

## Solution 4

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### Question 1: Eulerian versus Lagrangian description

We consider the following problem that in a one-dimensional flow, fluid particles are located all along the  $x$ -axis, let us assume there are infinitely many with an infinitesimal small distance between each other. Each particle carries a quantity  $u$ . At time  $t^0 := 0$ , fluid particles at each point  $x$  have the quantity  $u(x, t^0) := f(x)$  and begin motion in the  $x$ -direction with velocity  $v(x, t^0) := Kx$  and continue at that speed.

- a) In the Lagrangian description, we identify our control volumes with the fluid particles. Now we focus on one control volume  $p$ . At the time  $t^0 = 0$ , the control volume has the position  $x(t^0) := x_p^0$ . Since each particle moves at constant velocity, the position  $x_p$  and velocity  $v_p$  of our control volume, after a time  $t$  is given by

$$x_p(t) = x_p^0 + t v(x_p^0, t^0) \quad (1)$$

$$= x_p^0 + t K x_p^0 \quad (2)$$

$$v_p(t) = v(x_p^0, t^0) \quad (3)$$

$$= K x_p^0 \quad (4)$$

this would also follow by taking the first derivative from  $x_p(t)$  (with respect to time). The quantity  $u$  travels with the flow, hence with our control volume. Therefore, the quantity  $u_p$  carried by the control volume stays constant:

$$u_p(t) = u(x_p^0, t^0) \quad (5)$$

$$= f(x_p^0) \quad (6)$$

- b) In the Eulerian description, we identify our control volumes with stationary portions of the space. In this case, we chose that the control volumes are points and there are at  $t^0$  as many control volumes as fluid particles. Now we focus again on one control volume  $p$ . In the Eulerian framework, the control volume remains at the same position at all  $t$ , hence:

$$x_p = x_p^0 \quad (7)$$

$$v_p = 0 \quad (8)$$

In contrast to the control volume,  $u$  is traveling with the flow, which leads to a change of  $u$  within the control volume. At time  $t$ , the quantity  $u$  has traveled with the flow particle at constant velocity  $v = Kx$  to the position  $x_p$ . Hence, in order to determine

the quantity  $u_p(t)$  at position  $x_p$ , we need to find out where the starting location  $x_s$  of the flow particle has been.

At time  $t$ , the fluid particle has traveled from the position  $x_s$  with the velocity  $v = K x_s$  for a time duration of  $t$  to the position  $x_p$  of the control volume. Hence:

$$x_s + t K x_s = x_p \quad (9)$$

$$x_s = \frac{x_p}{1 + t K} \quad (10)$$

$$u_p(t) = u(x_s, t^0) \quad (11)$$

$$= f(x_s) \quad (12)$$

$$= f\left(\frac{x_p}{1 + t K}\right) \quad (13)$$

## Question 2: Conservation laws, diffusion and advection

We consider a chemical species  $C$  whose concentration  $c(x, t)$  varies in time and space (one dimension  $x$ !). The situation is illustrated in Figure 1 where the chemical species  $C$  is contained in a long, thin tube with constant cross-section  $A$ .

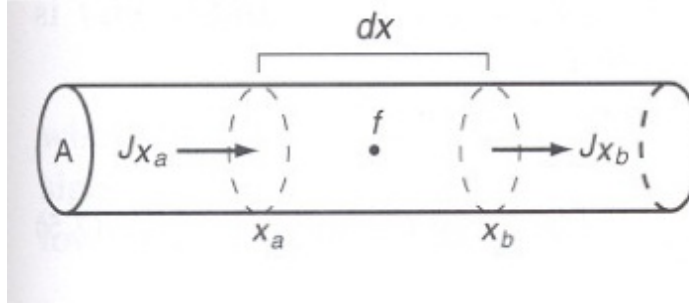


Figure 1: Conservation in thin long tube (3D), with variables varying only in one dimension (from C.P. Fall, 2005)

Let us think of the slice between  $x_a$  and  $x_b$  as our "control volume"  $V$ .

- a) The intensive quantity in the set-up is the concentration  $c(x, t)$  of the chemical species  $C$  (e.g. in units molecule number per litre or micromol/litre). Extensive quantities are e.g. the total mass  $m$  or the total amount  $N$  of  $C$ . We will focus on  $N$  in this exercise, because it relates to concentration. The dimension of  $N$  is simply the number of particles, in biology often in units micromoles (One mole contains Avogadro's number (approximately  $6.022 \times 10^{23}$ ) entities).

The flux rate  $J$  has the dimension amount/area/time.

The net rate of increase of  $C$   $f$  has dimension amount/time/volume.

- b) For the conservation law of the total amount of the  $C$  we need to specify the system as follows:

$$\begin{aligned} \text{Total amount of } C \text{ in the control volume, i.e. in } [x_a, x_b] &= \int_{x_a}^{x_b} c(x, t) A dx \\ \text{Net rate of entry of } C &= AJ(x_a, t) - AJ(x_b, t) \\ \text{Net rate of production of } C &= \int_{x_a}^{x_b} f(x, t, c(x, t)) A dx \end{aligned}$$

Then, the conservation of the total amount of  $C$  reads in :

$$\frac{d}{dt} \int_{x_a}^{x_b} c(x, t) A dx = AJ(x_a, t) - AJ(x_b, t) + \int_{x_a}^{x_b} f(x, t, c(x, t)) A dx$$

To get integral quantities, we can replace

$$AJ(x_b, t) - AJ(x_a, t) = A \int_{x_a}^{x_b} \frac{\partial}{\partial x} J(x, t) dx$$

and get

$$\frac{d}{dt} \int_{x_a}^{x_b} c(x, t) A dx = - \int_{x_a}^{x_b} \frac{\partial}{\partial x} J(x, t) A dx + \int_{x_a}^{x_b} f(x, t, c(x, t)) A dx$$

If the function  $c(x, t)$  is smooth enough, we can interchange integration and differentiation (Leibniz's rule). Furthermore, we can get rid of  $A$  and get:

$$\int_{x_a}^{x_b} \left[ \frac{\partial}{\partial t} c(x, t) + \frac{\partial}{\partial x} J(x, t) - f(x, t, c(x, t)) \right] dx = 0 \quad (14)$$

Since we did not assume anything about our control volume, this equation must hold for all control volumes. This can only be true if the integrand is zero, and we arrive at the differential form of the conservation law:

$$\frac{\partial}{\partial t} c(x, t) + \frac{\partial}{\partial x} J(x, t) - f(x, t, c(x, t)) = 0 \quad (15)$$

The general Reynolds transport theorem states:

$$\frac{D\phi}{Dt} = \int_{V(t)} \left( \frac{\partial f}{\partial t} + \nabla \cdot (f\mathbf{v}) \right) dV(t) = \int_{V(t)} \frac{\partial f}{\partial t} dV(t) + \oint_{S(t)} f\mathbf{v} \cdot \mathbf{n} dS(t) \quad (16)$$

for any intensive quantity  $f$  and the related extensive quantity  $\phi = \int_V f dV$ . Intuitively, this means: The temporal change of extensive property is equal the integral of the temporal change of intensive property plus the net flow out of the volume element. If we now compare equation (16) to the above derived equation (14) we can see that  $\frac{\partial}{\partial t} c(x, t)$  corresponds to  $\frac{\partial f}{\partial t}$  and  $\frac{\partial}{\partial x} J(x, t)$  corresponds to  $\nabla \cdot (f\mathbf{v})$ . The term  $f(x, t, c(x, t))$  in our derivation has not occurred in the lecture.  $f$  describes production and destruction of the chemical species  $C$  which is referred to as chemical reactions. Thus, we can call the derived equation (15) a general reactive flow equation.

In three dimension with  $\mathbf{x} = (x, y, z)$  Equation (15) reads:

$$\frac{\partial}{\partial t} c(\mathbf{x}, t) + \nabla \cdot J(\mathbf{x}, t) - f(\mathbf{x}, t, c(\mathbf{x}, t)) = 0$$

- c) A **constitutive** equation is a relation between two physical quantities that is specific to a material or substance, and does not follow directly from physical laws. It is combined with other equations that do represent physical laws to solve some physical problem. Some constitutive equations are simply phenomenological; others are derived from first principles.

Fick's law states that the flux  $J$  is proportional to the concentration gradient, where the proportionality constant is the diffusion coefficient  $D$  (it is in general a rank-2 tensor, and a diffusion *constant* only under additional assumptions):

$$J(x, t) = -D \frac{\partial}{\partial x} c(x, t)$$

$D$  is proportional to the velocity of the diffusing particles, which depends on the temperature, viscosity of the fluid and the size of the particles according to the Stokes-Einstein relation. For the biological molecules the diffusion coefficients normally range from  $10^{-11} \text{ m}^2 \text{ s}^{-1}$  to  $10^{-10} \text{ m}^2 \text{ s}^{-1}$

If the flux in Equation (15) is described by Fick's law, we get

$$\frac{\partial}{\partial t} c(x, t) + \frac{\partial}{\partial x} \left( -D \frac{\partial}{\partial x} c(x, t) \right) - f(x, t, c(x, t)) = 0 \quad (17)$$

which is the reaction-diffusion-equation in one dimension. In three dimensions Equation (17) reads:

$$\frac{\partial}{\partial t}c(\mathbf{x}, t) + \nabla \cdot (-D\nabla c(\mathbf{x}, t)) - f(\mathbf{x}, t, c(\mathbf{x}, t)) = 0$$

- d) Assuming in addition a uniform macroscopic flow of the solvent, with speed  $\nu$  along the x-axis, the advective flux for our problem is given by:

$$J(x, t) = \nu c(x, t)$$

Hence, the advection-reaction-diffusion-equation in one dimension reads

$$\frac{\partial}{\partial t}c(x, t) + \frac{\partial}{\partial x} \left( \nu c(x, t) - D \frac{\partial}{\partial x} c(x, t) \right) - f(x, t, c(x, t)) = 0 \quad (18)$$

and the three-dimensional form is:

$$\frac{\partial}{\partial t}c(\mathbf{x}, t) + \nabla \cdot (\nu c(\mathbf{x}, t) - D\nabla c(\mathbf{x}, t)) - f(\mathbf{x}, t, c(\mathbf{x}, t)) = 0$$

### Question 3: The Cable equation

We consider our tube to be bounded by a membrane. We keep track of the electrical potential across the membrane, rather than the chemical species within the tube! The total current along the interior of the axon is  $I(x)$ , positive from left ( $x_a$ ) to right ( $x_b$ ), and the transmembrane current per unit area  $I_T$ , positive outward.

- a) The conservation of current in the control volume with  $S$  being the circumference length of the tube is given by:

$$I(x_a, t) - I(x_b, t) = \int_{x_a}^{x_b} I_T(x) S dx$$

Using integral notation we can re-write this equation and get

$$- \int_{x_a}^{x_b} \frac{\partial}{\partial x} I(x, t) dx = \int_{x_a}^{x_b} I_T(x) S dx$$

for any control volume leading again to the differential expression:

$$-\frac{\partial}{\partial x} I(x, t) = I_T(x) S \quad (19)$$

- b) The total transmembrane current  $I_T$  consists of two components, a capacity and an ion current. The capacity current results from the fact that we assume that our membrane, which consists of a lipid-bilayer, behaves like a capacitor. Hence, the current through the capacitor can be modelled as:

$$I_{cap} = C_m \frac{\partial}{\partial t} V(x, t)$$

where  $V$  is the transmembrane potential, assuming the extracellular electric potential to be a constant, and  $C_m$  is the capacitance of the membrane. Furthermore, we have

an ion current  $I_{ion}$  due to a diversity of channels that are permeable for certain ions leading to

$$I_T = I_{cap} + I_{ion} = C_m \frac{\partial}{\partial t} V(x, t) + I_{ion}$$

We can embed this expression in Equation (19)

$$-\frac{\partial}{\partial x} I(x, t) = S (I_{cap} + I_{ion}) = S \left( C_m \frac{\partial}{\partial t} V(x, t) + I_{ion} \right) \quad (20)$$

- c) Finally, the constitutive equation for the relationship between the intracellular current  $I$  and intracellular voltage  $V$  is given by Ohm's law:

$$I(x, t) = -\frac{A}{R_c} \frac{\partial}{\partial x} V(x, t) \quad (21)$$

Again, we assume that the extracellular electric potential is a constant.  $R_c$  is the cytoplasmic resistance (dimension [Ohm L]). Embedding this relationship into Equation (22) we arrive at the general Cable Equation:

$$\frac{\partial}{\partial x} \left( \frac{A}{R_c} \frac{\partial}{\partial x} V(x, t) \right) = S \left( C_m \frac{\partial}{\partial t} V(x, t) + I_{ion} \right) \quad (22)$$

## Question 4: Conservation in the QS system

The QS is a coupled ODE/reaction-diffusion system. Outside the bacteria we have a normal diffusion equation for  $u_e$  with degradation, i.e. AHL molecules are allowed to deteriorate with rate  $\gamma$ . Hence, we arrive at

$$\frac{\partial}{\partial t} u_e(x, t) = D \Delta u_e - \gamma u_e \quad (23)$$

for AHL concentration  $u_e$  outside the cells.

The tricky part of the model is the handling at the boundary between the extracellular matrix and the bacteria. Assume, we model the bacteria as a sphere with radius  $R$ . Then, we model the exchange of AHL molecules by

$$\left( -D \frac{\partial}{\partial \nu} u_e(x, t) \Big|_{|x|=R} \right) = d_1 u_e(x, t) - d_2 u_c \quad (24)$$

where  $\nu$  is the normal to the cell surface. Notice that  $u_c$  is taken to be homogeneous throughout the bacteria cytosol. The different rates  $d_1$  and  $d_2$  are due to active pumps for AHL-molecule trans-membrane transport.

The evolution of  $u_c$  inside the cell is influenced by the reaction term  $f(u_c)$  and the net inflow into the cell via the cell membrane:

$$\text{Net inflow into the cell} = \int_{|x|=R} d_1 u_e(x, t) - d_2 u_c dx$$

Hence, we arrive at the evolution equation

$$\begin{aligned} \frac{d}{dt} u_c &= f(u_c) + \int_{|x|=R} d_1 u_e(x, t) - d_2 u_c dx \\ &= f(u_c) - 4\pi R^2 d_2 u_c + \int_{|x|=R} d_1 u_e(x, t) dx \end{aligned}$$

where we have used the surface area of the spherical cell  $S_{cell} = 4\pi R^2$ .

A word of caution about  $u_c$ . In the QS paper the authors call  $u_c$  the mass of the substance within the cell. Then,  $d_1$  and  $d_2$  would have, however, different dimensions. It seems more convenient to think of  $u_c$  as a density as well, i.e. mass ( $x_c$ ) divided by the volume of the cell  $V_{cell}$  which is in our case very easy to calculate, namely  $V_{cell} = \frac{4}{3}\pi R^3$

## Question 5: Something about numerics: Finite Volume methods

In the lecture, we derived the diffusion equation as follows: With density  $u(x, t)$  as intensive quantity and  $m = \int_V u dV$  as corresponding extensive quantity we find from mass conservation and using Gauss' theorem

$$0 = \frac{Dm}{Dt} = \int_{V(t)} \frac{\partial u}{\partial t} dV + \oint_{\partial V(t)} u \mathbf{v} \cdot \mathbf{n} dS.$$

With Fick's law  $u \mathbf{v} = -D \nabla u$  follows

$$\int_{V(t)} \frac{\partial u}{\partial t} dV = \oint_{\partial V(t)} D \nabla u \cdot \mathbf{n} dS.$$

For Finite Volume methods, each volume element  $V_i(t)$  is taken finite but small enough for variations of  $u$  to be negligible. Then  $u$  can be assumed as constant throughout  $V_i$ , this value  $u_i$  is stored in a mesh point within  $V_i$ , and the left hand side  $\int_{V_i(t)} \frac{\partial u}{\partial t} dV \approx \int_{V_i(t)} \frac{\partial u_i}{\partial t} dV = |V_i(t)| \frac{\partial u_i}{\partial t}$  can be discretised.

For the right hand side, let  $V_1(t), \dots, V_k(t)$  the neighbouring volume elements of  $V_i$  at time  $t$ . Then the surface  $\partial V_i(t)$  can be split into disjoint parts  $\partial V_i(t) \cap \partial V_j(t)$ ,  $j = 1, \dots, k$ , and each surface integral

$$\int_{\partial V_i(t) \cap \partial V_j(t)} D \nabla u \cdot \mathbf{n} dS$$

measures flux from one volume element ( $V_i$ ) into another ( $V_j$ ). As this expression occurs equally in each of the neighbouring volume elements, just with sign inverted because outer normal of  $V_i$  is inner normal of  $V_j$  on  $\partial V_i \cap \partial V_j$ , the Finite Volume methods are conservative.