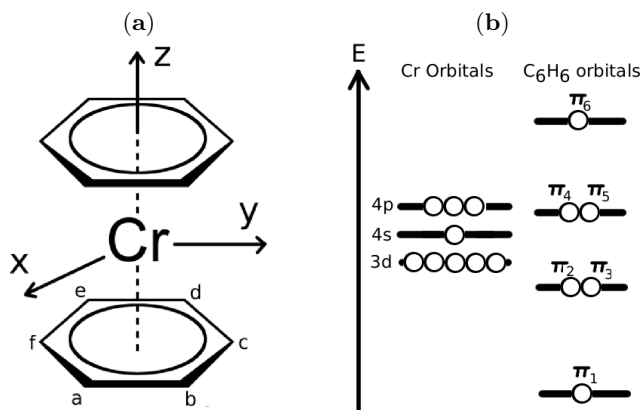


## Problem 1: Molecular-Orbital Theory for Dibenzenechromium

Dibenzenechromium  $\text{Cr}(\text{C}_6\text{H}_6)_2$  can be chosen as a prototype for the general class of organometallic  $\pi$  complexes of the transition metals.



The complex is composed by the  $d^6$  central atom Cr coordinated to two benzene molecules ( $\text{C}_6\text{H}_6$ , see Fig. **a**). The bonding in  $\text{Cr}(\text{C}_6\text{H}_6)_2$  is commonly described in terms of a molecular-orbital model starting with the delocalized  $\pi$  molecular orbitals of  $\text{C}_6\text{H}_6$  groups. The six  $\pi$  molecular orbitals of  $\text{C}_6\text{H}_6$  can be expressed as

$$\begin{aligned}
 E_1 & \quad \psi(\pi_1) = \frac{1}{\sqrt{6}} \left( p_z^{(a)} + p_z^{(b)} + p_z^{(c)} + p_z^{(d)} + p_z^{(e)} + p_z^{(f)} \right) \\
 E_2 = E_3 & \quad \begin{cases} \psi(\pi_2) = \frac{1}{2\sqrt{3}} \left( 2p_z^{(a)} + p_z^{(b)} - p_z^{(c)} + 2p_z^{(d)} - p_z^{(e)} + p_z^{(f)} \right) \\ \psi(\pi_3) = \frac{1}{2} \left( p_z^{(b)} + p_z^{(c)} - p_z^{(e)} - p_z^{(f)} \right) \end{cases} \\
 E_4 = E_5 & \quad \begin{cases} \psi(\pi_4^*) = \frac{1}{2} \left( -p_z^{(b)} + p_z^{(c)} - p_z^{(e)} + p_z^{(f)} \right) \\ \psi(\pi_5^*) = \frac{1}{2\sqrt{3}} \left( 2p_z^{(a)} - p_z^{(b)} - p_z^{(c)} + 2p_z^{(d)} - p_z^{(e)} - p_z^{(f)} \right) \end{cases} \\
 E_6 & \quad \psi(\pi_6^*) = \frac{1}{\sqrt{6}} \left( -p_z^{(a)} - p_z^{(b)} - p_z^{(c)} - p_z^{(d)} - p_z^{(e)} - p_z^{(f)} \right)
 \end{aligned}$$

where  $p_z$  is a  $p$  carbon atomic orbital orthogonal to the plane of the ring and the superscript letters refer to the heavy atom center along the ring. Molecular orbitals are ranked in energy starting from the lowest energy orbital ( $E_1$ ). The two pairs  $(\pi_2, \pi_3)$  and  $(\pi_4^*, \pi_5^*)$  are degenerate. For two benzene rings there are a total of twelve  $\pi$  molecular orbitals.

- Using orbital-symmetry considerations only, write down the occupied orbitals and the two lowest-energy anti-bonding molecular orbitals of the  $\text{Cr}(\text{C}_6\text{H}_6)_2$  complex as a linear combination of the metal  $3d$ ,  $4s$  and  $4p$  orbitals and the benzene  $\pi$  orbitals (use the reference system given in Fig. **a**);

2. Make a tentative energy ranking of the obtained molecular orbitals of the complex;
3. Using the simplified relative energy-level diagram given in Fig. **b** for the metal  $3d$ ,  $4s$  and  $4p$  orbitals and the benzene  $\pi$  orbitals, make an estimate of the relative magnitude of the coefficients in the linear combinations which define the first two occupied molecular orbitals.

## Problem 2: A One-Dimensional Stochastic Process

Consider the stationary stochastic process

$$x(t+1) = ax(t) + bG(t) \quad (1)$$

where  $b \neq 0$ ,  $-1 < a < 1$  and  $G(t)$  is a Gaussian process of variance zero and covariance one:

$$\begin{aligned} \langle G(t) \rangle &= 0 \\ \langle G^2(t) \rangle &= 1 \\ \langle G(t+1)G(t) \rangle &= 0 \end{aligned}$$

1. Determine the average value of  $x$
2. Determine the variance  $\langle x^2 \rangle - \langle x \rangle^2$  as a function of  $a$  and  $b$ . For  $b = 1$  draw a graph of the variance as a function of  $a$ .
3. Determine the correlation function  $\langle x(t+1)x(t) \rangle$  as a function of  $a$  and  $b$ .
4. Determine the probability  $P(x|x_0)$  that the system is in  $x$  at time  $t+1$  given that the system is in  $x_0$  at time  $t$  (hint:  $G$  is a Gaussian process, namely the probability distribution of  $G$  is  $P(G) = \frac{1}{\sqrt{2\pi}} \exp(-G^2/2)$ )
5. Describe a physical system that could be modeled by Eq. (1) with  $a$  close to one.
6. Describe a physical system that could be modeled by Eq. (1) with  $a = 1$

### Problem 3: Stretching of a freely-rotating chain

Consider a chain of  $N$  equally-long segments,  $\{\vec{t}_1, \vec{t}_2, \dots, \vec{t}_N\}$  embedded in a three-dimensional space. The segments, which have length  $b$ , are phantom (no self-avoidance) but are subject to the constraint that two consecutive segments must form an angle  $\theta$ , see figure.

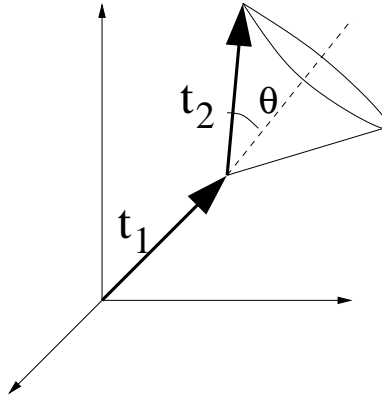


Figure 1: Example of chain configuration. The second bond forms an angle  $\theta$  with the preceding one and is hence restricted over the indicated cone.

(1) For a given orientation of the first bond,  $\vec{t}_1$ , calculate the average orientation of bonds,  $\vec{t}_2, \vec{t}_3, \dots, \vec{t}_N$ . Discuss after how many segments along the chain there is no more information/memory of the directionality of the first bond.

(2) By averaging over all configurations of the chain, calculate the average end-to-end distance,  $\langle \vec{R}_{ee} \rangle = \langle \sum_i \vec{t}_i \rangle$  and mean square end-to-end distance,  $\langle \vec{R}_{ee}^2 \rangle$  in terms of  $\cos(\theta)$ . Next, assuming that  $\cos(\theta)$  is small, write an approximate expression for how  $\langle \vec{R}_{ee}^2 \rangle$  grows as a function of  $N$ .

Consider now the application, to the chain ends, of a stretching force,  $\vec{f}$ . The energy of a given configuration is  $E = -\sum_i \vec{f} \cdot \vec{t}_i$ . Assuming that the force strength,  $f$ , is small, and averaging over all chain configurations:

(3) compute, to leading order in  $f$ , the average orientation of the first bond,  $\langle \vec{t}_1 \rangle$ . On the basis of your result discuss how the average end to end distance,  $\langle \vec{R}_{ee} \rangle$ , depends on  $\vec{f}$ .

(4) Show that  $\langle \vec{R}_{ee}^2 \rangle$  is affected by the applied force only to second order in  $f$ . Discuss this result in relation to the previous one.

## Problem 4: Medicinal Chemistry

Address one and only one of the following issues:

1. Describe a possible synthetic approach, mechanism of action, and structure-activity relationships (SAR) for one of the following classes of drugs: neuroleptic agents; opioid analgesic agents.
2. Describe the technique of QSAR (Quantitative Structure-Activity Relationship) and 3D QSAR applied to computational drug design, explaining the role of the principal component analysis and partial least squares in defining quantitative statistical models.

## Problem 5: Functional Genomics

Address one and only one of the following issues:

1. A large quantity of synuclein is believed to be a potential cause of Parkinson's disease (PD). The candidate proposes high-throughput strategies to identify molecules that decrease its expression as a therapeutic for PD.
2. How the sequences of the human genome has impacted our ability to design new drugs.
3. Techniques for gene expression analysis from cDA microarrays to Affymetrix to new generations of deep sequencing.
4. How gene expression analysis may help drug development.
5. The use of protein-protein interaction maps in drug development.
6. The candidate design an high-throughput screening to isolate small molecules to inhibt apoptosis.

## **Problem 6: Structural Biology**

Address one and only one of the following issues:

1. Mention two techniques to determine the structures of macromolecules, and discuss their relative strengths and weaknesses.
2. Describe the 3D structure of a particular protein and its relevance to the function.
3. The molecular basis of epigenetics.

## **Problem 7: Molecular Recognition and Self-Assembling in Biological Systems**

The candidate should select a scientific relevant example and write down a research proposal (few pages long) based on a set of selected experimental techniques. The motivation for the choice of the discussed problem should be clearly discussed, and potentialities and limitations of each selected technique properly highlighted.

In the last 1/2 page the candidate will write a summary of the whole proposal as self-consistently as possible. A paper that will contain also numbers with units (for instance about sensitivity levels) will be rated higher than a paper that contains only vague statements. Of course the proposal does not need to be original but, please, pay attention to the paper's organization and logic that will need to be present especially in absence of original ideas and specific numbers.