virology blog

About viruses and viral disease

Multiplicity of infection

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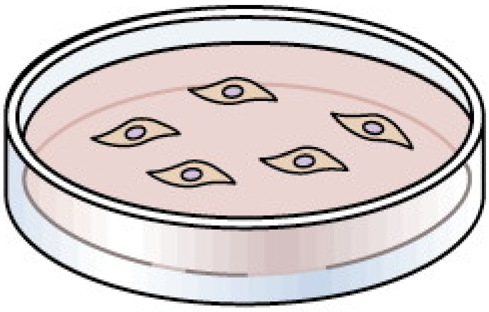

Multiplicity of infection (MOI) is a frequently used term in virology which refers to the number of virions that are added per cell during infection. If one million virions are added to one million cells, the MOI is one. If ten million virions are added, the MOI is ten. Add 100,000 virions, and the MOI is 0.1. The concept is straightforward.

But here is the tricky part. If you infect cells at a MOI of one, does that mean that each cell in the cutlure receives one virion?

The answer is no.

Here is another way to look at this problem: imagine a room containing 100 buckets. If you threw 100 tennis balls into that room – all at the same time – would each bucket get one ball? Most likely not.

How many tennis balls end up in each bucket, or the number of virions that each cell receives at different MOI, is described by the Poisson distribution:

$$P(k) = e^{-m}m^k/k!$$

In this equation, P(k) is the fraction of cells infected by k virus particles, and m is the MOI. The equation can be simplified to calculate the fraction of uninfected cells (k=0), cells with a single infection (k=1), and cells with multiple infection (k>1):

$$P(0) = e^{-m}$$

$$P(1) = me^{-m}$$

$$P(>1) = 1-e^{-m}(m+1)^*$$

*this value is obtained by subtracting from unity (the sum of all probabilities for any value of k) the probabilities P(0) and P(1)

Here are some examples of how these equations can be used. If we have a million cells in a culture dish and infect them at a MOI of 10, how many cells receive 0, 1, and more than one virion? The fraction of uninfected cells – those which receive 0 particles – is

$$P(0) = e^{-10}$$

$$= 4.5 \times 10^{-5}$$

In a culture of one million cells this is 45 uninfected cells. That's why an MOI of 10 is used in many virology experiments – it assures that essentially every cell is infected.

At the same MOI of 10, the number of cells that receive 1 particle is calculated by

$$P(1) = 10e^{-10}$$

$$= 10 \times 4.5 \times 10^{-5}$$

$$= 4.5 \times 10^{-4}$$

In a culture of one million cells, 450 cells receive 1 particle.

How many cells receive more than one particle is calculated by

$$P(>1) = 1 - e^{-10}(10+1)$$

$$=0.995$$

In a culture of one million cells, 999,500 cells receive more than one particle.

Using the same formulas, we can determine the fraction of cells receiving 0, 1, and more than one virus particle if we infect one million cells at a MOI of 1:

$P(0) = e^{-1} = 0.37$ = 37% of cells are uninfected

$P(1) = 1 \times e^{-1}$ = 37% of cells receive one virion

$P(>1) = 1 - e^{-1}(1+1)$ = 26% of cells are multiply infected

An assumption inherent in these calculations is that all cells in a culture are identical in their ability to be infected. In a clonal cell culture (such as HeLa cells) the deviations in size and surface properties are small enough to be negligible. However, in a multicellular animal there are substantial differences in cell types that affect susceptibility to infection. Under these conditions, it is experimentally difficult to determine how many virions infect different cells.

High MOI is used when the experiment requires that every cell in the culture is infected. By contrast, low MOI is used when multiple cycles of infection are required. However, it is not possible to calculate the MOI unless the virus titer can be determined – for example by plaque assay or any other method of quantifying infectivity.