-H_w dan bilangan integrasinya yang diperoleh dari simulasi klasik MM 2-badan + 3-badan ion Zr^{4+} dalam larutan amoniak 18,6%

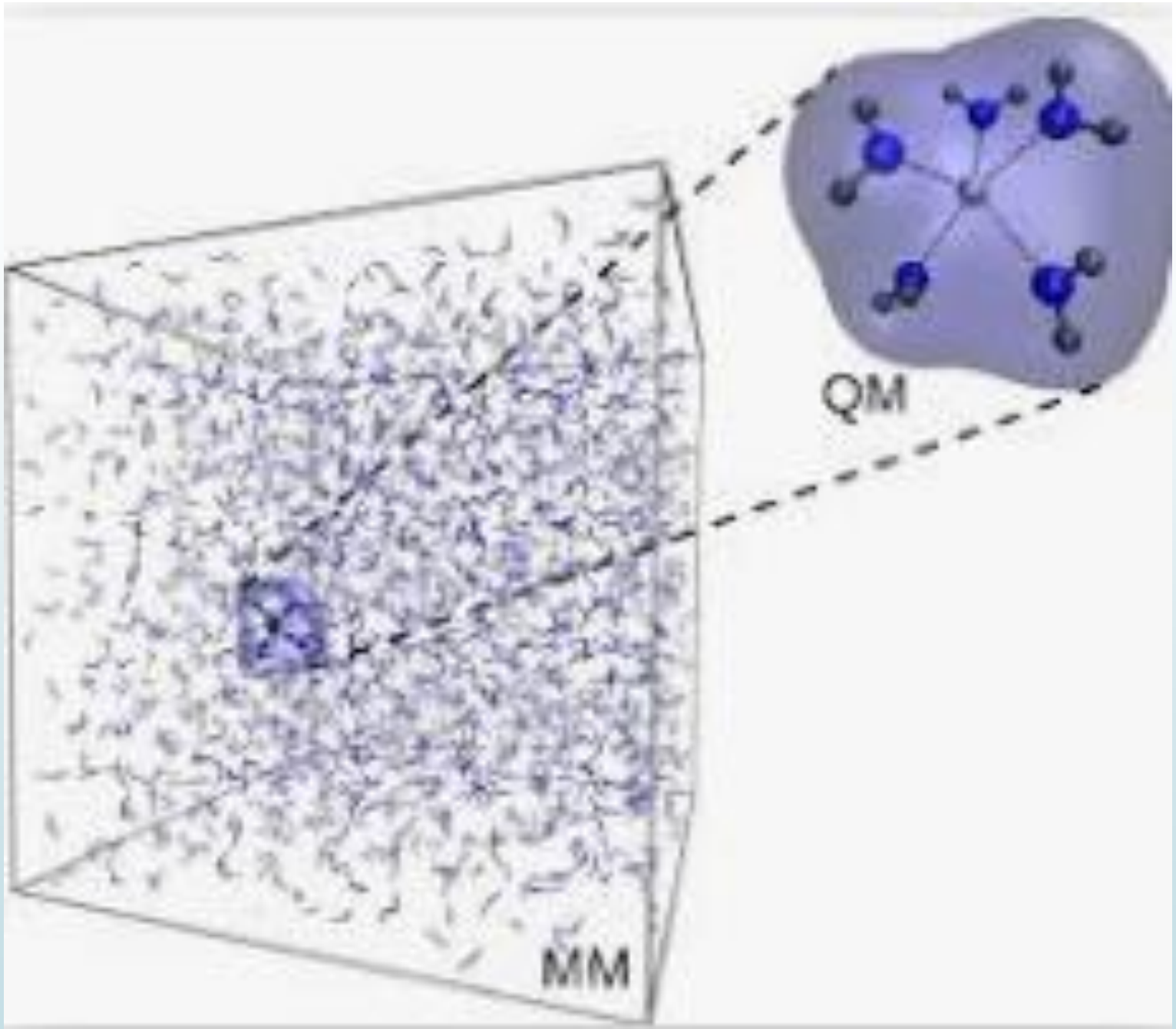


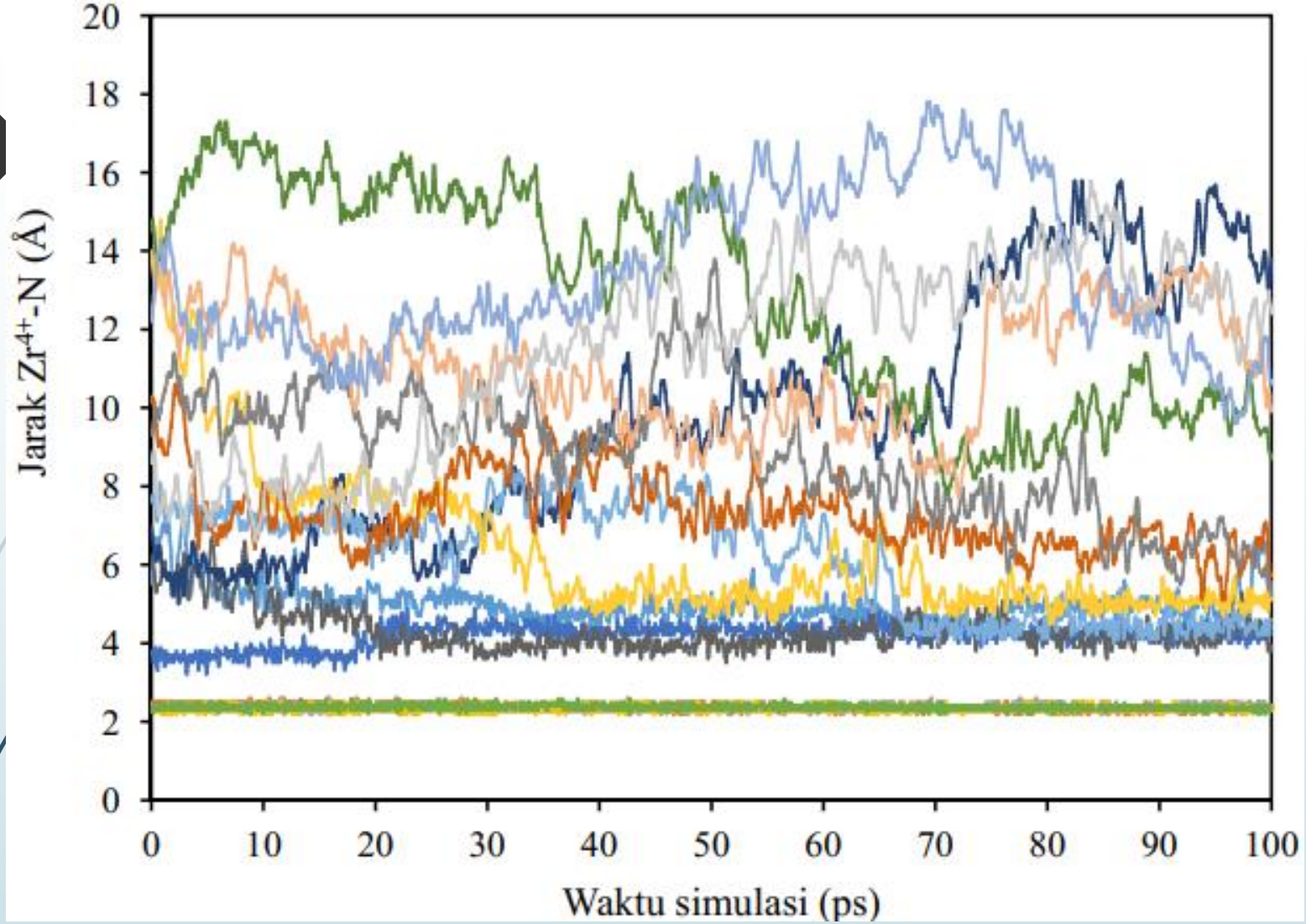
Potret struktur a) $[Zr(NH_3)_4(H_2O)_6]^{4+}$, b) $[Zr(NH_3)_3(H_2O)_5]^{4+}$ dalam kulit pertama masing-masing hasil simulasi klasik MM 2-badan dan MM 2-badan + 3-badan (potret diambil melalui Tmolex), c) $[Zr(NH_3)_3(H_2O)_5]^{4+}$ yang dikelilingi molekul air dan amoniak dalam kulit kedua. Oksigen (merah), hijau (nitrogen), abu-abu (hidrogen) dan biru (ion zirkonium)





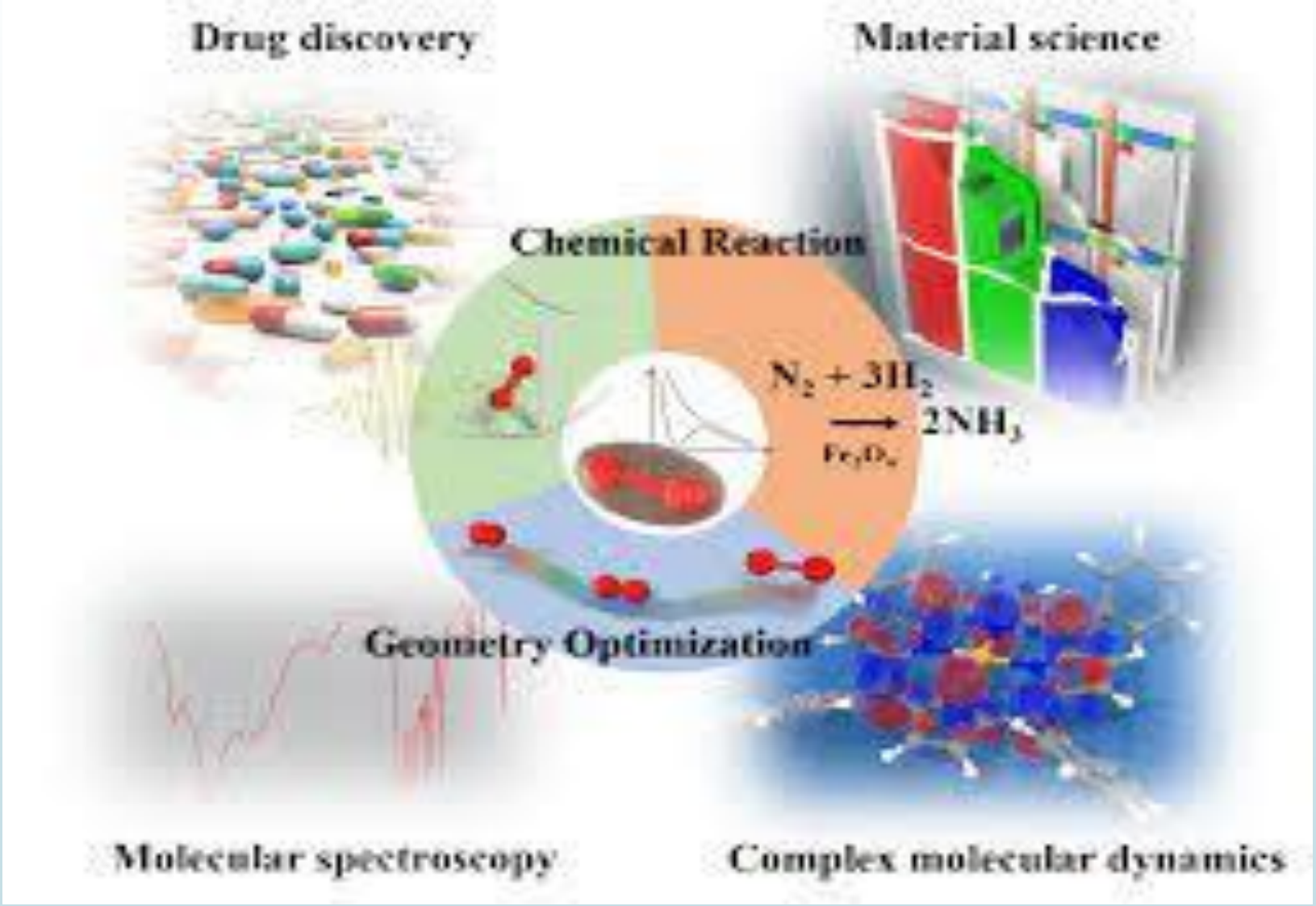
Gambar 5.54 Distribusi bilangan koordinasi solvasi Zr^{4+} dalam larutan amoniak 18,6% pada kulit pertama dan kedua a) air dan b) amoniak yang diperoleh dari simulasi MK/MM


QM
MM

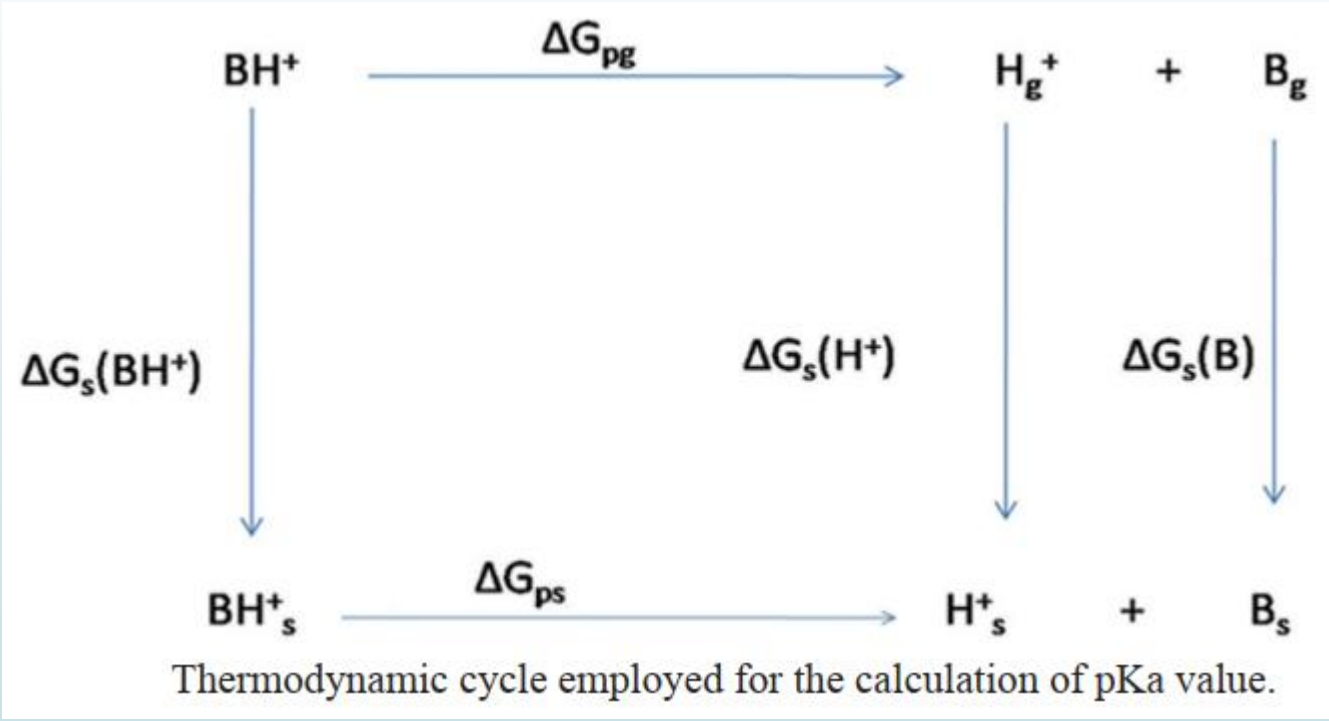


Variasi jarak Zr^{4+}-O dan Zr^{4+}-N selama simulasi klasik MM 2-badan yang menunjukkan tidak terjadi pertukaran ligan air dan amoniak dalam kulit solvasi pertama

Riset Dalam Kimia Komputasi



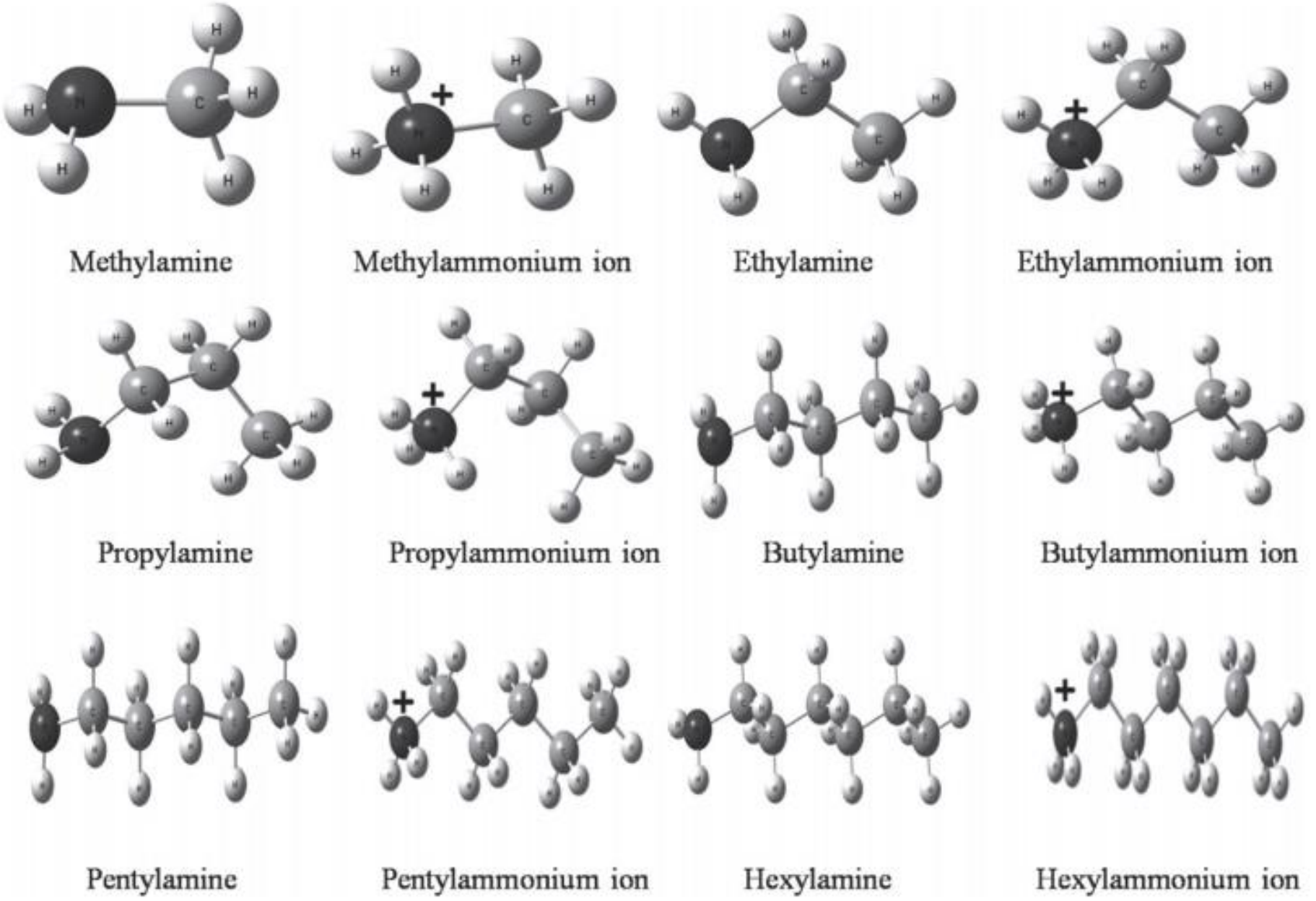
STUDI pKa



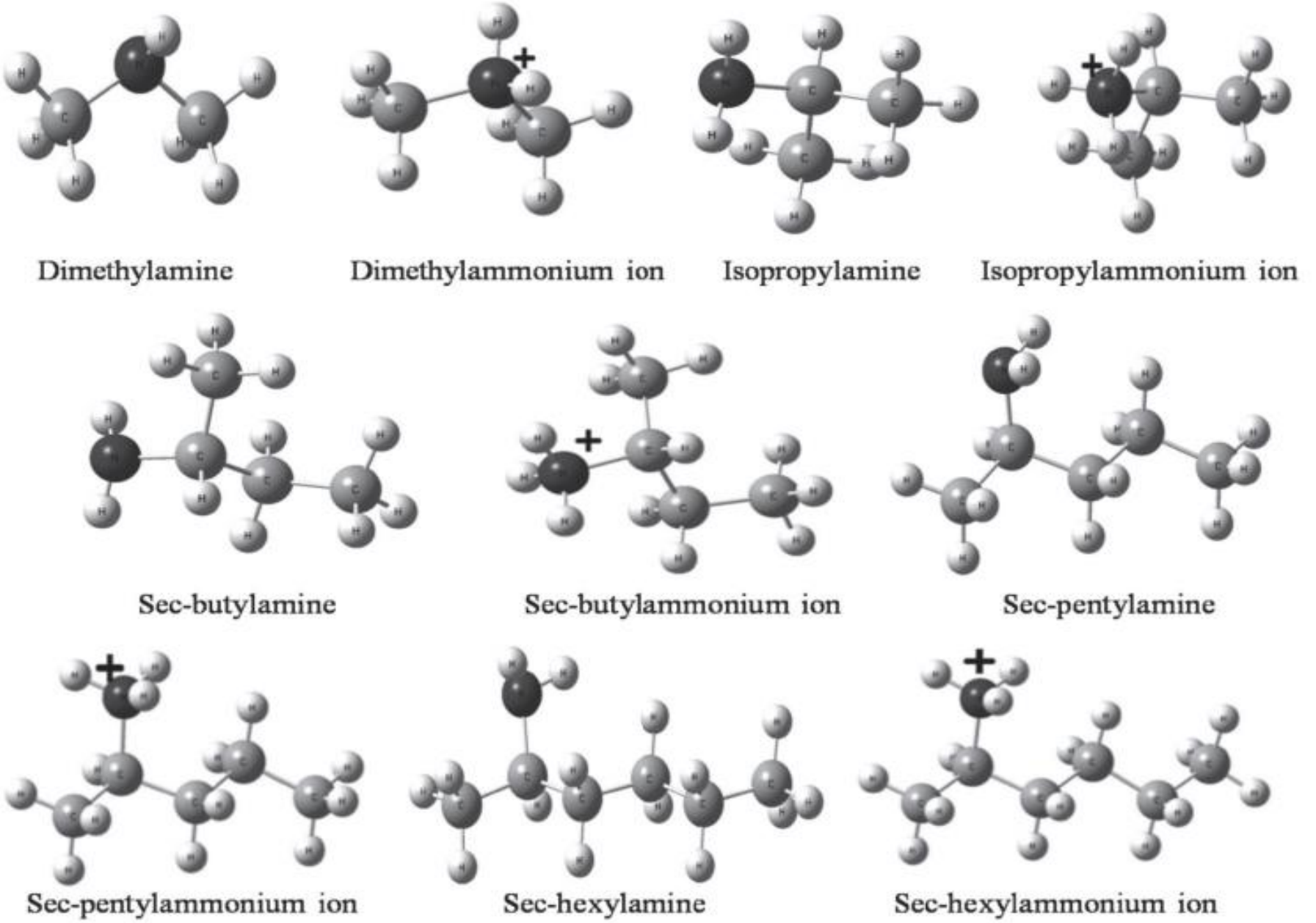
Thermodynamic cycle employed for the calculation of pKa value.

TABLE 1.1 pKa Values of Methylamine Obtained by Using Different Basis Sets

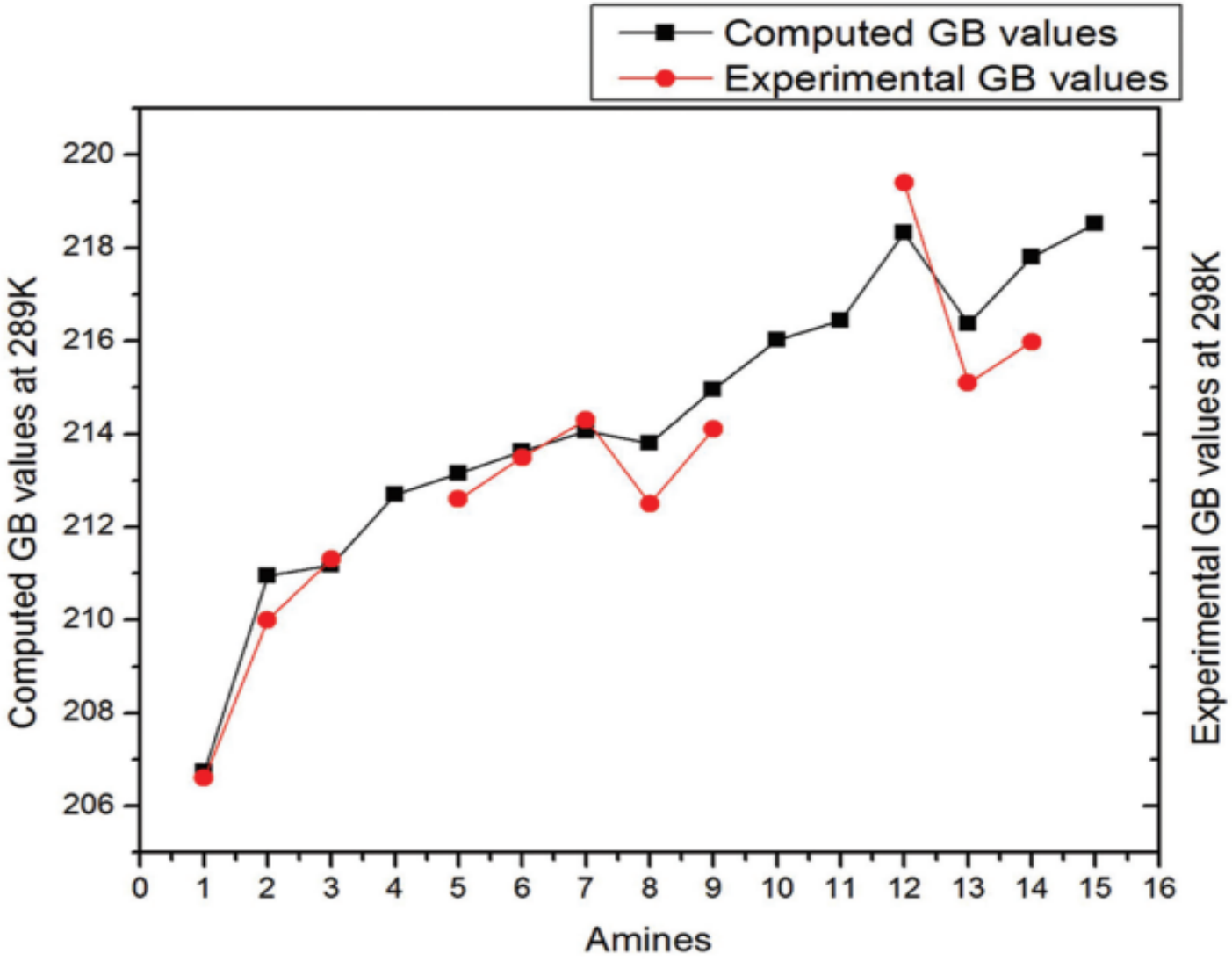
Basis set	pKa values at 298 K		Relative deviation (%)
	Calculated	Experimental	
6–31G	16.34	10.50	55
6–31G(d)	14.15	10.50	38
6–31G(d,p)	14.90	10.50	41
6–31++G	12.21	10.50	16
6–31++G(d)	9.99	10.50	4
6–311++G(d,p)	10.45	10.50	**0.4**



Optimized geometries of neutral and protonated primary amines.



Optimized geometries of neutral and protonated secondary amines.



Calculated and experimental gas phase basicity values of different alkylamines at 298K.

TABLE 1.4 pKa Values (Calculated and Experimental) of Different Alkylamines

Number	Amine	pKa values at 298 K	
		Calculated	Experimental
1	Methylamine	10.44	10.50
2	Dimethylamine	10.74	10.73
3	Trimethylamine	10.10	09.80
4	Ethylamine	10.42	10.60
5	Propylamine	10.55	10.67
6	Isopropylamine	10.61	10.63
7	Butylamine	10.66	10.68
8	Sec-butylamine	10.89	10.80
9	Tret-butylamine	10.44	10.43
10	Pentylamine	10.79	10.63
11	Sec-pentylamine	10.83	–
12	Tert-pentylamine	11.01	10.85
13	Hexylamine	10.72	10.56
14	Sec-hexylamine	10.95	–
15	Tert-hexylamine	10.36	–

KEYWORDS

- alkylamines
- density functional theory
- free energy of solvation
- gas phase basicity
- gas phase proton affinity
- pKa values

MOLECULAR DOCKING

DOCKING MOLECULAR

Struktur kompleks tiga dimensi (3D) yang terbentuk antara target obat dan kandidat obat memainkan peran penting dalam desain obat berbasis struktur (SBDD), molekul kandidat obat dirancang dengan mengacu pada struktur 3D target obat.

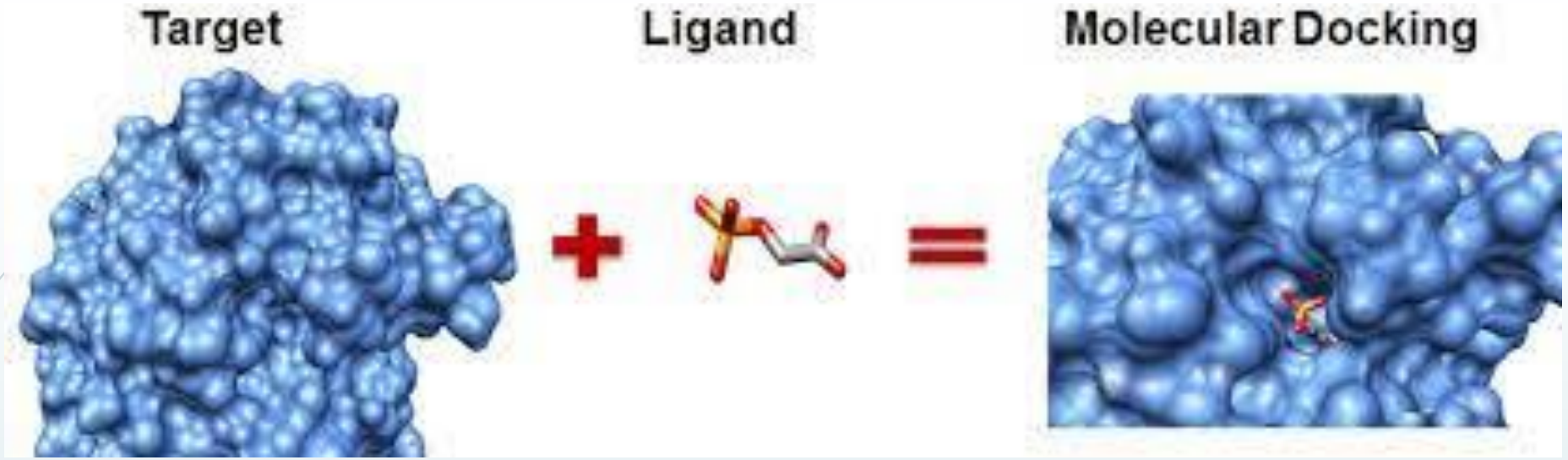
Dengan demikian, prediksi komputasi struktur kompleks protein-ligan, yaitu komputasi docking, memainkan peran penting dalam SBDD

Bahan

Bahan yang digunakan dalam penambatan molekul berupa model protein 2BK5 diunduh dari situs Protein Data Bank (http://www.rcsb.org/), dan data struktur senyawa ligand (PUBCHEM).

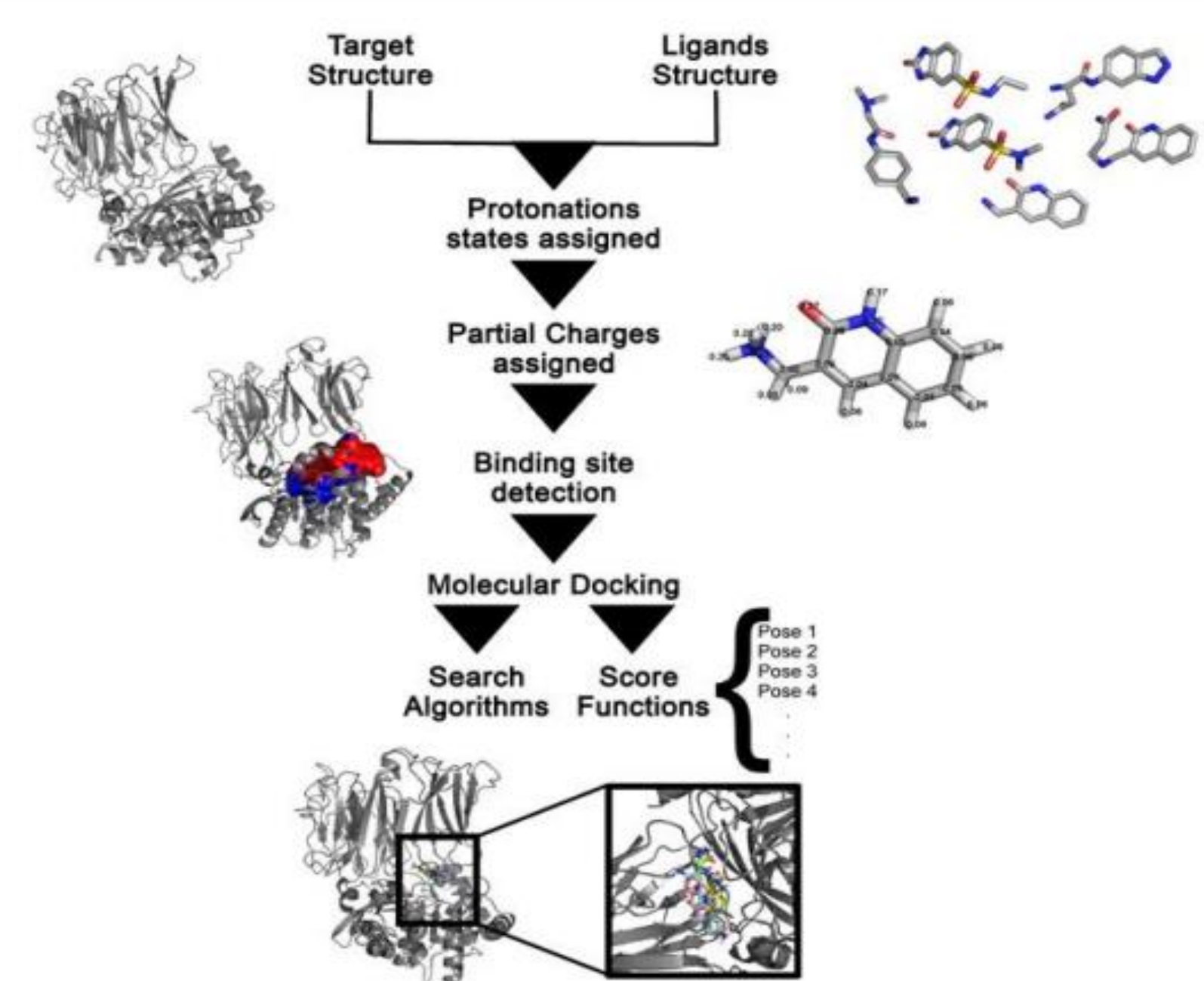
Perangkat

Perangkat lunak yang digunakan yaitu, Sistem Operasi Windows 10, Autodock Tools, Autodock Vina, MOE, PyMol, Gaussview dan Biovia Discovery Studio 2017, dan Desmond. Perangkat keras yang digunakan pada penelitian ini adalah computer dengan spesifikasi *processor* AMD Quad core CPU @ 2.50GHz, dan RAM 6 GB.

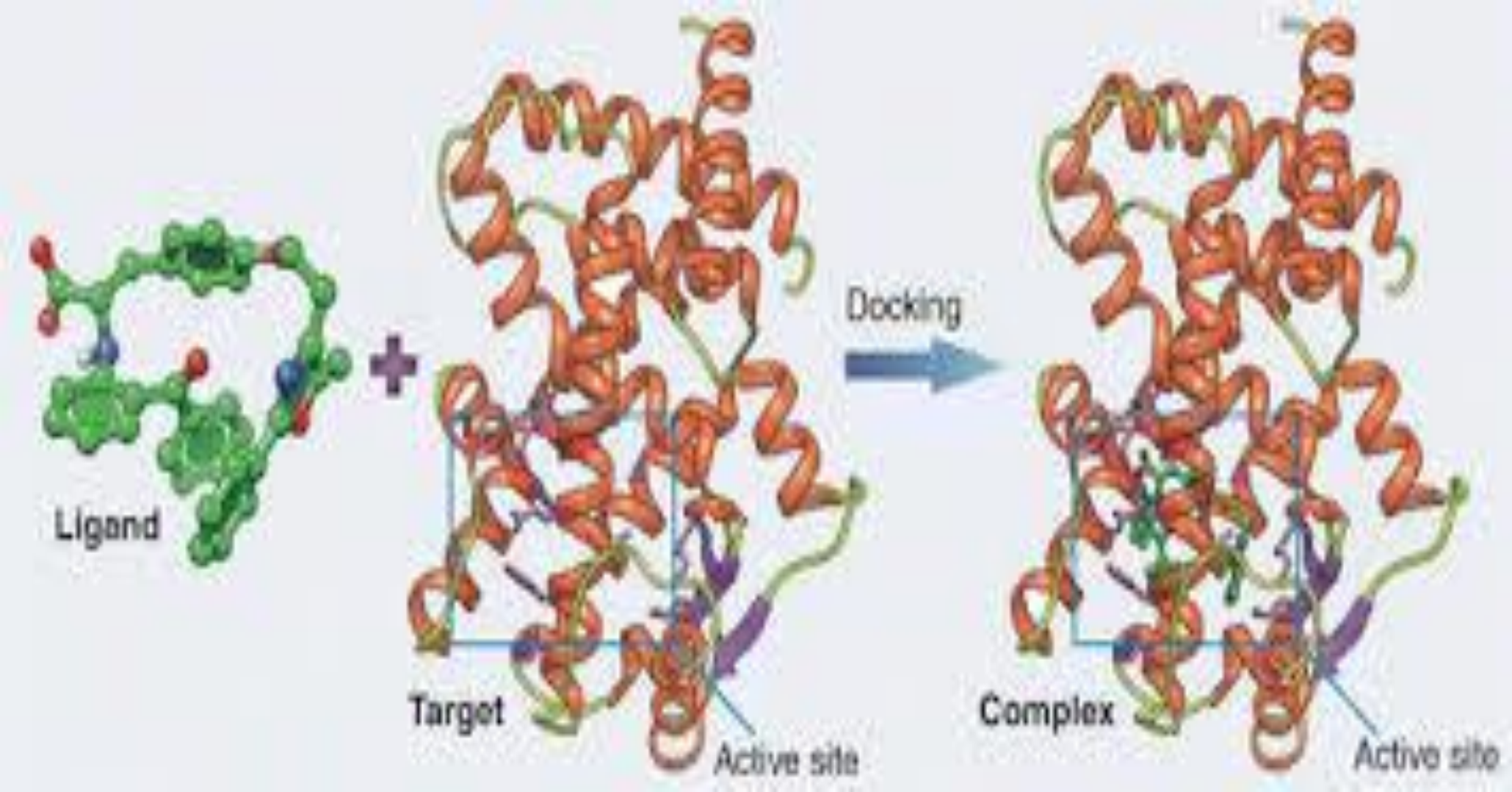


Pengertian Docking Molekul

Prosedur Docking



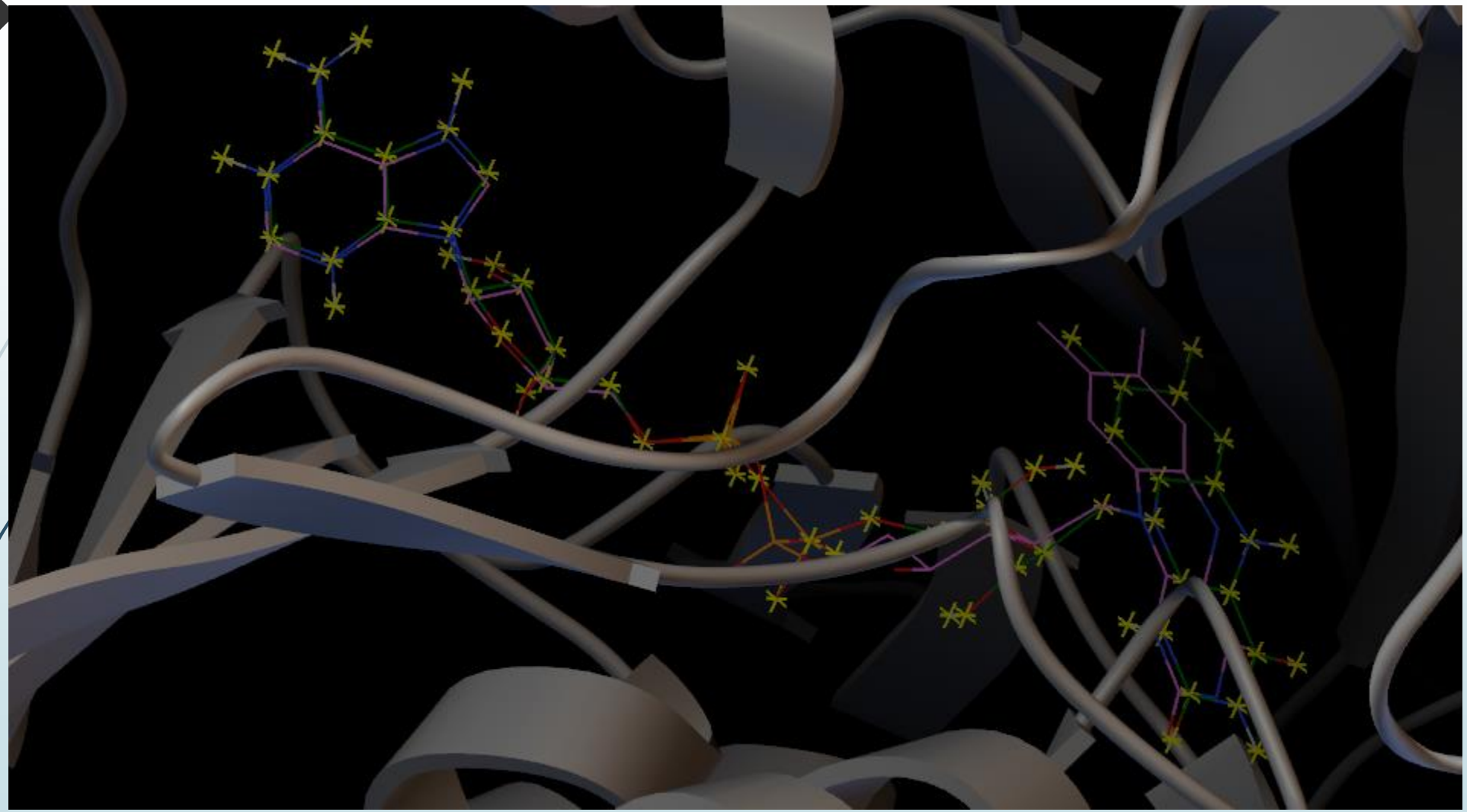
Docking ligand ke Target (Protein)

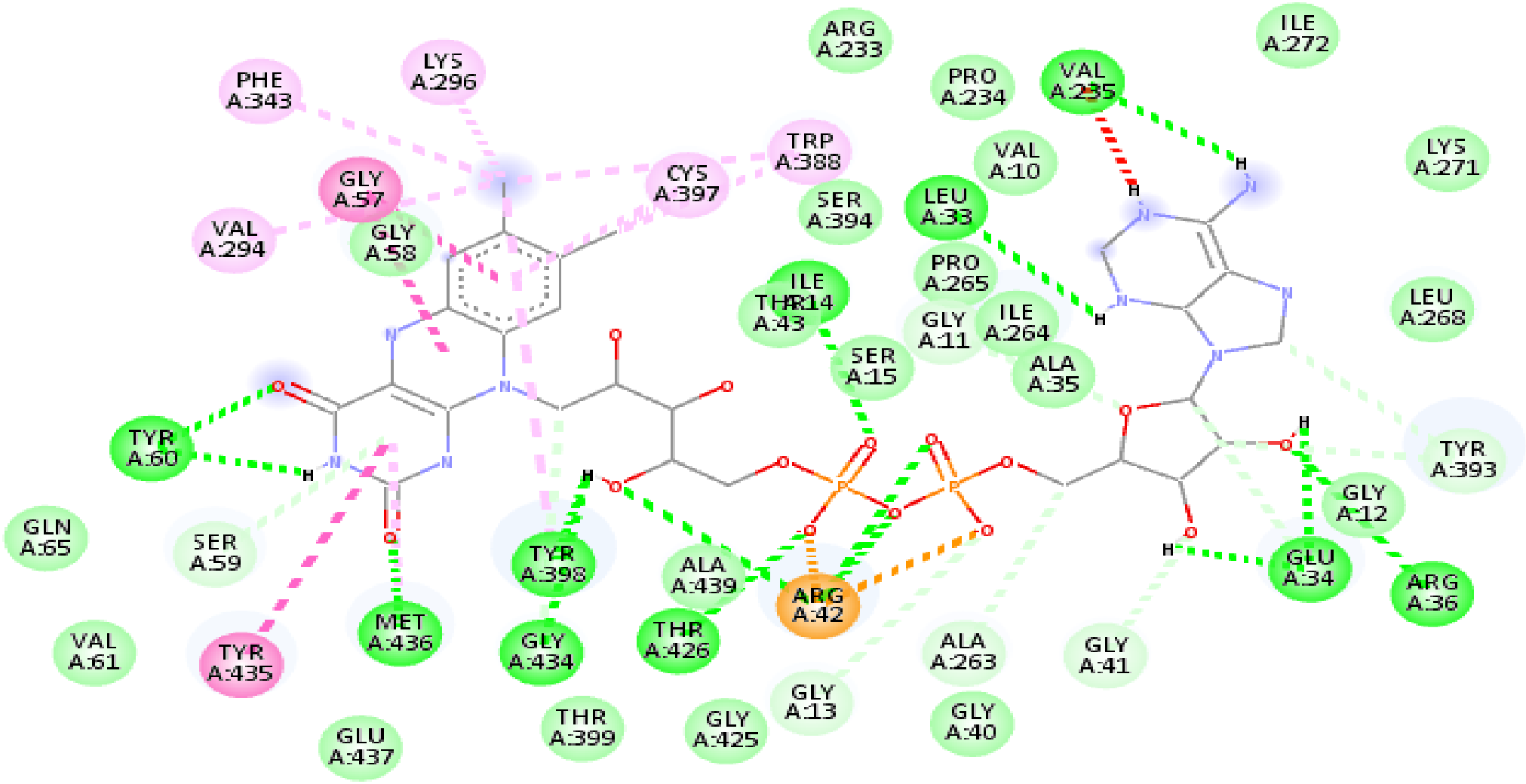


log - Notepad

File Edit Format View Help

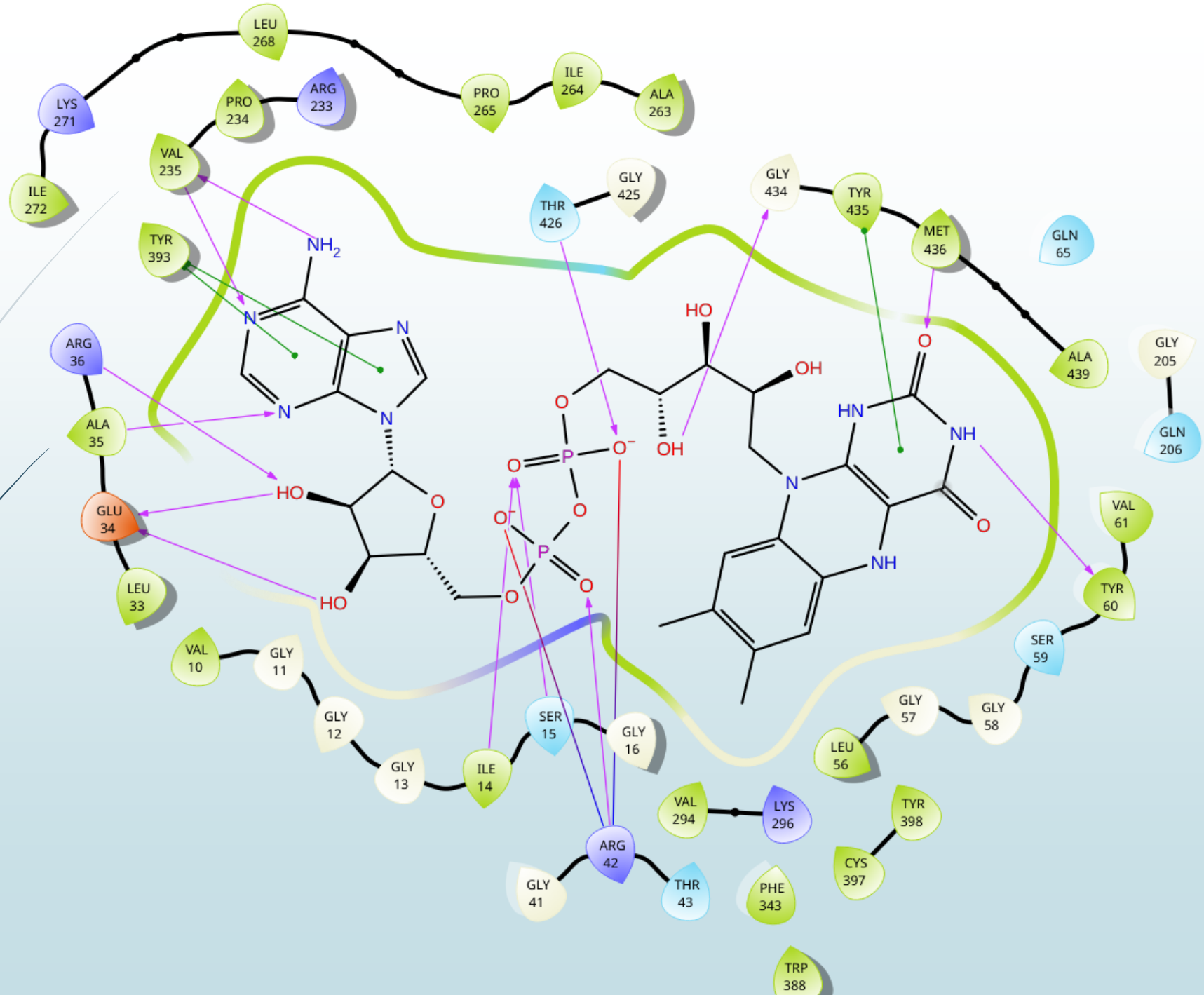
```
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1096075048
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -14.0     0.000     0.000
   2        -11.1    27.854    30.333
   3        -10.7    27.418    30.214
   4        -10.6    24.839    27.899
   5        -10.6    30.339    34.134
   6        -10.5    27.876    31.206
   7        -10.4    28.397    30.878
   8        -10.4    27.670    30.699
   9        -10.4    28.243    31.137
  10        -10.4    23.834    27.574
Writing output ... done.
```





Interactions

- van der Waals
- Attractive Charge
- Conventional Hydrogen Bond
- Carbon Hydrogen Bond
- Unfavorable Donor-Donor
- Pi-Donor Hydrogen Bond
- Pi-Pi T-shaped
- Amide-Pi Stacked
- Alkyl
- Pi-Alkyl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LYS 271
PRO 234
ARG 233
PRO 265
ILE 264
ALA 263
VAL 235
ILE 272
THR 426
GLY 425
GLY 434
TYR 435
MET 436
GLN 65
TYR 393
NH2
ARG 36
ALA 35
GLU 34
LEU 33
HO
HO
HO
OH
OH
HN
NH
NH
O
ALA 439
GLY 205
GLN 206
VAL 61
TYR 60
SER 59
GLY 57
GLY 58
LEU 56
VAL 10
GLY 11
GLY 12
GLY 13
ILE 14
SER 15
GLY 16
VAL 294
LYS 296
TYR 398
CYS 397
ARG 42
GLY 41
THR 43
PHE 343
TRP 388


Terima
kasih