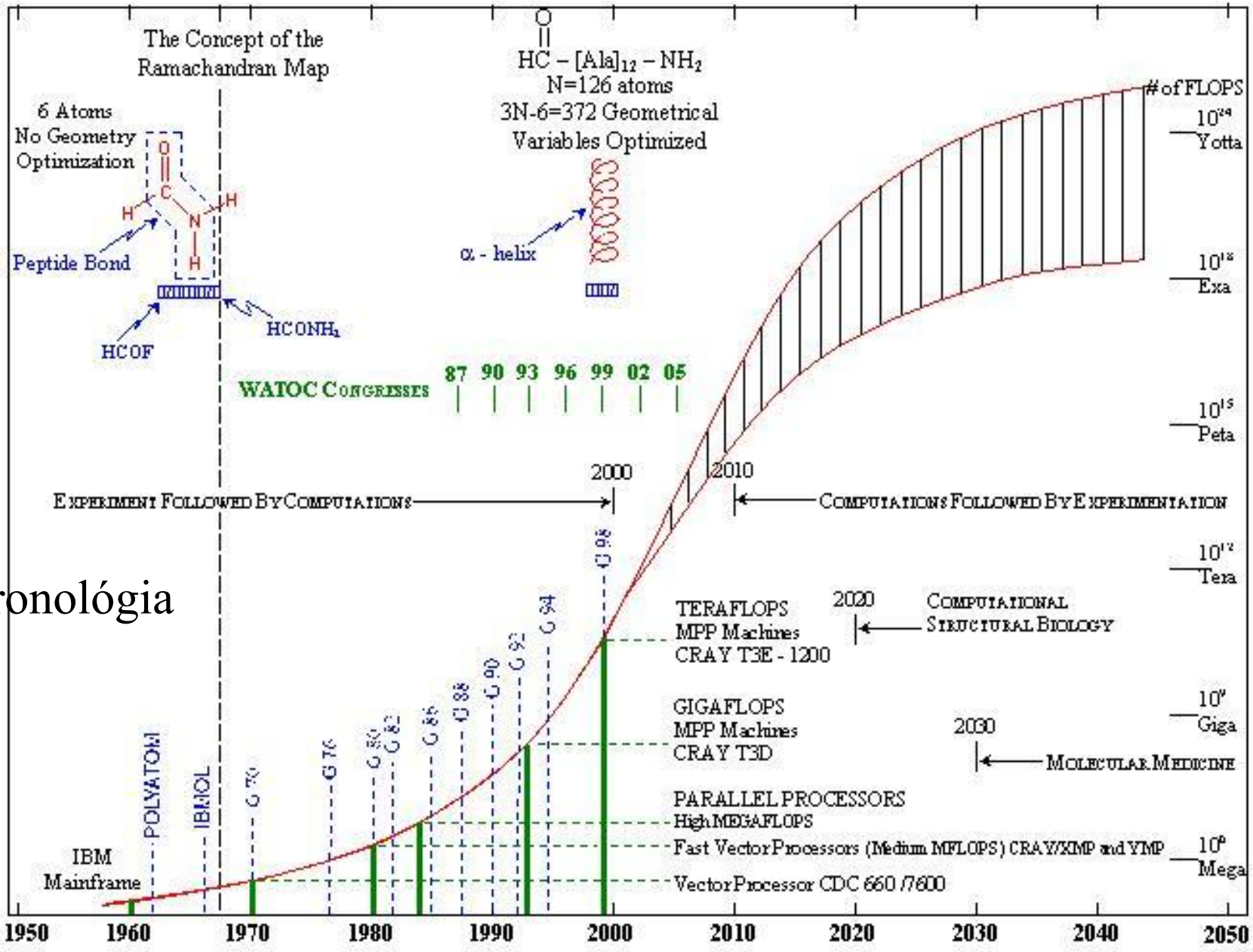
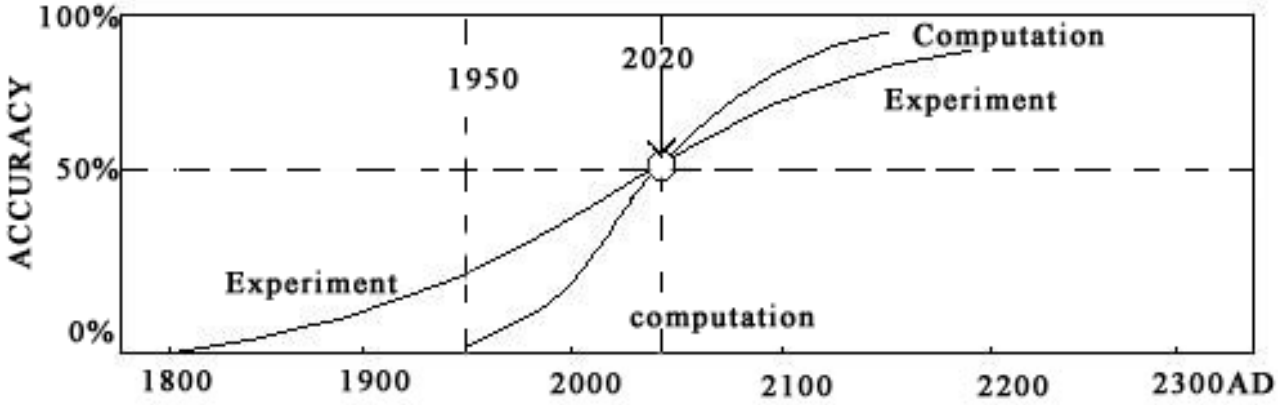
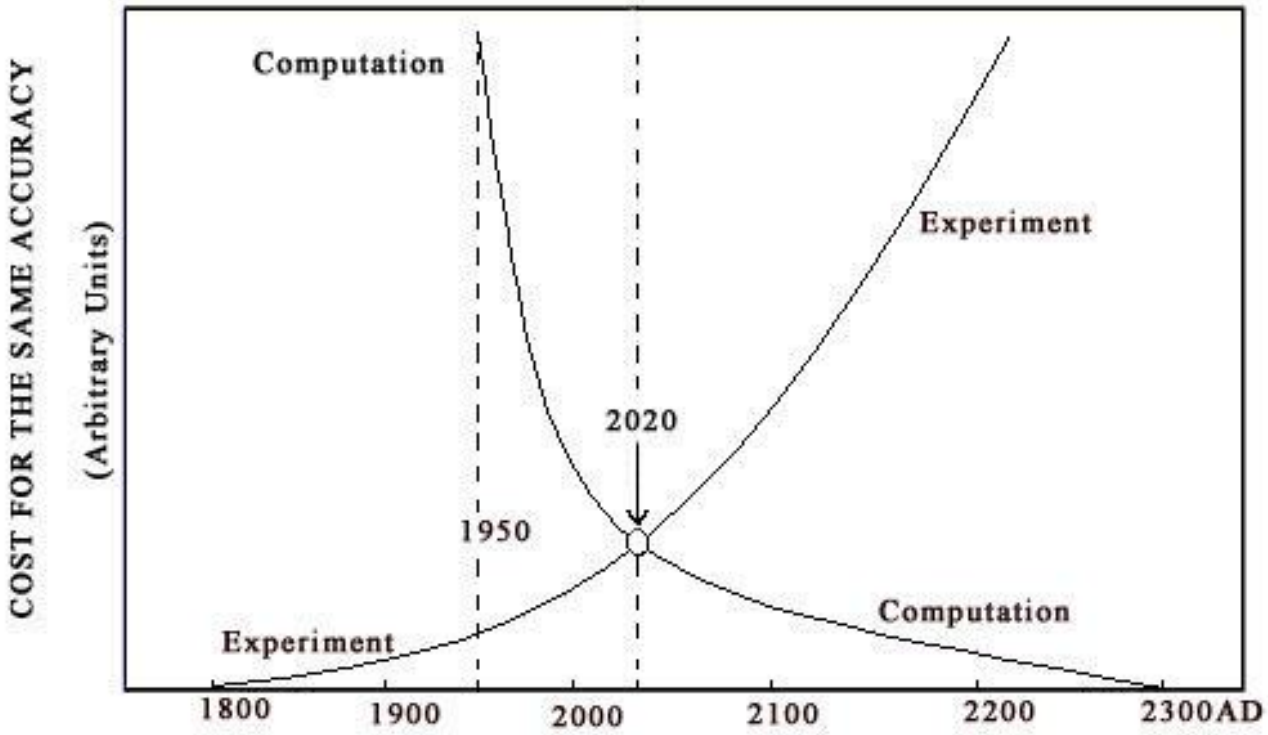
Gázfázisú peptidek és fehérjék konformációs tulajdonságai

kronológia

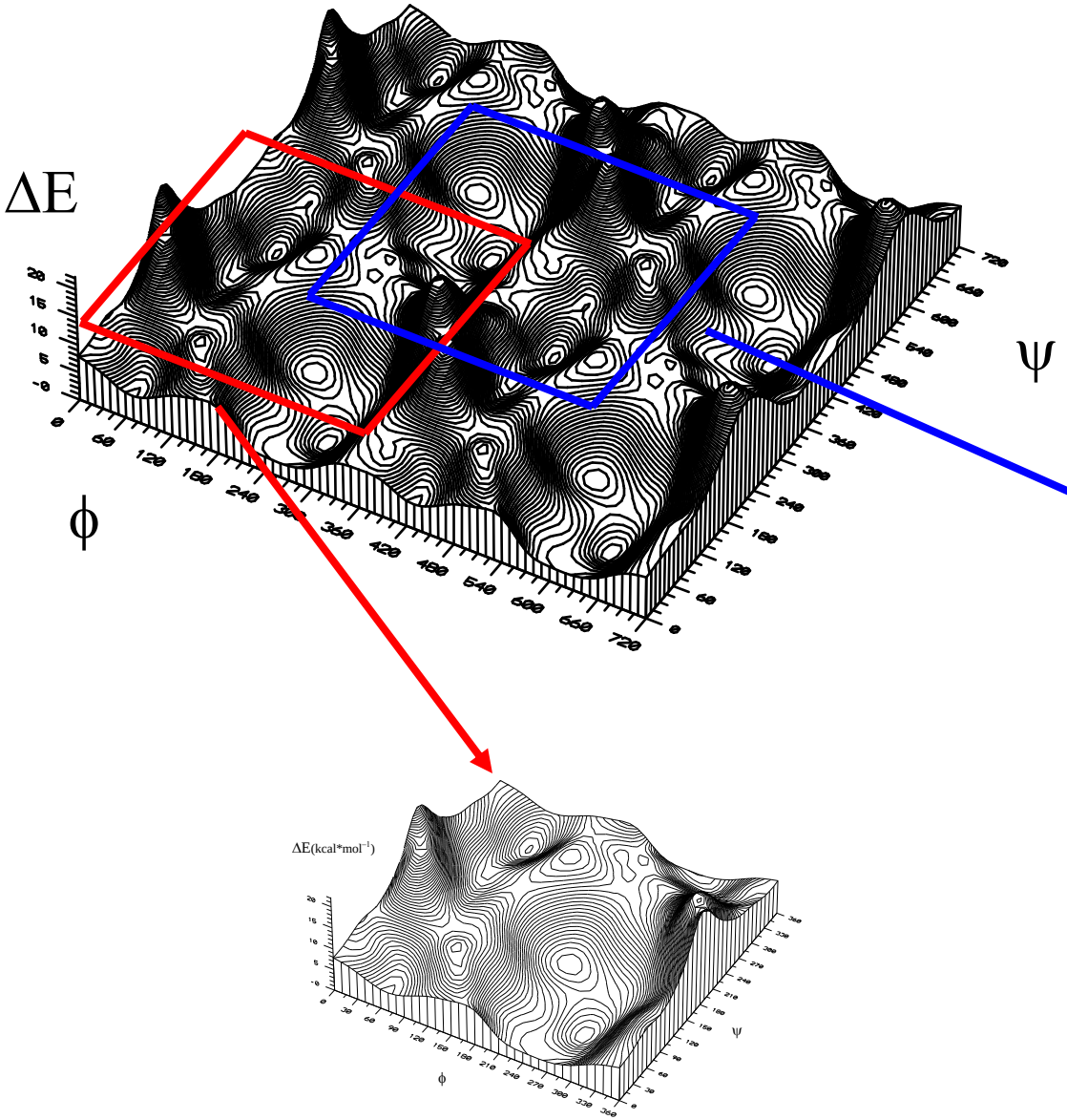

The Concept of the Ramachandran Map
6 Atoms No Geometry Optimization
Peptide Bond
HCOF
HCONH2
HC – [Ala]12 – NH2
N=126 atoms
3N-6=372 Geometrical Variables Optimized
α - helix
WATOC Congresses
87 90 93 96 99 02 05
# of FLOPS
10^24 Yotta
10^18 Exa
10^15 Peta
10^12 Tera
10^9 Giga
10^6 Mega
2000
2010
Experiment Followed By Computations
Computations Followed By Experimentation
TERAFLOPS
MPP Machines
CRAY T3E - 1200
2020
Computational Structural Biology
GIGAFLOPS
MPP Machines
CRAY T3D
2030
Molecular Medicine
PARALLEL PROCESSORS
High MEGAFLOPS
Fast Vector Processors (Medium MFLOPS) CRAY/XMP and YMP
Vector Processor CDC 660 /7600
IBM Mainframe
POLYATOM
IBMOL
1950 1960 1970 1980 1990 2000 2010 2020 2030 2040 2050

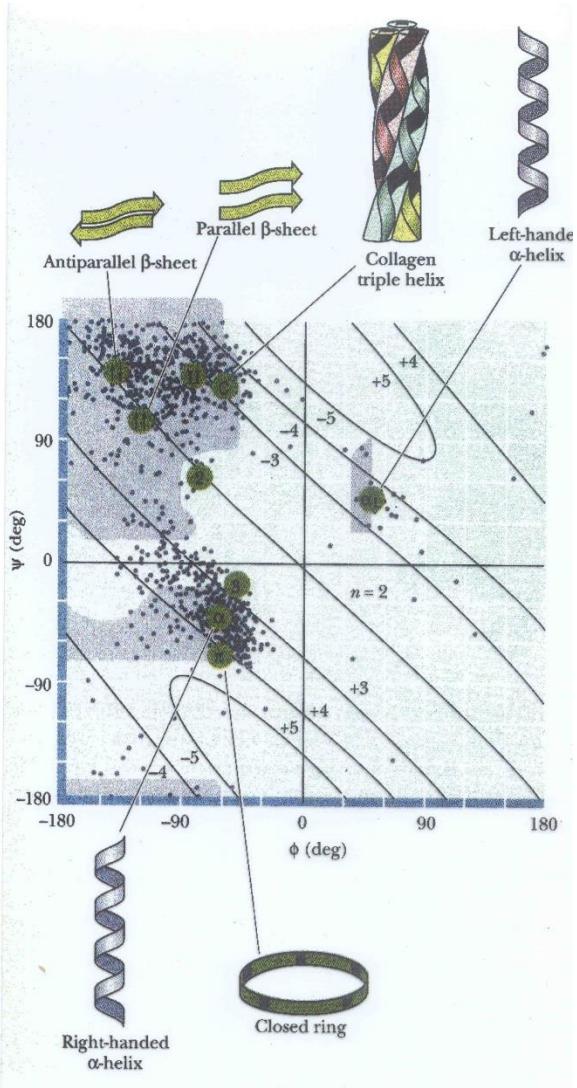
tapasztalat és jóslás





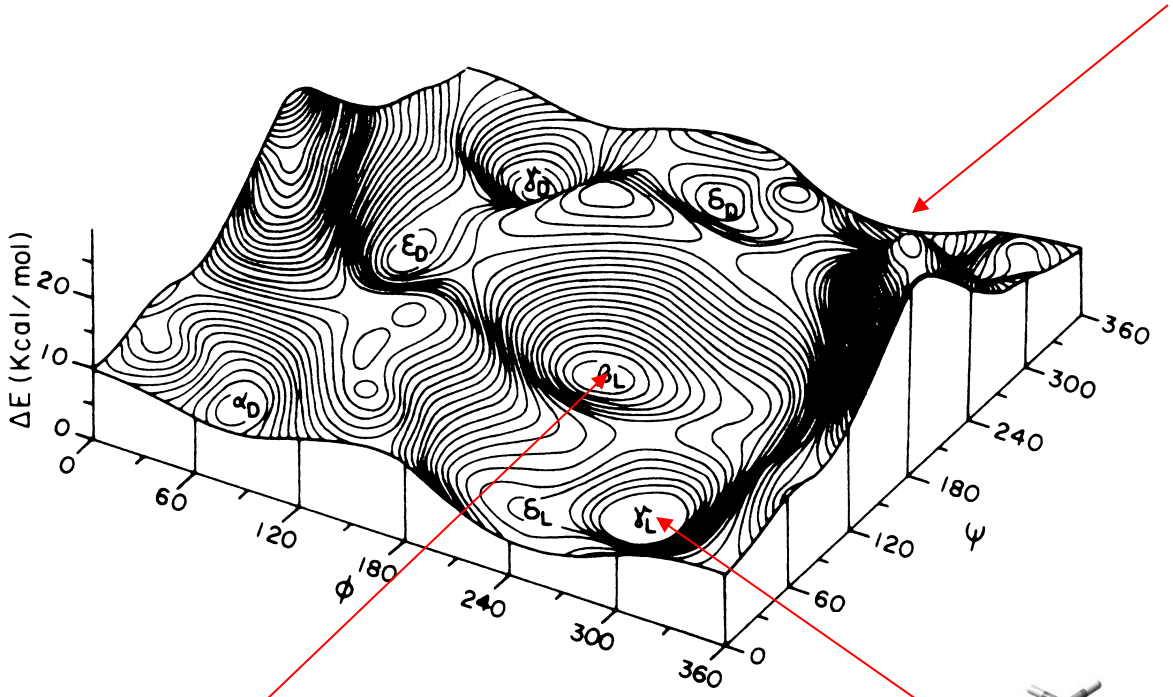
Ramachandran térkép, konformációs építőelemek

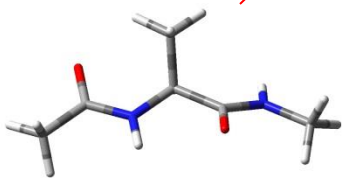


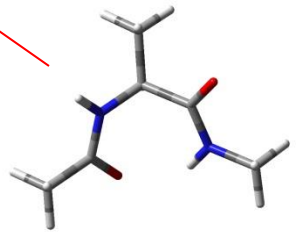


Meglevő és hiányzó „lego” elemek

α-hélix ?
poli Prolin II ?







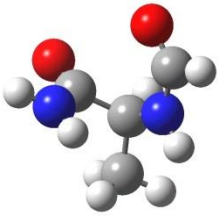
β-redő

γ-kanyar

α-hélix modell

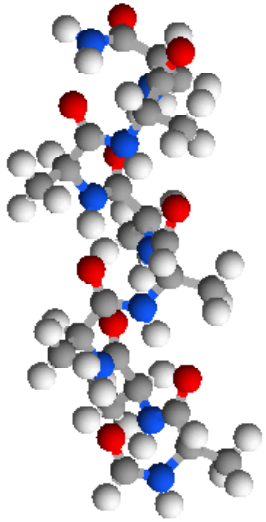
$HCO\text{-}(L\text{-}Ala)_n\text{-}NH_2$

n=1

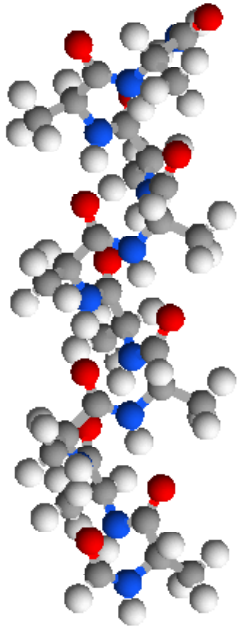


monomer

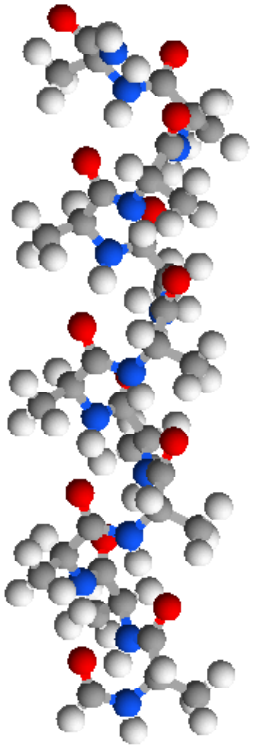
n=8



n=10

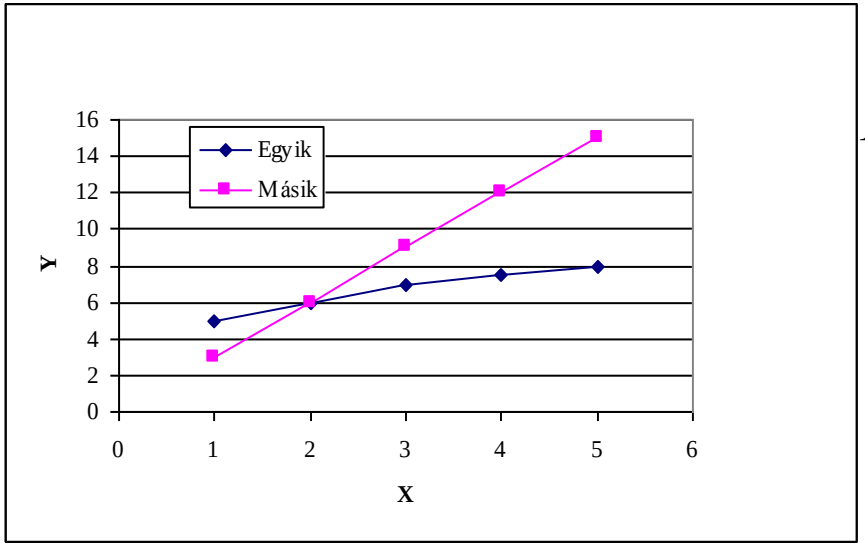


n=12



oligomer

Hogyan értelmezzük a konformerek stabilitásának az oligomer hossza szerinti változását?



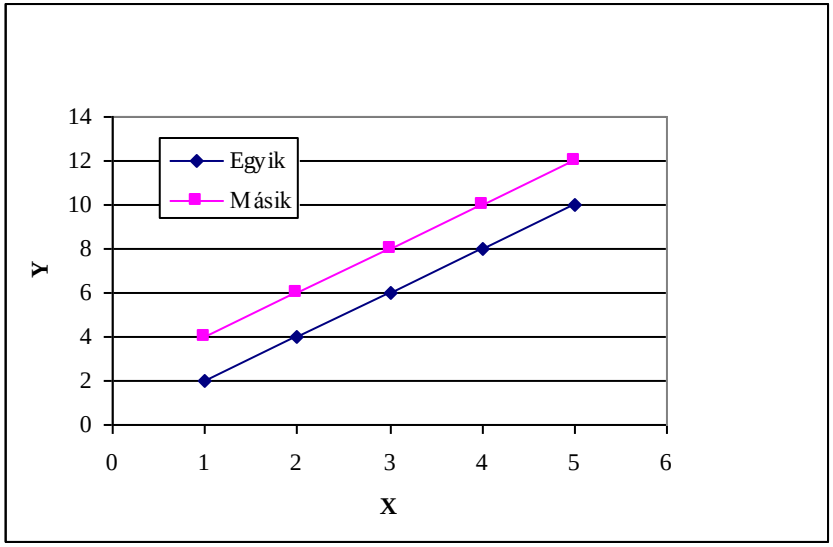
Egymást keresztező stabilitási sorozatok:

a hossz függvényében a két konformer stabilitása eltérően változik.

For-$(Aaa)_x$-NH_2 x=1,2,..6

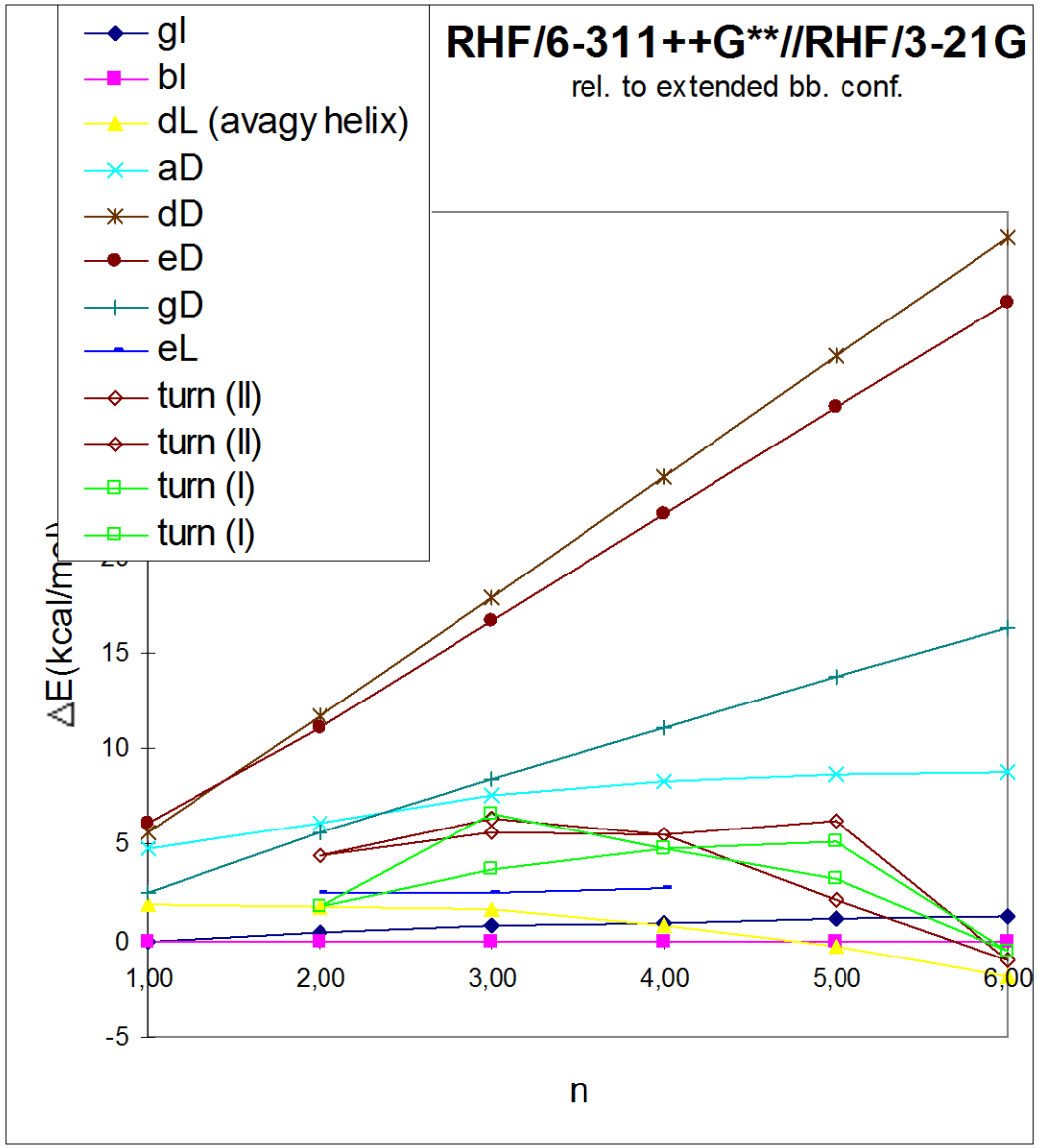
Kvázi párhuzamos lefutású stabilitási sorozatok:

a hossz függvényében a két konformer stabilitása kvázi azonos módon változik.

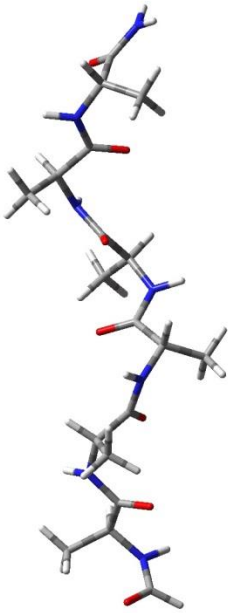


Relatív stabilitás

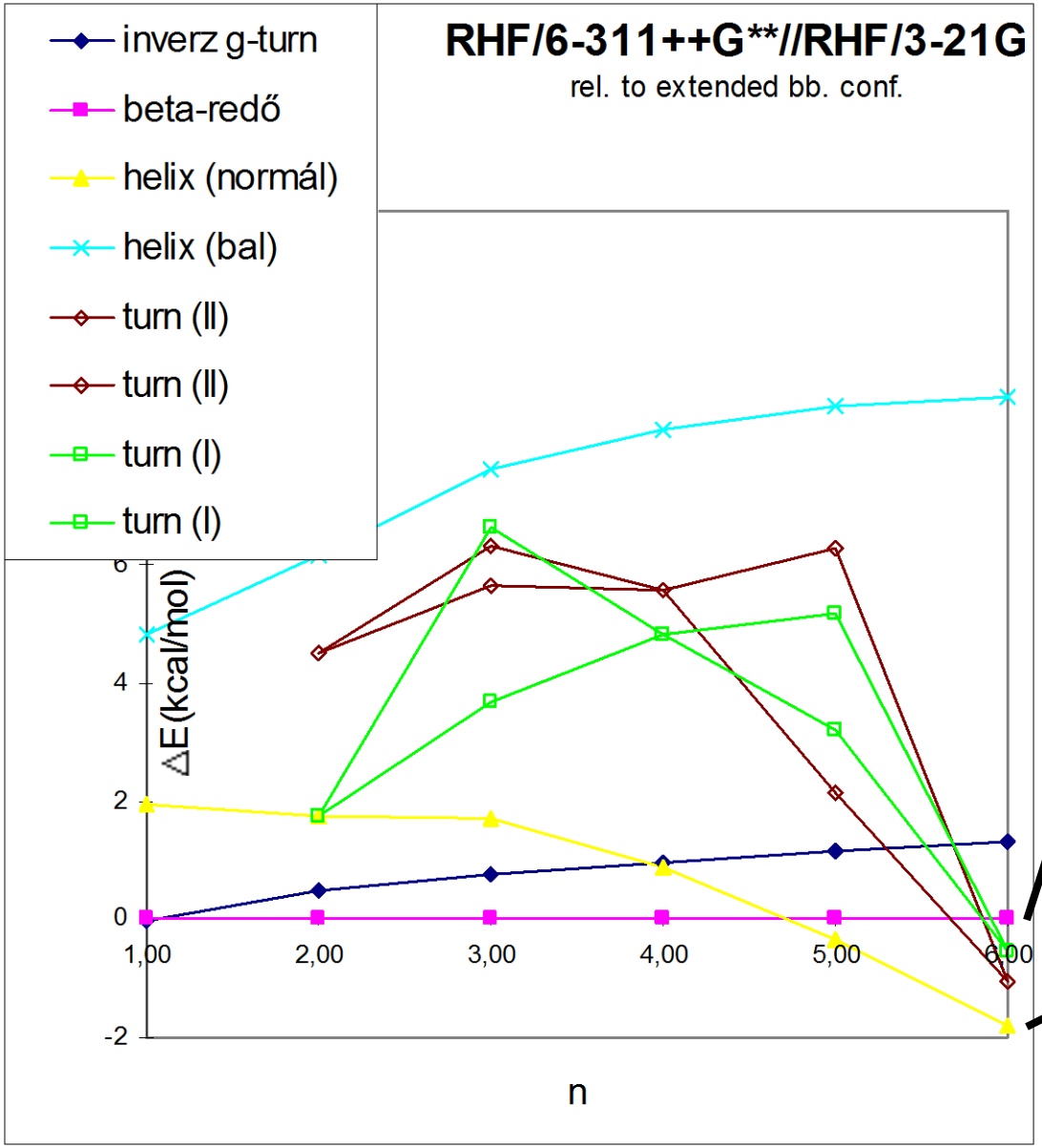
A konformerek relatív energiája
az oligomer hosszának függvényében

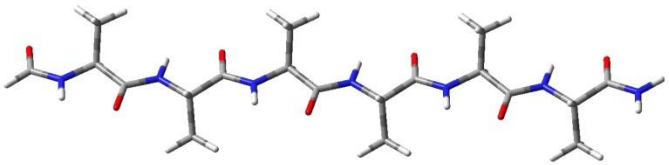


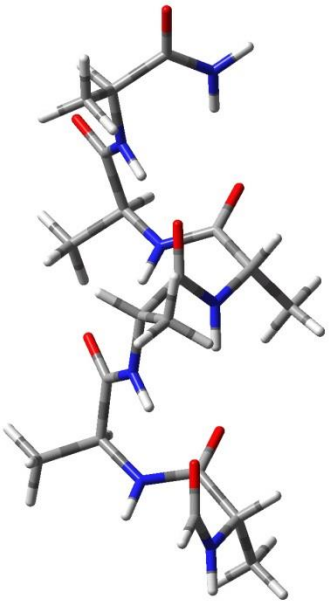
$(\varepsilon_D)_n$



A konformerek relatív energiája az oligomer hosszának függvényében

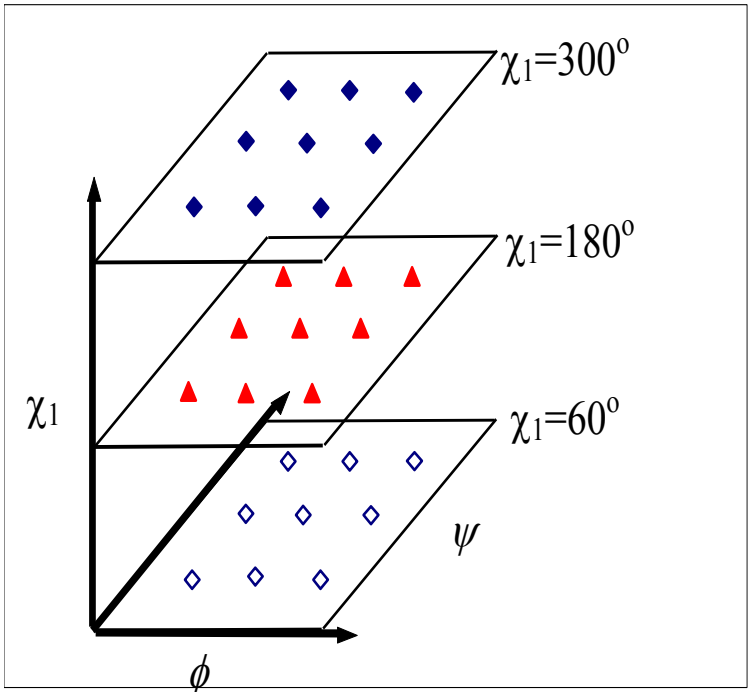


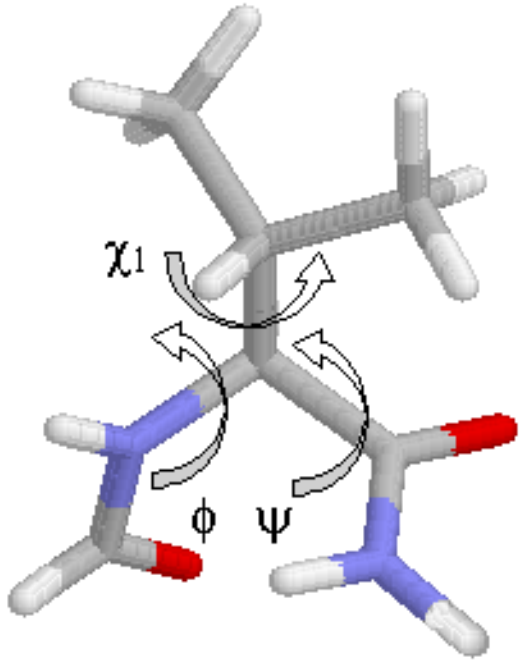




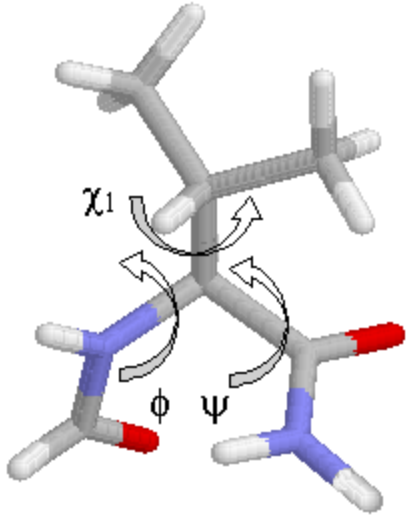
ab initio rendszerek alkalmazása

pl.**For-L-Val-NH2**





legyen ω_0 és $\omega = 180^o$,
belátható hogy a konformerek maximális száma **27**

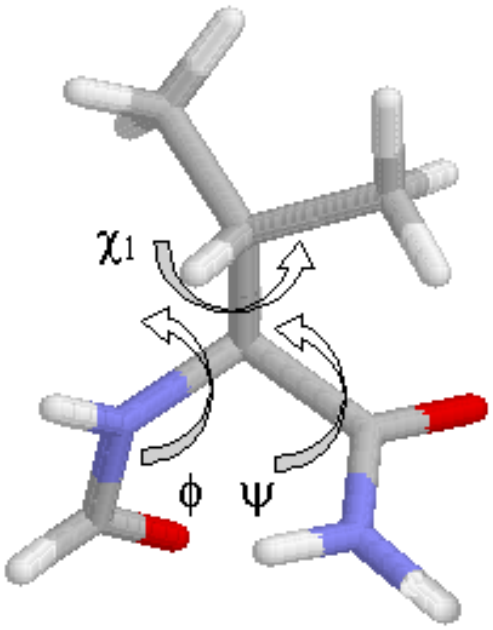


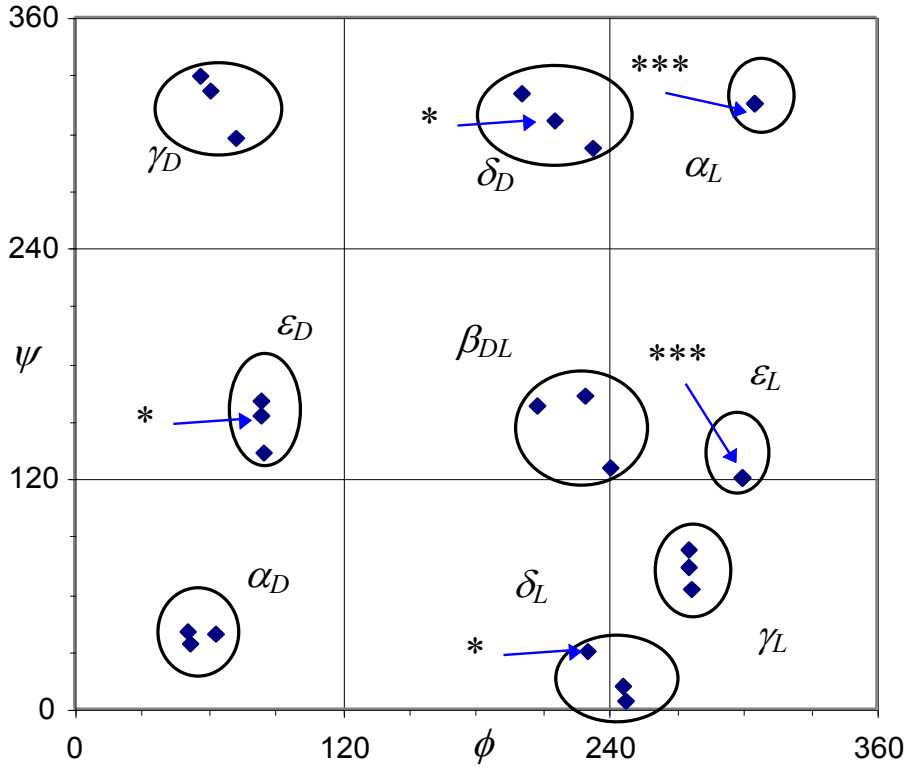
Energy calculation	**Optimized geometry used**	**Conformer categories**
3-21G RHF	3-21G RHF	*20 full opt. +7 [,]-constr. opt.*
6-31+G* RHF	3-21G RHF	*20 full opt. +7 [,]-constr. opt.*
6-311++G** B3LYP	3-21G RHF	*20 full opt. +7 [,]-constr. opt.*
6-311++G** B3LYP	6-311++G** B3LYP	*18 full opt. +9 [,]-constr.* opt.
TZ2P RHF	6-311++G** B3LYP	*18 full opt. +9 [,]-constr. opt.*

Aims of the research:

- -correlation of
- the ab initio data of different levels of theory:
- - structural properties (ϕ, ψ, $\chi 1$ etc.)
- - relative energies (ΔE)
- - CSA values (σ, δ)
- - comparison of
- experimental (X-ray/PDB) and theoretical probabilities
- experimental (shift values /BMRB) and ab initio NMR chemical shifts

Locations of the different conformers of **For-L-Val-NH2** (6-311++G** B3LYP) on a Ramachandran surface

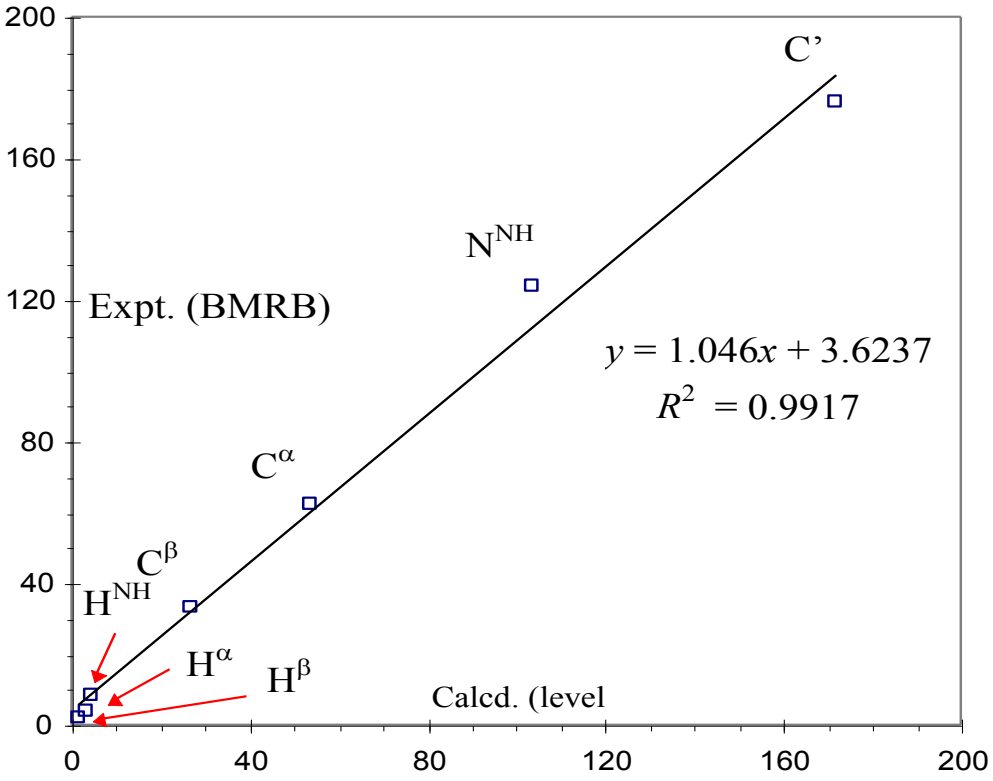


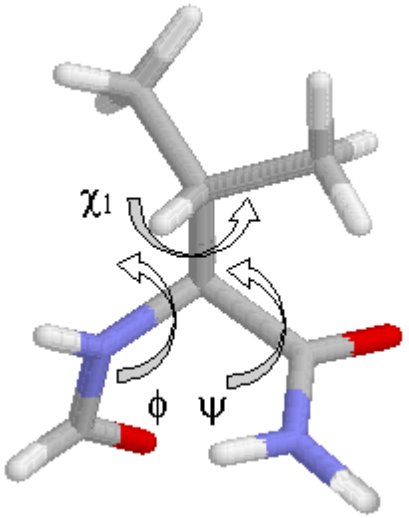


* structures with constrained [ϕ, ψ].

Correlation between *ab initio* and experimentally determined average (conformation independent) chemical shifts of nuclei in For-L-Val-NH_2

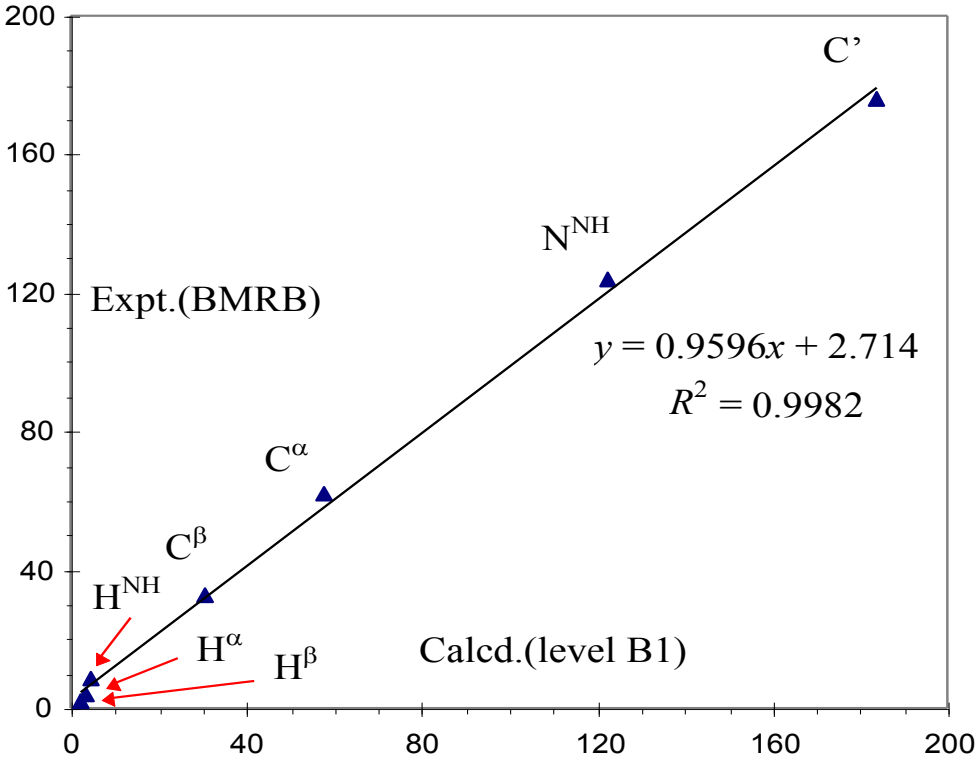
(GIAO–RHF/6-31+G*//RHF/3-21G)

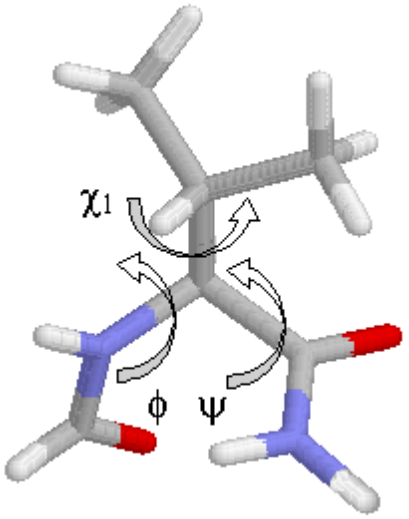




Correlation between *ab initio* and experimentally determined average (conformation independent) chemical shifts of nuclei in For-L-Val-NH_2

(GGIAO–RHF/TZ2P//B3LYP/6-311++G**)

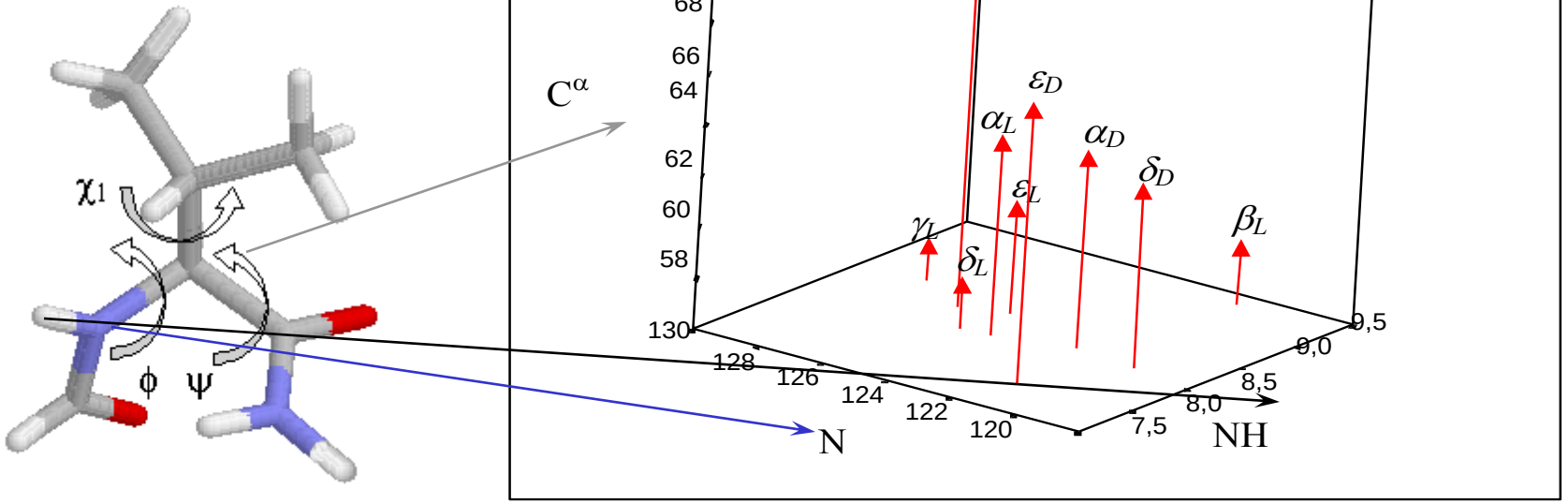




$^{15}N^{NH}$ – $^{1}H^{NH}$ – $^{13}C^{\alpha}$ correlated 3D-plots for For-L-Val-NH_2

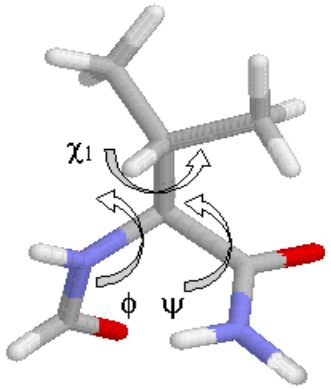
(GIAO–RHF/TZ2P // B3LYP/6-311++G**)

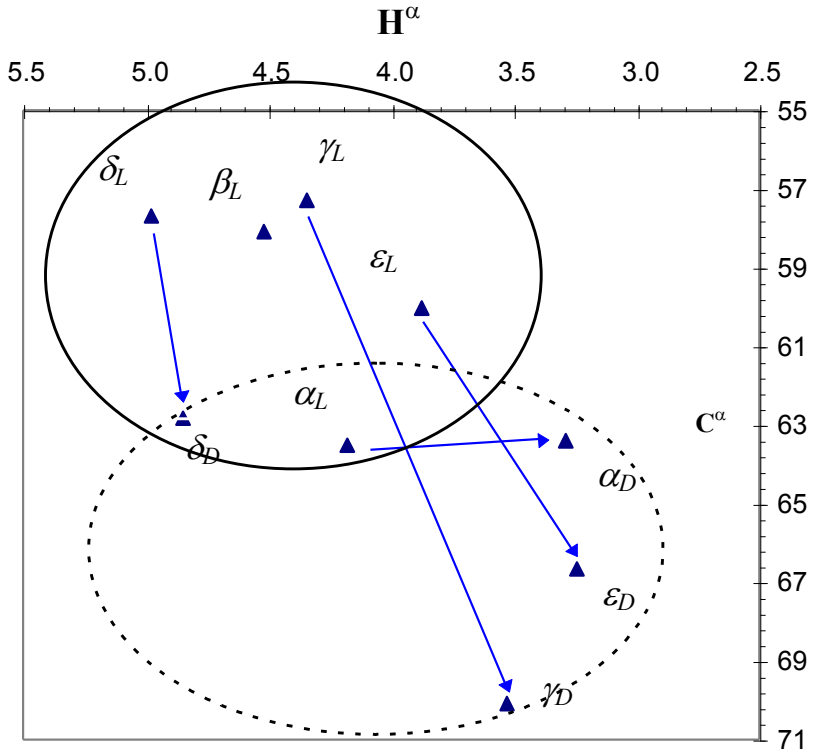
Chemical shifts for each backbone type were obtained by averaging all three side-chain rotamers.



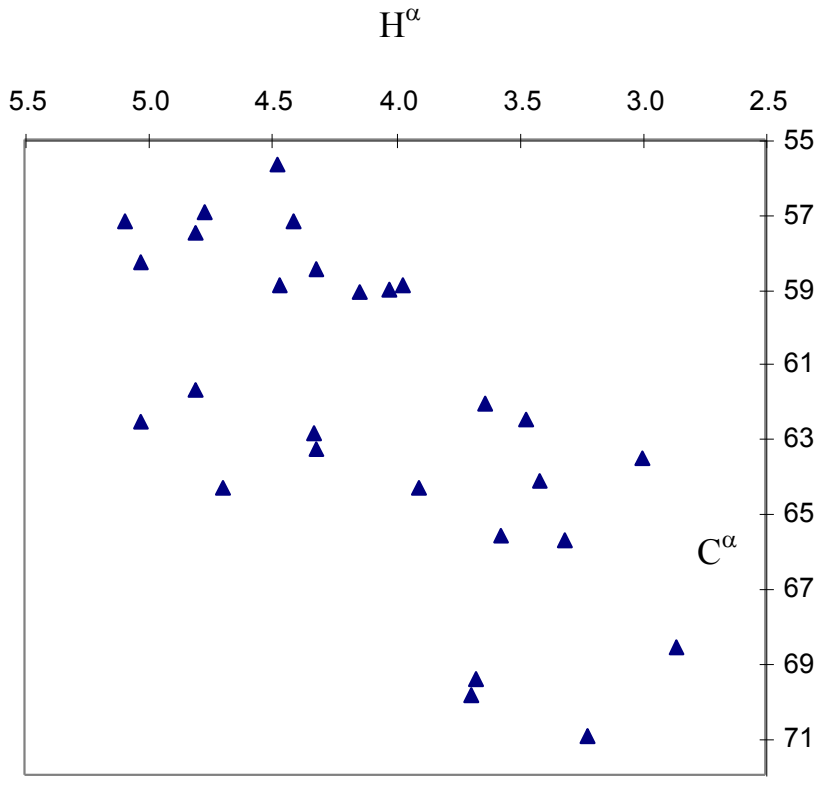
$^{1}H - {}^{13}C$ correlated 2D-plots for For-L-Val-NH_2

(GIAO–RHF/TZ2P//B3LYP/6-311++G**)



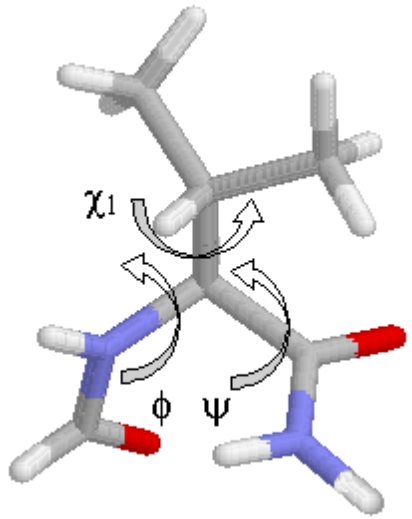


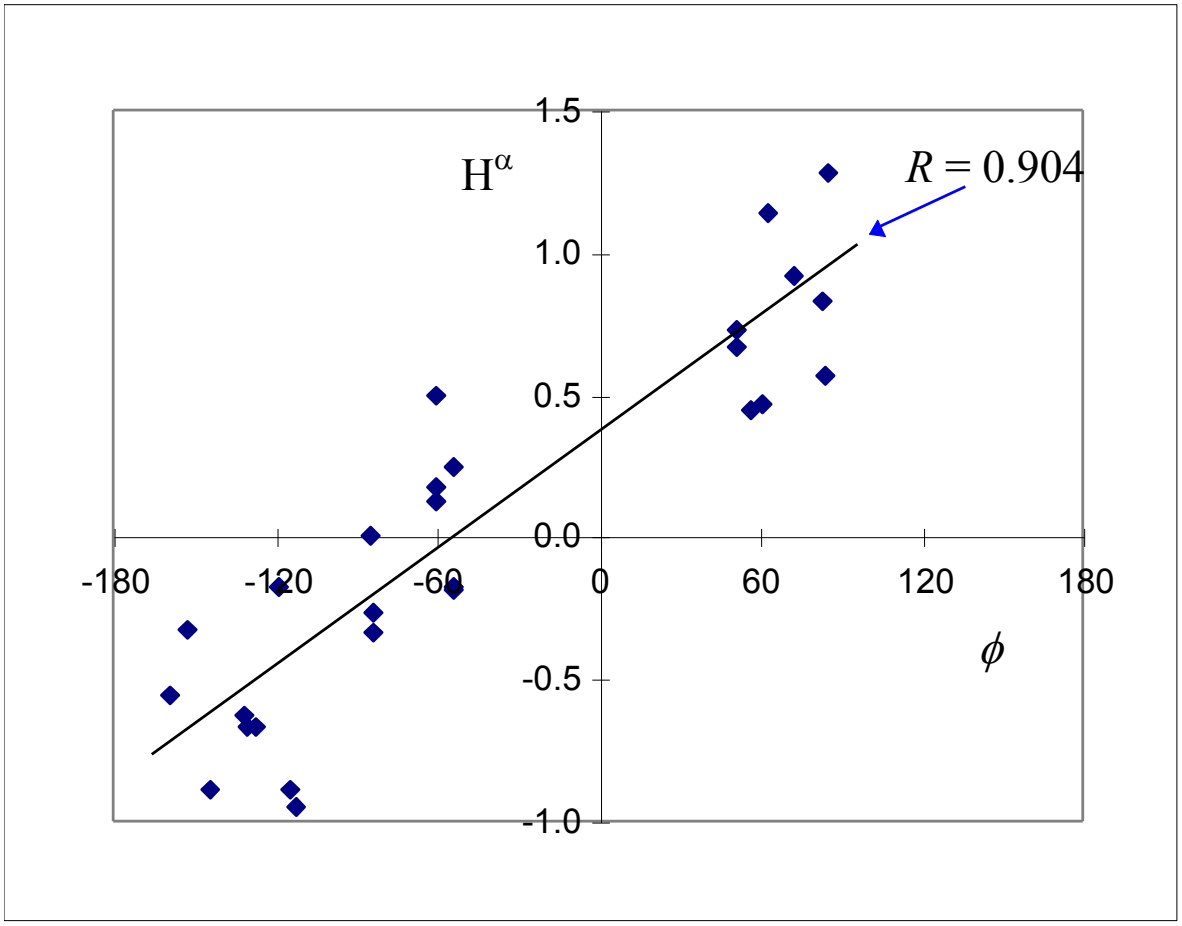
averaging the effect of side-chain orientation



all 27 conformers

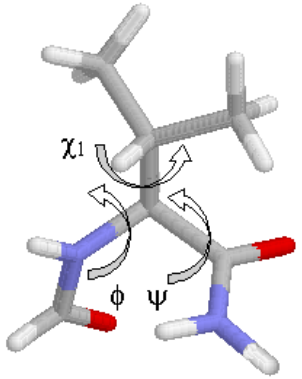
The maximized fit between 1Hα and ϕ at level B1 ($R2$ = 0.818)



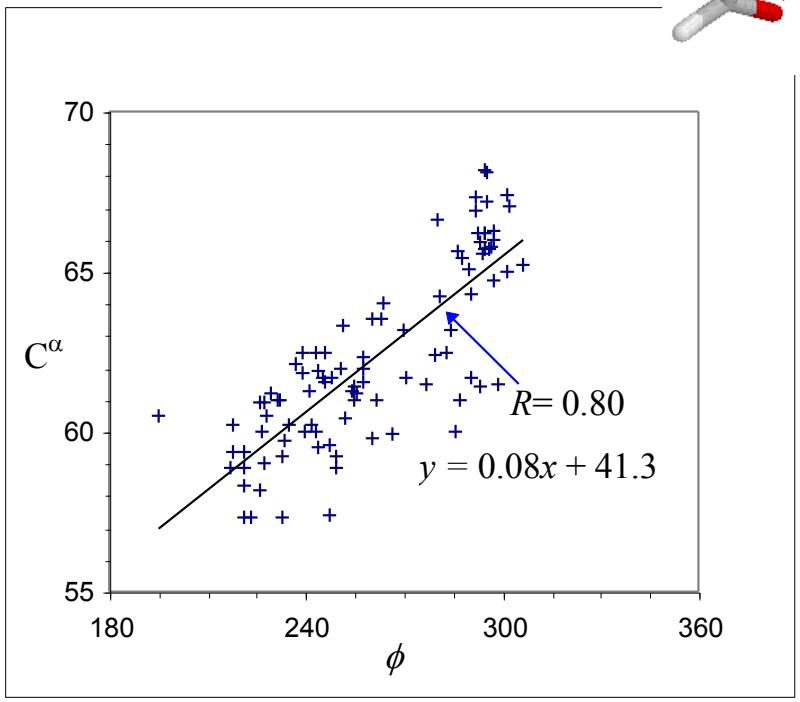


$^{13}C^{\alpha}$– $^{1}H^{\alpha}$ chemical shift – chemical shift correlation plot for 93 valines found in 18 proteins

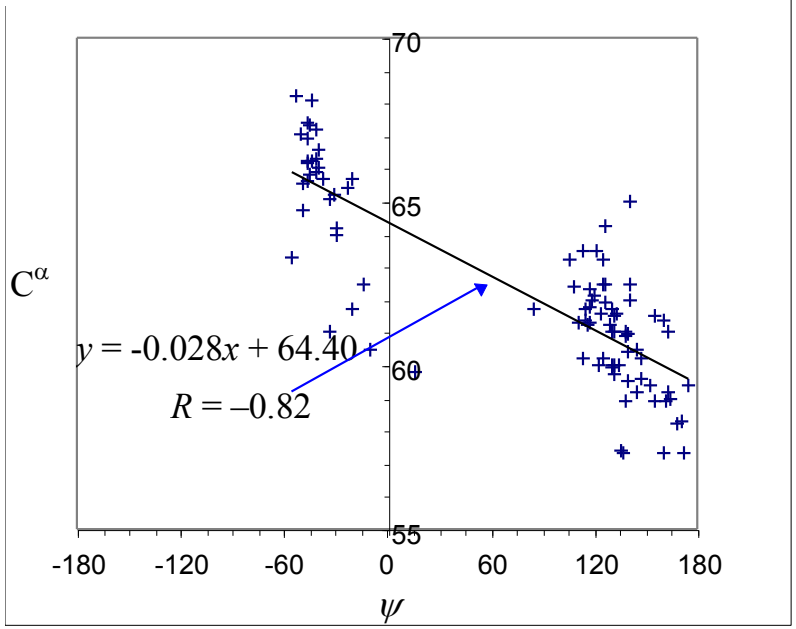
13C$^{\alpha}$/ϕ



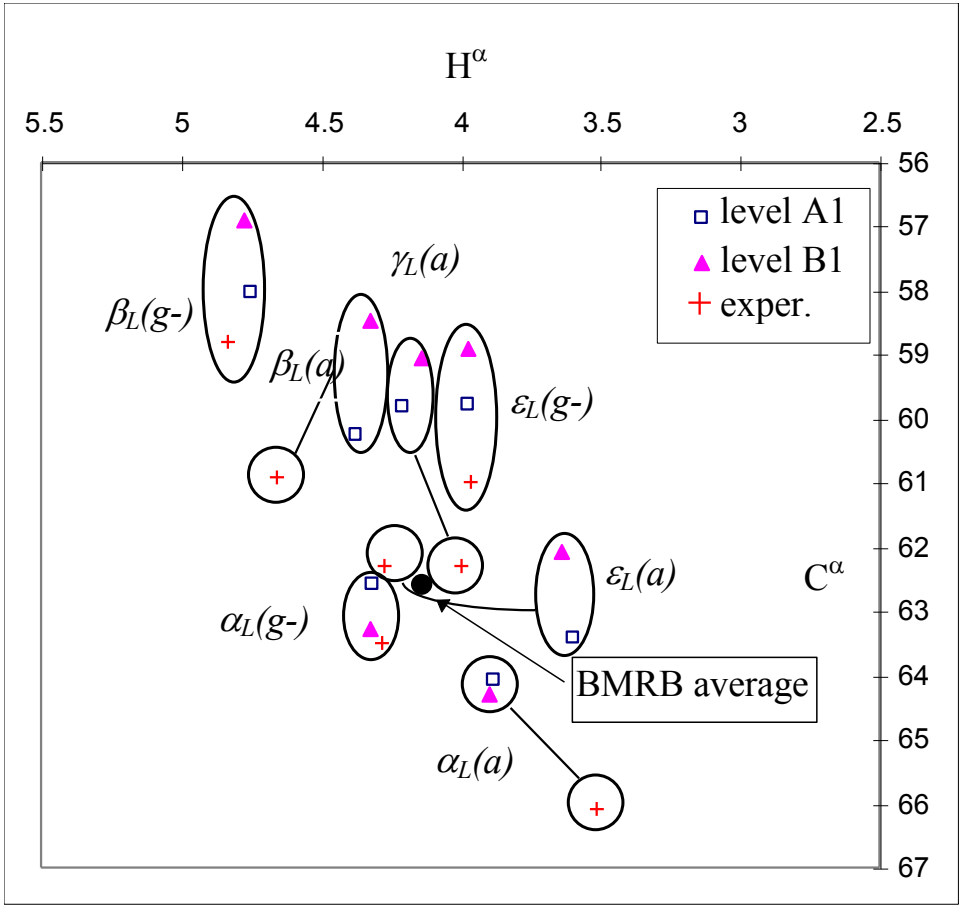
$^{13}C^{\alpha}/\psi$

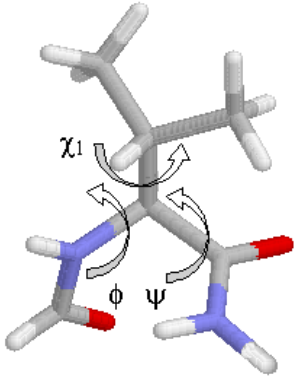


B



Experimentally determined and *ab initio* calculated H^{α} and C^{α} chemical shifts of valine conformers





(Computed values are uniformly shifted by 8.04 ppm [C^{α}] and 0.63 ppm [H^{α}] at level A1, and by 4.12 ppm [13Cα] and 0.35 ppm [Hα] at level B1 to match BMRB experimental average values 13Cα =62.17 ppm and 1Hα = 4.09 ppm.) Only those conformers are plotted which were found in the 18 proteins more than twice.