1 Diffusion limit for the precision of chemical detection

Here we will derive the Berg-Purcell limit to the precision of chemical detection. This has been considered specifically for the case of chemotaxis performance by Escherichia coli, which can respond to very small gradients in concentration, in a beautiful paper by Berg and Purcell, Biophys J 20: 193 (1977). Here we will ask a simple question: if the average ligand concentration is $c$ and we have a small measurement apparatus (e.g. the receptor protein) that attempts to measure this concentration, how precisely can this be done?

1) Suppose the measurement apparatus has linear size $a$. What is the approximate number of molecules of ligand in the volume occupied by the apparatus? Note that the ligand must diffuse into this volume if you want to detect it! Suppose the ligand is present at $1$ nM or $1$ µM concentration, and the apparatus is either a single receptor protein $a \sim 1$ nm or the whole cell $l \sim 1$ µm. What is the average number of molecules in all these cases?

2) While what you computed is the average number of detected molecules, from measurement to measurement the real number will fluctuate. Can you argue that detecting molecules is a point process? What is the error (variance) in the number of detected molecules on a single measurement (express it in terms of $c$ and $a$)?

3) The error in a measurement can be reduced by repeating the measurement over and over again. Recall from the statistics that after $K$ measurement, the error becomes $\sigma^2_K = \sigma^2_1/K$. What is the condition on those measurements (Does the error go down when you duplicate measurements)?

4) So our chemical detector wants to reduce the variance from question (2) by making more measurements, as in question (3). Suppose the total time you have to measure concentration is $\tau$. What is roughly the maximal number of measurements $K$ the detector can make?

5) Putting everything together, what is the effective error in the number of molecules in a box of size $a$, if the detector can measure during time $\tau$, ligand is present at average concentration
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c and diffuses with constant $D$? Express the result in terms of these quantities. Turn the error in the number of molecules into the error in concentration measurement and show that it is

$$\left(\frac{\sigma_c}{c}\right)^2 \sim \frac{1}{Da\tau} \quad (1.1)$$

There is an apparent paradox here. If this is the error for detection by a single receptor, then by having $M$ receptors in the cell, I should be able to suppress this error even further (by doing more simultaneous measurements), such that:

$$\left(\frac{\sigma_c}{c}\right)^2 \sim \frac{1}{MDa\tau} \quad (1.2)$$

For large $M$ (by making many many receptors) I can obviously make this as small as possible. On the other hand, if I think of the whole E. coli as a detector apparatus of size $l \sim 1 \mu$m, the same argument says that I can never measure better than

$$\left(\frac{\sigma_c}{c}\right)^2 \sim \frac{1}{Dl\tau} \quad (1.3)$$

6) Can you figure out what is going on (and what should be the true error in concentration)? Hint: think whether the conditions of (3) hold again when I have more and more receptors, $M \to \infty$? Based on this consideration, estimate of how many receptors the bacteria should have for a minimum error.

7) If the diffusion constant of the ligand is $D \sim 1 \cdot 10^{-9} \text{ m}^2/\text{s}$ and the measurement time $\tau \sim 10 \text{ s}$ (typical run/tumble time for bacterial chemotaxis), what is the precision by which the whole bacterium, $l \sim 1 \mu$m, can measure the concentration?