

# Mathematical Oncology

Quasi Stationary Steady State

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In mathematical modelling, the concept of a quasi-stationary steady state (QSSS) is often employed to simplify complex systems under specific constraints. This approach is justified based on several underlying principles and assumptions:

1. **Separation of time scales:** QSSS assumptions are primarily justified when the dynamical system exhibits separation of time scales between *fast and slow variables*, allowing for the assumption that the fast processes reach a steady state (almost) instantaneously.
2. **Reduction of model complexity:** This assumption can significantly reduce the model's complexity by decreasing the number of differential equations that need to be solved simultaneously.
3. **Enhanced analytical insights:** Simplification under the QSSS assumption can facilitate analytical solutions or methods, providing better understanding of the system's behaviour.
4. **Empirical justification:** QSSS assumptions are often empirically justified by experimental observations that indicate the rapid equilibration of certain variables.
5. **Mathematical formalism:** Theoretical justifications of QSSS come from mathematical formalisms such as [singular perturbation theory](#), which helps identify the conditions under which the QSSS assumption is valid.
6. **Predictive accuracy:** The use of QSSS is justified if it leads to models that accurately predict experimental outcomes or observed phenomena.

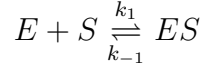
## Example: Michaelis-Menten Enzyme Kinetics

An typical example of the application of the QSSS assumption is found in enzyme kinetics, specifically in the Michaelis-Menten mechanism. This mechanism describes the conversion of a substrate ( $S$ ) into a product ( $P$ ) with the help of an enzyme ( $E$ ), and through the formation of a intermediate  $E$ - $S$  complex. More specifically the Michaelis-Menten mechanism is described in the following steps:

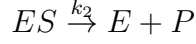
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1. Fast: formation of the enzyme-substrate ( $ES$ ) complex:



2. Slow: conversion to product  $P$ :



Mathematically, the system of equations that describe the time evolution of the concentrations of  $S$ ,  $E$ ,  $ES$ , and  $P$  reads as follows:

$$\begin{aligned}\frac{d[S]}{dt} &= -k_1[E][S] + k_{-1}[ES], \\ \frac{d[E]}{dt} &= -k_1[E][S] + (k_{-1} + k_2)[ES], \\ \frac{d[ES]}{dt} &= k_1[E][S] - (k_{-1} + k_2)[ES], \\ \frac{d[P]}{dt} &= k_2[ES].\end{aligned}$$

The QSSS assumption *can be applied under the premise that the formation of the  $ES$  complex and its dissociation (back to  $E$  and  $S$ ), are much faster than its conversion to the product  $P$* . This simplification allows to write

$$\frac{d[ES]}{dt} = 0 \implies k_1[E][S] - (k_{-1} + k_2)[ES] = 0,$$

i.e.

$$[ES] = \frac{k_1}{k_{-1} + k_2} [E][S],$$

Assuming now that the total enzyme concentration  $[E]_{tot}$ , which is the sum of the free enzyme  $[E]$  and the enzyme bound within the complex  $[ES]$ , remains constant:

$$[E]_{tot} = [E] + [ES]$$

allows to solve for  $[E]$  and after substituting back in the  $[ES]$  formula (and after some algebra), we obtain

$$[ES] = \frac{[E]_{tot}[S]}{K_M + [S]}$$

where  $K_M = \frac{k_{-1} + k_2}{k_1}$  is the Michaelis constant.

The rate of product  $P$  formation is then given by:

$$\frac{d[P]}{dt} = k_2[ES] = \frac{k_2[E]_{tot}[S]}{K_M + [S]}$$

Defining the maximum rate  $V_{max} = k_2[E]_{tot}$ , we finally obtain the Michaelis-Menten equation:

$$\frac{d[P]}{dt} = V_{max} \frac{[S]}{K_M + [S]}$$

Clearly, these calculations would not have been carried through with the QSSS assumption  $\frac{d[ES]}{dt} = 0$ .