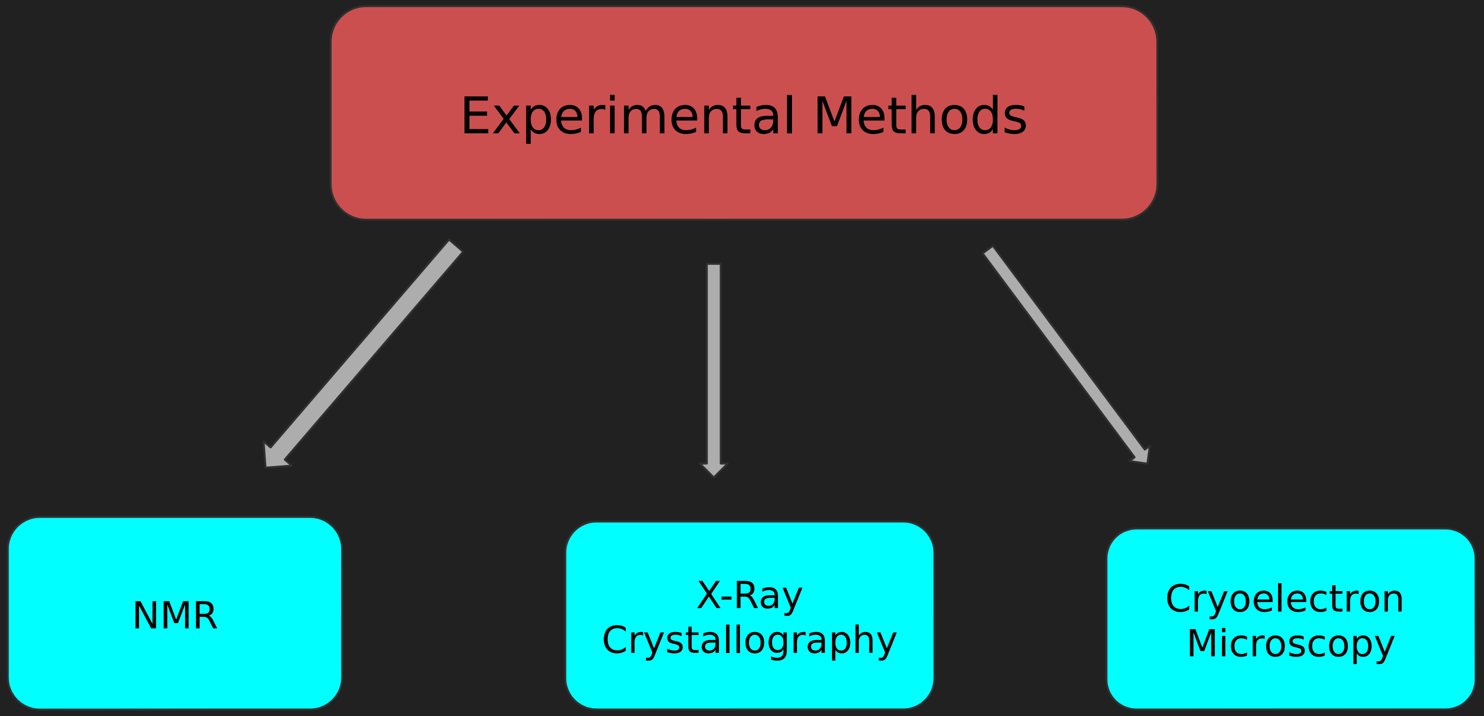
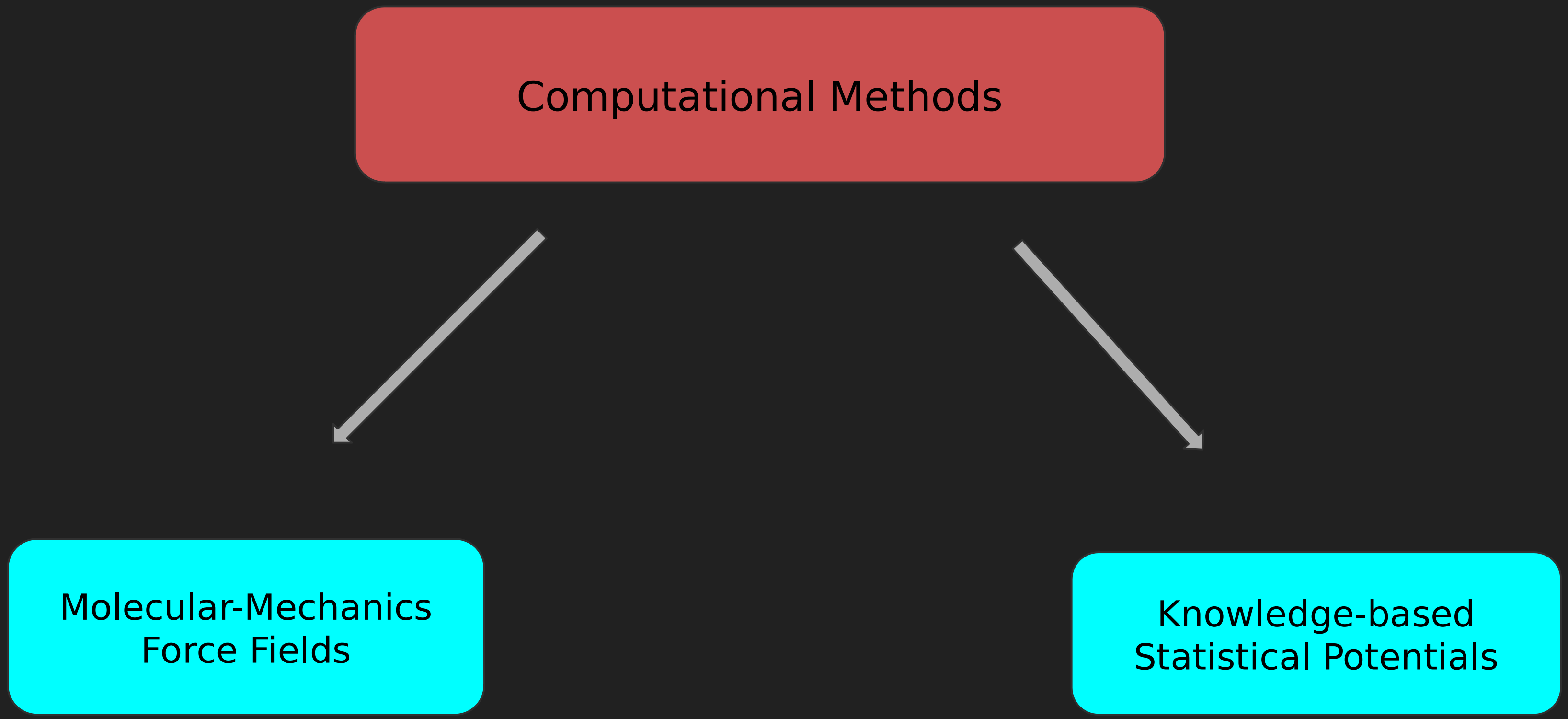
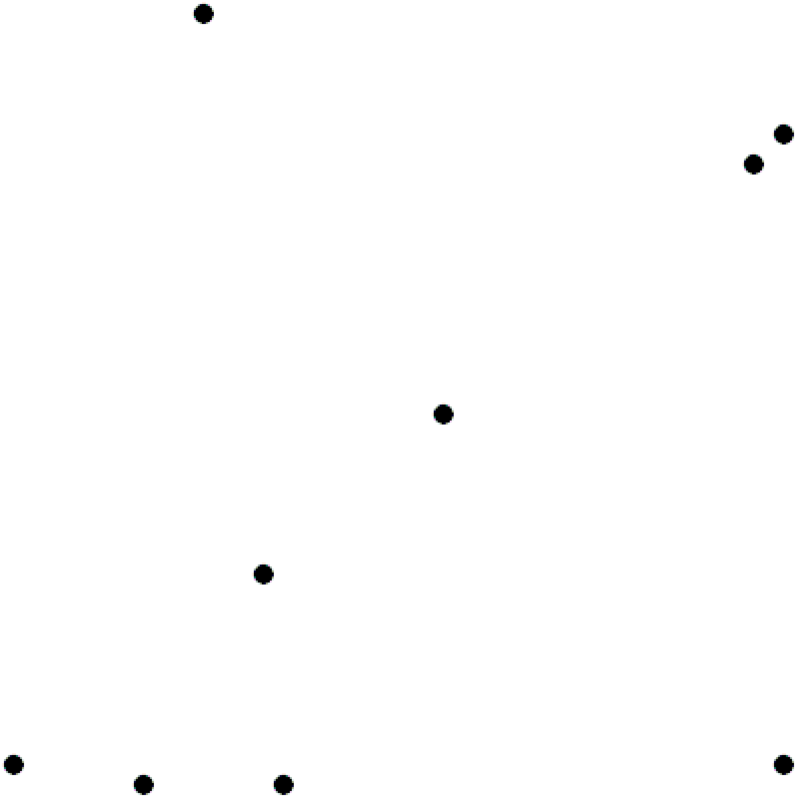
Knowledge-Based Statistical Potentials

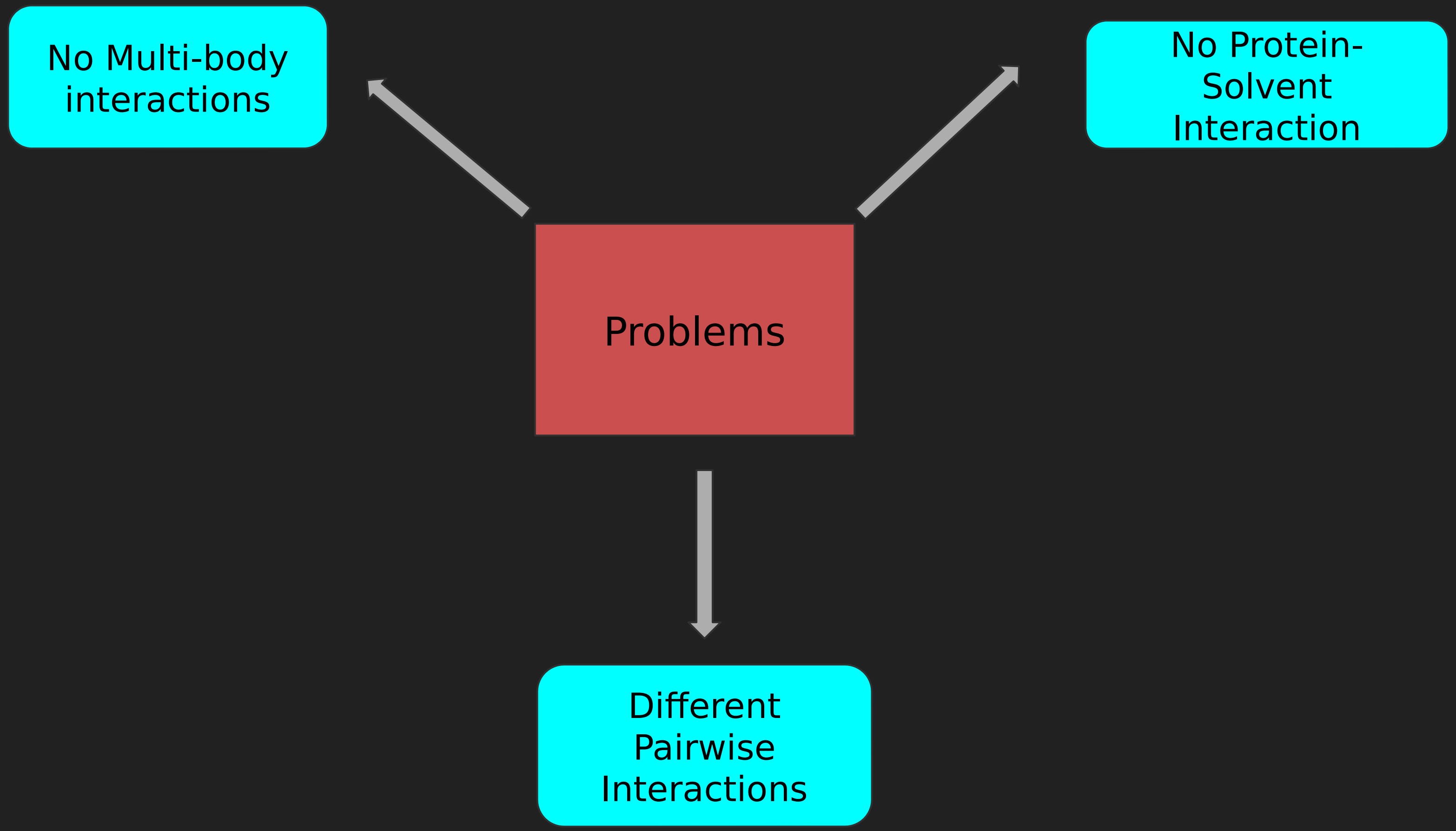

Experimental Methods
NMR
X-Ray Crystallography
Cryoelectron Microscopy


Computational Methods
Molecular-Mechanics Force Fields
Knowledge-based Statistical Potentials



$$P(r) = \frac{1}{Z} e^{-\frac{F(r)}{kT}}$$

$$\Delta F(r) = -kT \ln \frac{P(r)}{Q_R(r)} - kT \ln \frac{Z}{Z_R}$$


No Multi-body interactions
No Protein-Solvent Interaction
Problems
Different Pairwise Interactions

$$F = -K_B T ln(Z)$$

$$H = \sum_{i=1}^{N} \frac{p_i^2}{2m} + \sum_{i<j} U(r_{ij})$$

$$Z(N,V,T) = \frac{1}{N!(2\pi\hbar)^{3N}} \int \prod_{i=1}^{N} d^3p_i d^3r_i e^{-\beta H}$$

$$Z(N,V,T) = \frac{1}{N!(2\pi\hbar)^{3N}} \left[\int \prod_i d^3p_i e^{-\beta \sum_j \frac{p_j^2}{2m}}\right] \times \left[\int \prod_i d^3r_i e^{-\beta \sum_{j<k} U(r_{jk})}\right]$$

$$Z(N,V,T) = \frac{1}{N!\lambda^{3N}} \int \prod_i d^3r_i e^{-\beta \sum_{j<k} U(r_{jk})}$$

Cluster Expansion and f-Mayer Function

$$f(r) = e^{-\beta U(r)} - 1$$

$$f_{ij} = f(r_{ij})$$

$$Z(N,V,T) = \frac{1}{N!\lambda^{3N}} \int \prod_i d^3r_i \prod_{j>k}(1 + f_{jk})$$

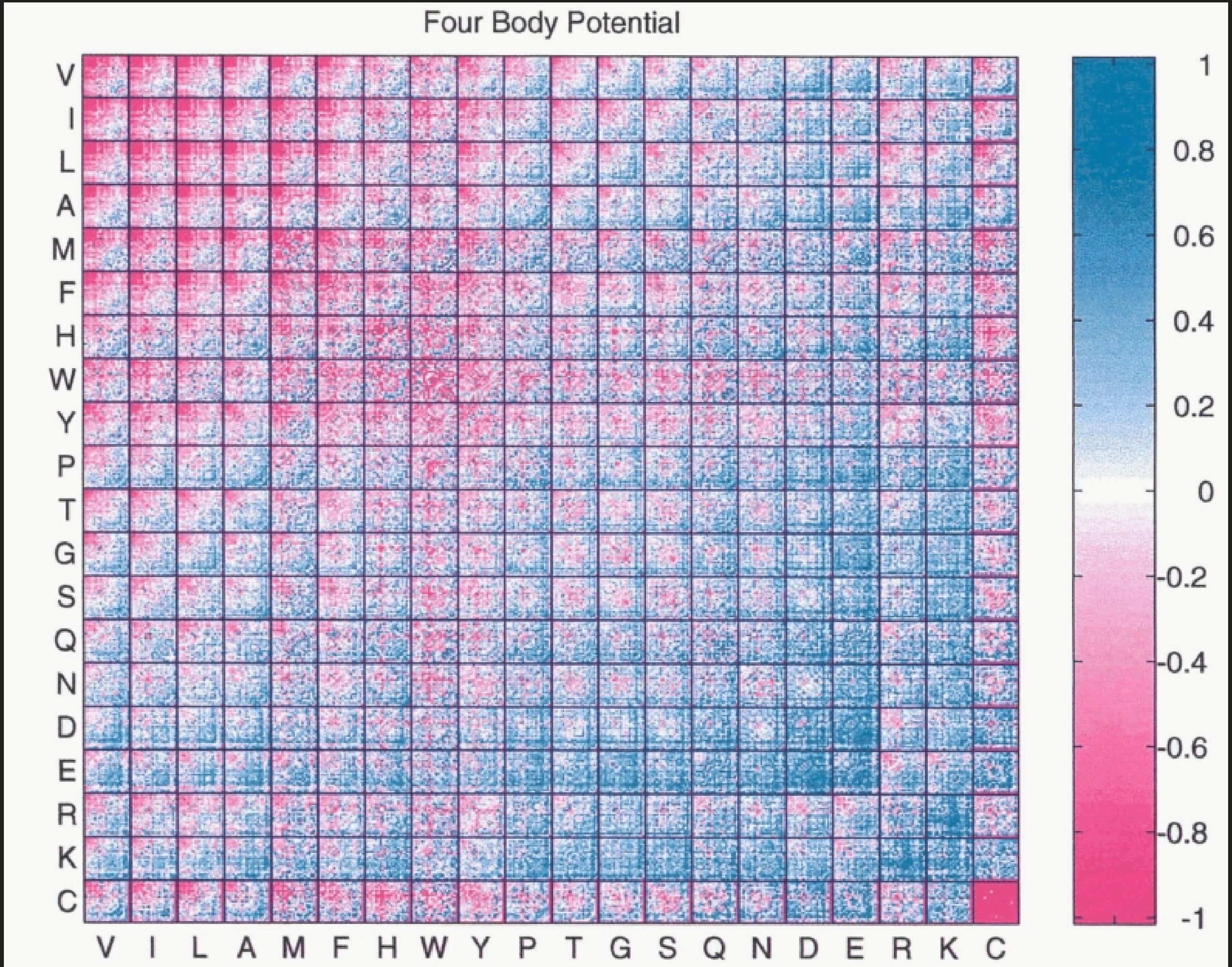
$$Z(N,V,T) = \frac{1}{N!\lambda^{3N}} \int \prod_i d^3r_i \left(1 + \sum_{j<k} f_{jk} + \sum_{j>k,l>m} f_{jk} f_{lm} + \ldots\right)$$

$$Z(N,V,T) = \frac{1}{N!\lambda^{3N}} \sum_G W[G]$$

$$Z(N,V,T) = \frac{1}{\lambda^{3N}} \sum_{\{m_l\}} \prod_l \frac{U_l^{m_l}}{(l!)^{m_l} m_l!}$$

Hypothesized Knowledge-based Statistical Potential

$$F = -K_B T ln \left(\frac{1}{\lambda^{3N}} \sum_{m_l} \prod_l \frac{U_l^{m_l}}{(l!)^{m_l} m_l!} \right)$$



Four Body Potential
V
I
L
A
M
F
H
W
Y
P
T
G
S
Q
N
D
E
R
K
C
V I L A M F H W Y P T G S Q N D E R K C
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
-1

Advantages of the Statistical Potential

1. Now we have multiple body interaction. We have been able to derive a general N-body interaction term.
2. Adding a weight factor to f-Mayer function corresponding to the depth of interaction of amino residues, we can take into account the protein-solvent interactions.
3. f-Mayer function represents the strength of the interaction. So giving different ranks to different kind of interactions allows us to include multiple interactions.

References

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3. Potentials of Mean Force for Protein Structure Prediction Vindicated, Formalized and Generalized by Thomas Hamelryck1 * ., Mikael Borg1., Martin Paluszewski1., Jonas Paulsen1 , Jes Frellsen1 , Christian Andreetta1 , Wouter Boomsma2,3, Sandro Bottaro2 , Jesper Ferkinghoff-Borg2 *
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Thank You for your attention