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Property density function

By the end of this lesson, you will be able to... use the uniform probability distribution graph a normal curve state the properties of the normal curve explain the role of area in the normal density function For a quick overview of this section, feel free to watch this short video summary: In Chapter 6, we focused on discrete random variables, random variables which take on either a finite or countable number of values. Continuous random variables, which have infinitely many values, can be a bit more complicated. Consider the rand() function in the computer software Microsoft Excel. It returns a random number between 0 and 1. There are infinitely many possibilities, so each particular value has a probability of 0! When we consider continuous random variables, we need to instead consider the probability "density", which might not always be the same for each value. Some ranges might be more likely, and hence the probability would be more "dense" near those values. To make this easier to understand, we need a new concept called a probability density function. Let's look at Example 4, from Section 6.1, in which two dice were tossed and X = the sum of the two dice. The histogram below highlights P(X k_{co}\) for μ > 1, the mutation will lead to an increased probability of being in the open state.The system governing the open and closed probability densities now takes the form $$\displaystyle\begin{array}{rcl} \frac{\partial \rho _{o}} {\partial t} + \frac{\partial } {\partial x}\left (a_{o}\rho _{o}\right) =\mu k_{co}\,x\rho _{c} - k_{oc}\rho _{o},& &{}\end{array}$$ (4.43) $$\displaystyle\begin{array}{rcl} \frac{\partial \rho _{c}} {\partial t} + \frac{\partial } {\partial x}\left (a_{c}\rho _{c}\right) = k_{oc}\rho _{o} - \mu k_{co}\,x\rho _{c},& &{}\end{array}$$ (4.44) where, as above, we have $$\displaystyle\begin{array}{rcl} a_{o} = v_{r}(c_{1} - x) + v_{d}(c_{0} - x),& & \\ a_{c} = v_{d}(c_{0} - x).& &{}\end{array}$$ (4.45) Note that in this model the opening rate depends on the concentration x. Model parameters are given in Table 4.2.Table 4.2 Parameter values for the model (4.43) and (4.44) In Fig. 4.3, we show the results of Monte Carlo simulations (histograms) and solutions of the probability density system (4.43) and (4.44) (red solid line) for the wild type case (μ = 1) and mutant case (μ = 3). As above, we see that these two computational approaches give more or less the same answer. It is more interesting to observe the effect of the mutation. We see that the mutation tends to shift the open probability density function toward the upper boundary, where the function becomes very large. This shows that, in the case of mutation, it is very likely to have a high concentration and an open channel—much more likely than in the wild type case.Fig. 4.3 Upper panel: Wild type open (left) and closed (right) probability density functions computed using Monte Carlo simulations (histogram) and by solving the probability density system (red line). The integral of the open probability density function is 0.811 (0.189 for the closed state probability density function). Lower panel: Similar figure as for the mutant case (μ = 3). The integral of the open probability density function is 0.962 (0.038 for the closed state probability density function) The statistical characteristics introduced above are given in Table 4.3. We note that the total open probability π o increases from 0.811 for the wild type to 0.962 for the mutant. Also, we note that the expected concentration, E o , for open channels is given by 81.91 \(\upmu\) M for the wild type and 87.95 \(\upmu\) M for the mutant. The standard deviation, on the other hand, is significantly reduced (by a factor of three) in the mutant case compared to the wild type. The probability of being in the closed state decreases by a factor of five in the mutant case compared to the wild type, whereas the expected concentration is doubled and the standard deviation is reduced by a factor of seven.Table 4.3 Statistical properties of the wild type and mutant cases We have seen a few examples indicating how changes in the reaction rates k co and k oc change the probability density functions. Since we are able to solve the stationary case analytically, this issue can be studied in great detail. Let us start by recalling that we model the effect of the mutation by introducing a severity index μ. The stationary model is then $$\displaystyle\begin{array}{rcl} \frac{\partial } {\partial x}\left (a_{o}\rho _{o}\right) =\mu k_{co}\,x\rho _{c} - k_{oc}\rho _{o},& &{}\end{array}$$ (4.46) $$\displaystyle\begin{array}{rcl} \frac{\partial } {\partial x}\left (a_{c}\rho _{c}\right) = k_{oc}\rho _{o} -\mu k_{co}\,x\rho _{c},& &{}\end{array}$$ (4.47) where we recall that μ = 1 is the wild type case. We discussed above how to solve the steady state model analytically (see Sect. 2.6, page 41) and we can use the analytical solution to investigate how the mutation affects the probability density functions. Since the steady state open probability density function is given by the solution of $$\displaystyle{\rho _{o}^{{\prime}} = -\alpha (x)\rho _{ o}}$$ with$$\displaystyle{\alpha (x) = \frac{\mu k_{co}\,x} {v_{d}(c_{0} - x)} - \frac{v_{p} - k_{oc}} {v_{p} (c_{+} - x)},}$$ where$$\displaystyle{v_{p} = v_{r} \frac{c_{1} - c_{0}} {c_{+} - c_{0}},}$$ we have solutions of the form $$\displaystyle{ \rho _{o,\mu }(x) = K_{\mu }e^{\frac{\mu k_{co}\,x} {v_{d}} }(c_{+} - x)^{\frac{k_{oc}} {v_{p}} -1}(x - c_{0})^{\frac{c_{0}\mu k_{co}} {v_{d}} }, }$$ (4.48) where K μ is a constant given by the somewhat complicated expression $$\displaystyle{1/K_{\mu } = (c_{+}-c_{0})^{a+b}e^{a}\Gamma (a)\Gamma (b)(_{ 1}\!F_{1}(a,a+b,c)+k_{oc}\frac{v_{p} - v_{d}} {v_{d}v_{p}} _{1}\!F_{1}(a,a+b+1,c)).}$$ Here \(_{1}\!F_{1}\) is Kummer’s regularized hypergeometric function and $$\displaystyle{a = c_{0}\mu k_{co}/v_{d},b = k_{oc}/v_{p},c = (c_{+} - c_{0})\mu k_{co}/v_{d}.}$$ It is useful to consider the ratio of the mutant solution to the wild type solution and we find that$$\displaystyle{ \frac{\rho _{o,\mu }(x)} {\rho _{o,1}(x)} = \frac{K_{\mu }} {K_{1}}e^{\frac{\left (\mu -1\right)xk_{co}} {v_{d}} }(x - c_{0})^{\frac{\left (\mu -1\right)c_{0}k_{co}} {v_{d}} }.}$$ In Fig. 4.4, we graph this relation as a function of the severity index μ and the concentration x. We observe that, close to the maximum concentration, the open probability density function of the mutant is much larger than for the wild type.Fig. 4.4 Contours of the function \(\frac{\rho _{o,\mu }(x)} {\rho _{o,1}(x)}\). Note that the open probability density function of the mutant is much greater than the open probability density function of the wild type for large values of the concentration and for large values of the mutation severity index μ As seen in both the numerical and analytical solutions above, the probability density functions may have singularities at the endpoints. It is easily seen from (4.48) that ρo, μ has a singularity at the endpoint \(x = c_{+}\) whenever$$\displaystyle{\frac{k_{oc}} {v_{p}}