Entrance Examination Physics and Chemistry of Biological Systems
September 2013

Solve **one** of the following problems (no extra credit is given for attempts to solve more than one problem). Write out solutions clearly and concisely. State each approximation used. Diagrams welcome. Number page, problem, and question clearly. All essays/solutions should be written in English. Do not write your name on the problem sheet, but use extra envelope.

Problem n. 1 – Langevin equation of a charged particle in a magnetic field

Consider the Langevin equation:

$$\gamma\,\vec{v} = q\,\vec{v}\wedge\vec{B} + \vec{\eta}(t) \tag{1}$$

describing the stochastic motion of a point particle of charge q and friction γ in a heat bath at temperature T and in the presence of a magnetic field $\vec{B}$. $\vec{v}$ is the particle velocity. $\vec{\eta}(t)$ is the stochastic force acting on the particle, which obeys thermal averages:

- $\langle\vec{\eta}(t)\rangle = 0$;
- $\langle\eta_i(t)\,\eta_j(t')\rangle = 2\,\gamma\,\kappa_B\,T\,\delta_{i,j}\,\delta(t-t')$ where κ_B is the Boltzmann constant, $\delta_{i,j}$[1] is the Kronecker delta, and $\delta(t)$ is the Dirac δ-function.

By assuming, that $\vec{B} = B\,\hat{z}$ is a uniform magnetic field oriented along the z-direction:

1. Find the explicit expression of particle velocity, $\vec{v}$, in terms of q, $\vec{B}$, γ, $\vec{\eta}$. Show, in particular, that it can be expressed as $\begin{pmatrix}\gamma_x\,v_x(t)\\ \gamma_y\,v_y(t)\\ \gamma_z\,v_z(t)\end{pmatrix} = \begin{pmatrix}\xi_x(t)\\ \xi_y(t)\\ \xi_z(t)\end{pmatrix}$ where γ_i and $\xi_i(t)$ are *new* frictions and stochastic forces, satisfying: $\langle\vec{\xi}(t)\rangle = 0$ and $\langle\xi_i(t)\,\xi_j(t')\rangle = 2\,\gamma_i\,\kappa_B\,T\,\delta_{i,j}\,\delta(t-t')$.
2. Calculate the mean-square-displacement $\delta r^2(t) \equiv \left\langle(\vec{r}(t)-\vec{r}(0))^2\right\rangle$. Show, in particular, that $\delta r^2(t) = 6\,D\,t$, where D is the diffusion coefficient. Express D in terms of γ, q, B. Sketch a plot of D as a function of B.
3. For which value of B, D has the same value as in two-dimensional diffusion?

[1] i and j run through the 3 spatial components (x, y, z).

Problem n. 2 – Lotka-Volterra model for predator-prey dynamics

Consider the dynamical system

$$\begin{aligned} \frac{dx}{dt} &= \alpha x - \beta xy \\ \frac{dy}{dt} &= -\gamma y + \delta xy \end{aligned} \tag{1}$$

where $x(t)$ and $y(t)$ represent the prey and predator populations, and the parameters α, β, γ, δ are all positive.

1. Give an interpretation of the different terms in (1) and of the meaning of the 4 parameters.
2. Compute the equilibrium points and discuss their stability. What can be deduced about the overall behavior of the system?
3. Show that the system (1) has an integral of motion (hint: look at $\frac{dx}{dy}$). Derive its expression and use it to characterize the global behavior of the system.
4. Describe what happens when you use a logistic growth for the prey, i.e., you replace the system (1) with the following

$$\begin{aligned} \frac{dx}{dt} &= \alpha x \frac{(k-x)}{k} - \beta xy \\ \frac{dy}{dt} &= -\gamma y + \delta xy \end{aligned} \tag{2}$$

   where $k > 0$ is the carrying capacity of the prey.

5. How would you modify (1) to represent a competing species scenario (i.e., x eats y and y eats x)?

Problem n. 3 – Mobile ions in an oppositely charged background

Consider a system where mobile ions of charge q are immersed in a uniformly charged medium of dielectir costant ϵ. The number density of the mobile ions is n and the system is overall neutral.

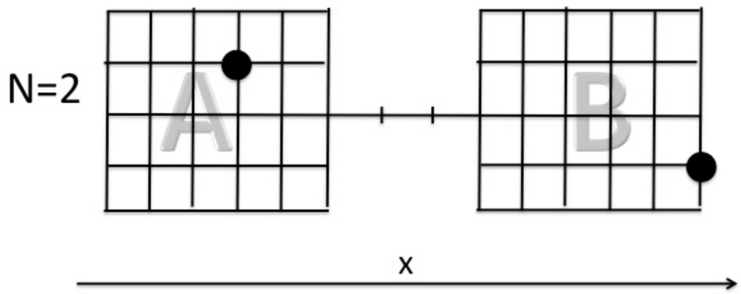
- Write down the Poisson equation for the potential ϕ for an instantaneous configuration of the mobile ions.

  Assume now that the system is in thermal equilibrium at a temperature T.

- Write down the expression for the local concentration of the mobile ions.
- Write down the self-consistent Poisson equation for the canonical average of the potential, $\langle \phi \rangle$.
- Specify the conditions which allow for linearising the previous equation, $\nabla^2 \langle \phi \rangle \propto \langle \phi \rangle$. What is the physical interpretation of the proportionality constant?
- Using the previous linearised expression, calculate $\langle \phi \rangle$ for a semi-infinite sample of the system ending a flat wall with positive surface charge density, ρ.

Problem n. 4 – Rare transitions of a particle between two containers

Consider a system with N particles moving on the square lattice depicted in figure, at a temperature $T = 1$. Each site can be occupied only by one particle at a time.



1. For N=1 compute the free energy as a function of the coordinate x of the particle
2. For N=2 compute the free energy as a function of the coordinate x of one of the two particles.
3. For N=2, using Arrenius law, estimate the rate for a transition of one of the two particles from the region labeled A to the region labeled B. Comment on the dependence on the temperature T. Assume that the kinetic prefactor is equal to 1.

Assume now that when the two particles occupy neighbouring sites they interact with an attractive potential $-\varepsilon$.

4. Repeat point 2 in the limit of infinite ε
5. Repeat point 2 and 3 for a generic value of ε.

Problem n. 5 – Generalization of Stokes formula for drag in a viscous fluid

Stokes formula states that a ball B_R of radius R moving at speed $V\mathbf{e}$ (here, $\mathbf{e}$ is a unit vector) in a Stokes fluid with viscosity $\eta > 0$ (see reminder later) experiences a drag given by

$$\begin{aligned} \mathbf{F}_{drag} &= -F_{drag}\,\mathbf{e} \\ F_{drag} &= 6\pi\eta R V\,. \end{aligned}$$

Consider an ellipsoid of revolution, whose longer axis is the axis of rotation, and moves at speed $\mathbf{V}$. The Stokes formula generalizes to

$$\mathbf{F}_{drag} = -\mathbf{K}\,\mathbf{V} \tag{3}$$

where the matrix $\mathbf{K}$ is symmetric and positive definite. Discuss why this is the case. In particular, answer to the following questions:

1. Which is the eigenvector of $\mathbf{K}$ corresponding to the largest eigenvalue?
2. Which is the eigenvector of $\mathbf{K}$ corresponding to the smallest eigenvalue?
3. Why is the matrix $\mathbf{K}$ positive definite?
4. Why is the matrix $\mathbf{K}$ symmetric ?
5. The following question is more advanced: try to answer to it *only if* you have already answered to the previous four questions. Drop the assumption that Ω is an ellipsoid, and assume now that it is a generic bounded region of R^3. Why is still true that (3) holds, with $\mathbf{K}$ a symmetric and positive definite matrix?

Reminder

The flow generated by a ball B_R of radius R moving at speed $V\mathbf{e}$ (here, $\mathbf{e}$ is a unit vector) in a Stokes fluid at rest, with viscosity $\eta > 0$, is described by the velocity field $\mathbf{v}$ and the scalar pressure field p obtained by solving the system

$$\begin{aligned} \eta\Delta\mathbf{v} - \nabla p &= 0 \quad \text{in } R^3 \setminus B_R \\ \operatorname{div}\mathbf{v} &= 0 \quad \text{in } R^3 \setminus B_R \\ \mathbf{v}(x) &= V\mathbf{e} \quad \text{on } \partial B_R \\ \mathbf{v}(x) \to 0\,,\ p(x) &\to 0 \quad \text{for } |\mathbf{x}| \to \infty \end{aligned}$$

Problem 6 -- Electronic structure and reactivity of 'piano-stool' anticancer compounds

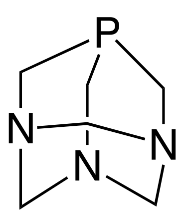
The Ru(η^6-arene)Cl_2pta complex (with pta = 1,3,5-triaza-7-phopsphaadamantane, in Figure) is a potential anticancer compound. Its active metabolite, formed after hydrolysis of Cl- ligands, targets Guanine bases in the major groove (N7-Gua) of double strand DNA.

According to the Hückel MO theory write the energy level diagram of the benzene molecular orbitals, and sketch corresponding MOs. Write the $E\pi$ electron energy and the delocalization energy of benzene.

Explain how benzene binds to the Ru metal center in Ru(η^6-arene)Cl_2pta and make a sketch of the structure of the inorganic complex.

According to the 18 e- rule, which is the possible oxidation state of metal Ru (electronic configuration $5s^2 4d^6$)?

Considering the following DNA sequence of a DNA duplex d[5'-CCTCTGGTCTCC-3']$_2$ how would you expect the Ru(η^6-arene)Cl_2pta compound to covalently bind to DNA?



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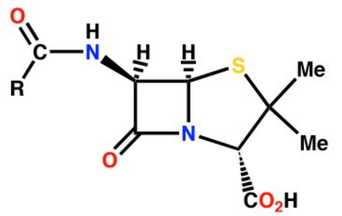
Problem 7 -- The chemical properties of beta-lactam antibiotics

Beta-lactams are commonly used class of antibiotics to fight bacterial infections. Serine-beta-lactamases are bacterial enzymes, which hydrolyze beta-lactam antibiotics. This hydrolysis occurs thanks to a serine aminoacid, which performs the nucleophilic attack on the beta-lactam ring. To counteract the action of these enzymes, clavulanic acid is used in combination with the antibiotics as it has a synergic effect on their activity.



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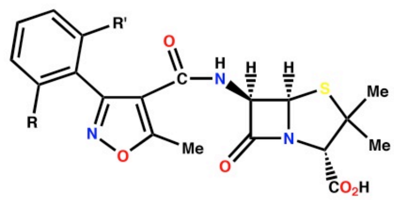

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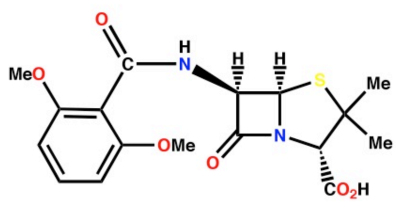
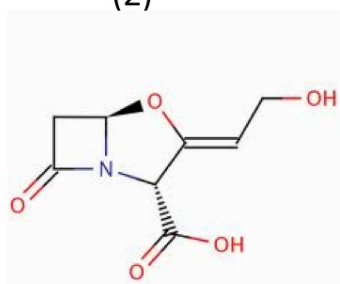


(3)



(4)

Describe the chemical characteristics of beta-lactam antibiotics, sketch the tridimensional structure of a generic beta-lactam antibiotic, and discuss the reasons of their high reactivity on the basis of their molecular orbital description.

Which is the reason of the sensitivity of the antibiotics to acid conditions? How would you expect benzyl-penicillin (in which R in 1 is a benzyl group) to increase/decrease this sensitivity? Comment on the chemical transformations of penicillins occurring in acidic solution and the effect of the substituents on these chemical transformations.

In contrast to benzyl-penicillin, oxacillin (2 with R=R'=H) and methicillin (3) are resistant to beta-lactamase enzymes. Which is the physical-chemical principle of their higher activity? Considering the sensitivity of beta-lactam antibiotics to acidic media, which of these two drugs is better for an oral administration?

Which are the reasons of the poor antibiotic activity of clavulanic acid (4) and of its high affinity towards beta-lactamases enzymes?