



INTERNATIONAL COLLEGE  
OF PHARMACEUTICAL  
INNOVATION

国际创新药学院

<b>Class</b>	Pharm, BioPharm
<b>Course</b>	Fundamentals of Medicinal & Pharmaceutical Chemistry
<b>Code</b>	FUNCHEM.9
<b>Title</b>	Collision theory & rate equation
<b>Lecturer</b>	Prof. Xincheng Teng
<b>Date</b>	2024-11-22

## Recommended Reading

- General Chemistry - The Essential Concepts  
by Chang and Goldsby (7th edition)  
Chapter 14: Chemical Kinetics  
14.1 The rate of reaction 470  
14.2 The rate laws 474  
14.3 Relation between reactants concentration and time  
14.4 Activation Energy and Temperature  
14.5 Reaction Mechanisms

# Learning Outcomes

- Explain the 'Collision Theory' in relation to 'molecular orientation', 'frequency of collisions' and 'energy of collisions'.
- Recall and explain factors affecting reaction rates.
- Calculate the rate of a reaction at a given time from a graph of reactant (or product) concentration versus time.
- Explain the 'rate law' or 'rate equation' in terms of partial orders and overall order of reaction.
- Define 'reaction order'.
- Using the base hydrolysis of aspirin as an example, explain what you understand by a 'pseudo-first order' reaction.
- Demonstrate an understanding of how a knowledge of reaction order with respect to a particular drug can affect drug dosage for the treatment of a particular disease.

# What is 'Chemical Kinetics'?

The area of chemistry concerned with the **speed** or **rate** at which a chemical reaction occurs is called:

## **“Chemical Kinetics”**

The word **“Kinetic”** suggests movement or change.

**Chemical kinetics** is therefore the study of:

- the **rates** of chemical reactions
- the **factors** that **affect** rates of reactions
- the **mechanisms** by which reactions occur

# Why study chemical kinetics?

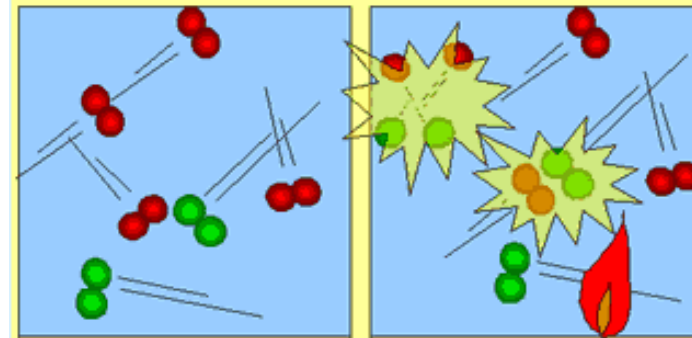
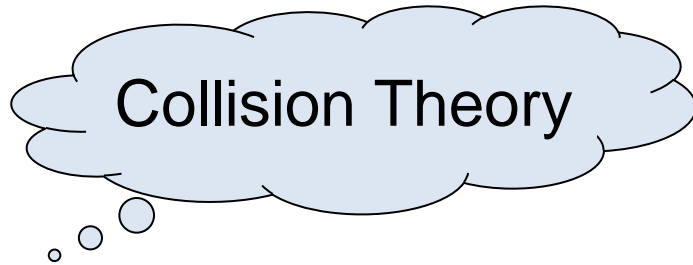
- How molecules react in the body
- Shelf-life of pharmaceuticals
- Onset and duration of action of various drugs
- Some medications need to be fast acting eg. pain killers
- Some others need to be slow



# Factors Affecting Reaction Rates

1. **Concentration** of reactants
2. **Temperature** e.g. Reactions are faster
3. **Catalysis** e.g. biological enzymes
4. **Surface area** e.g. powders versus lumps!

# Theories about Reaction Rates

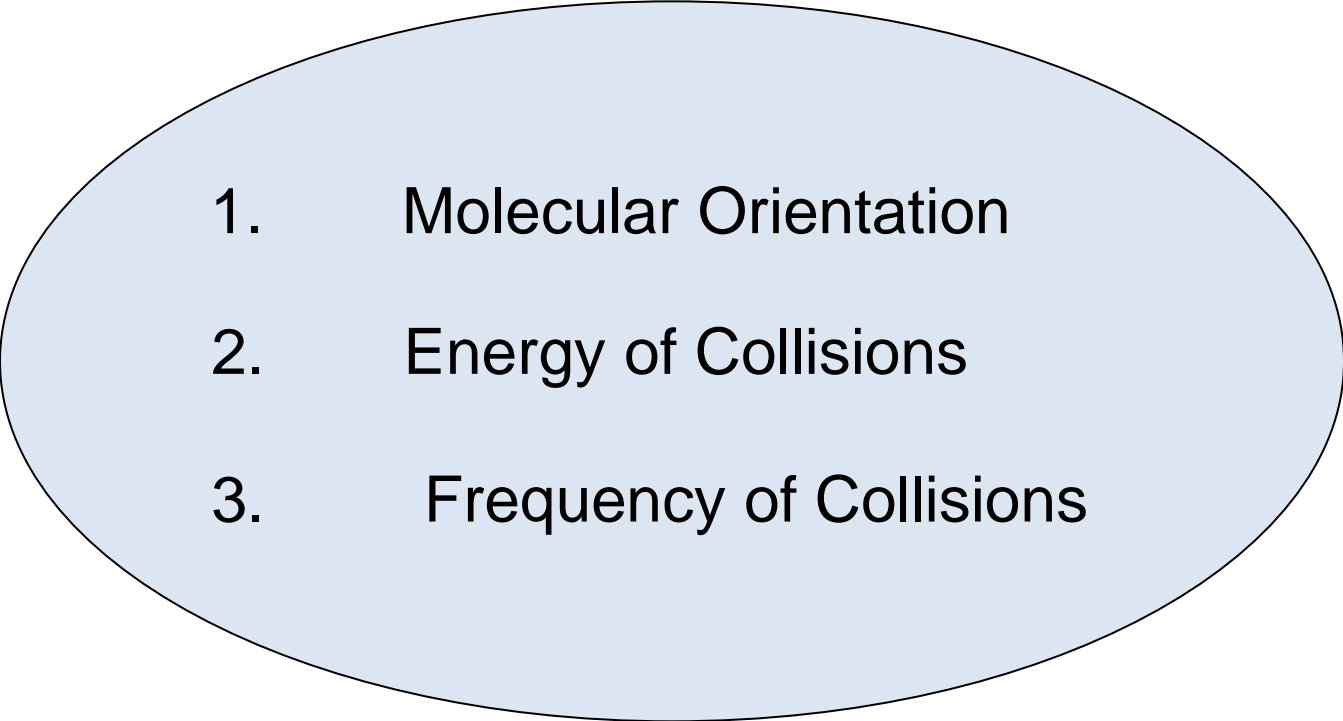


Effective model of what happens to molecules in a reacting system

It tells us that:

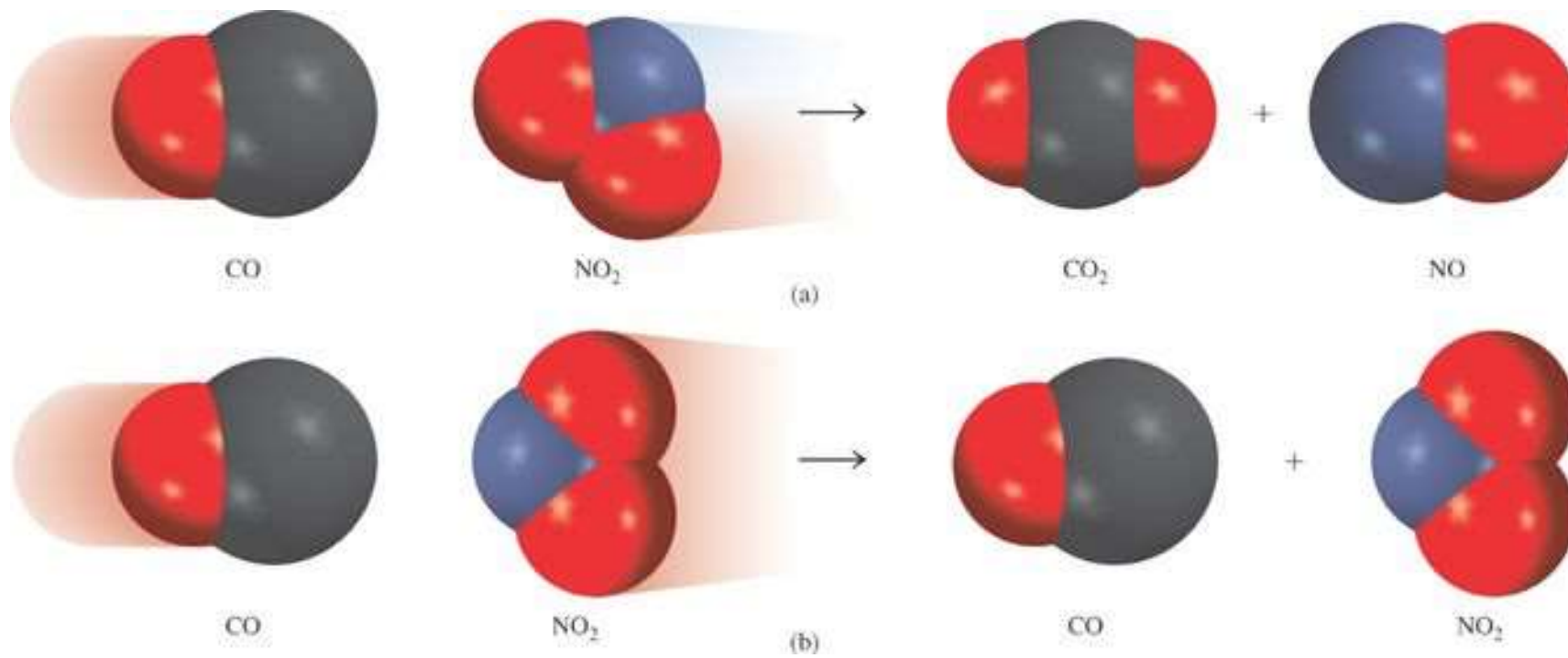
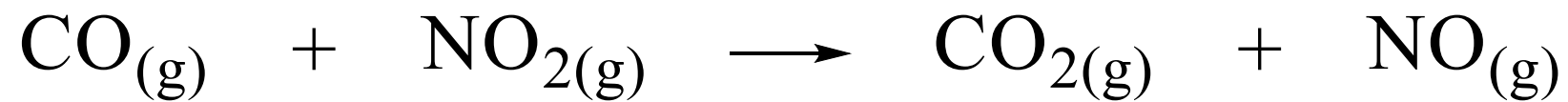
for a reaction to occur, an **effective collision** must take place between reactants

## What makes a collision an “effective collision”?

- 
1. Molecular Orientation
  2. Energy of Collisions
  3. Frequency of Collisions

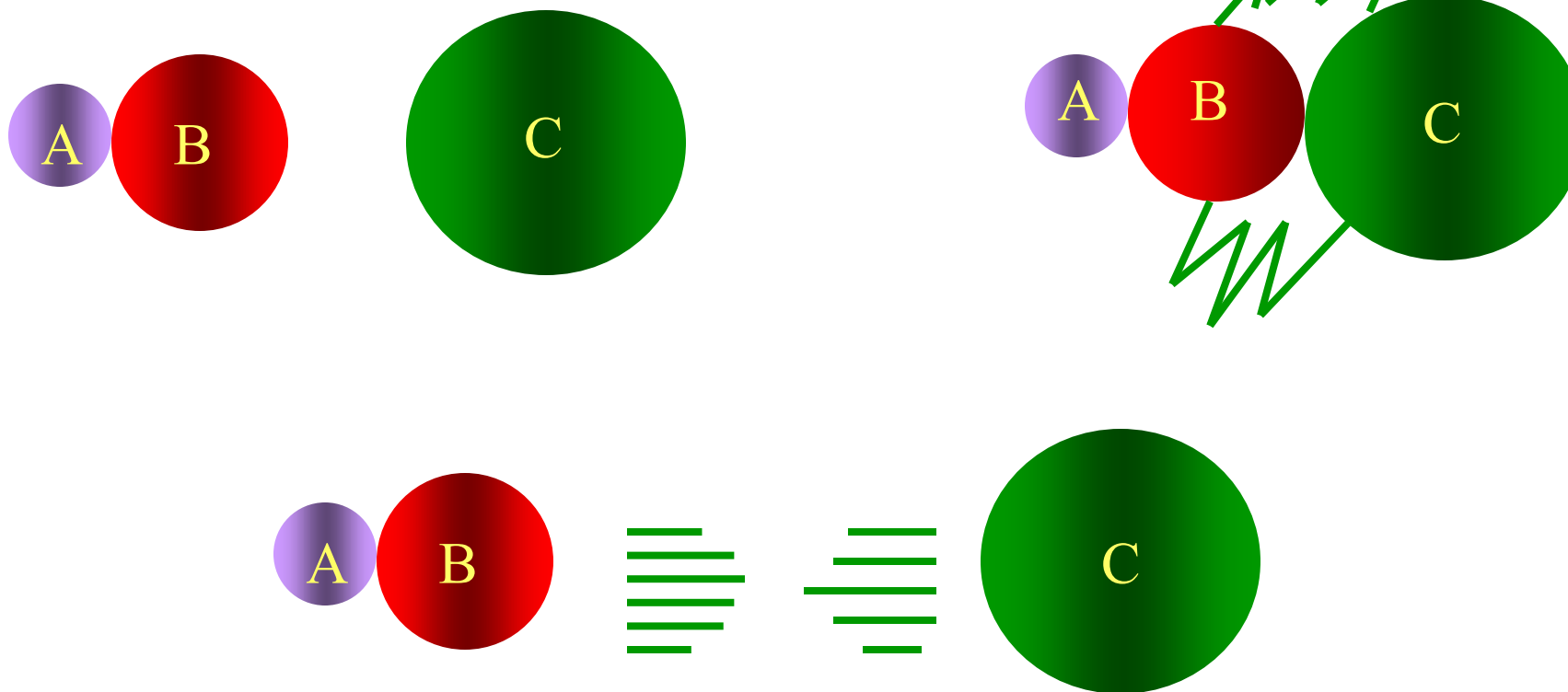


# 1. Molecular Orientation



## 2. Energy of Collisions

Two slow moving molecules collide

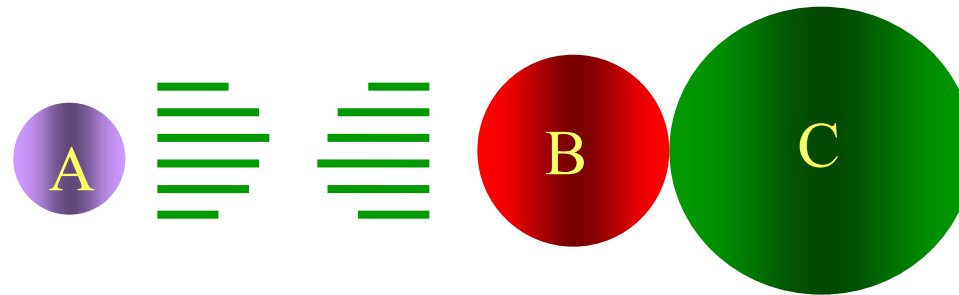
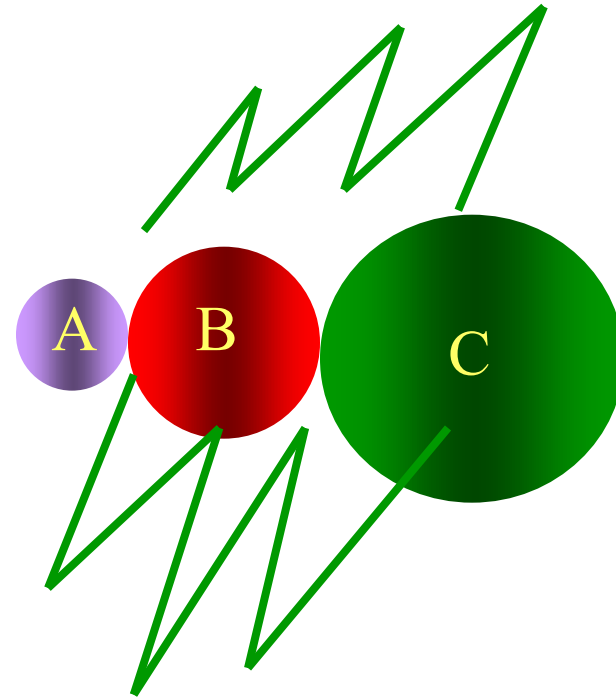
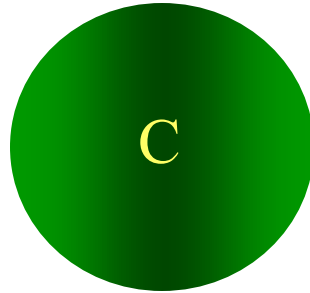
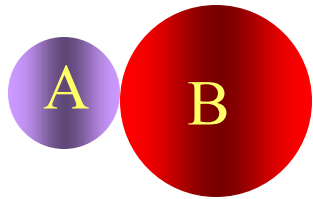


**Repulsion due to electron clouds**

**No product formation**

## 2. Energy of Collisions

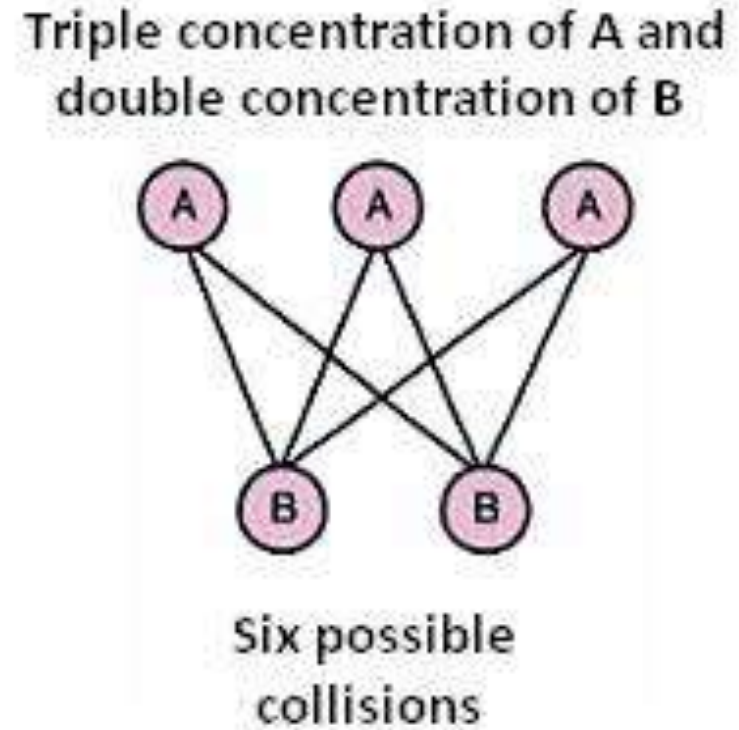
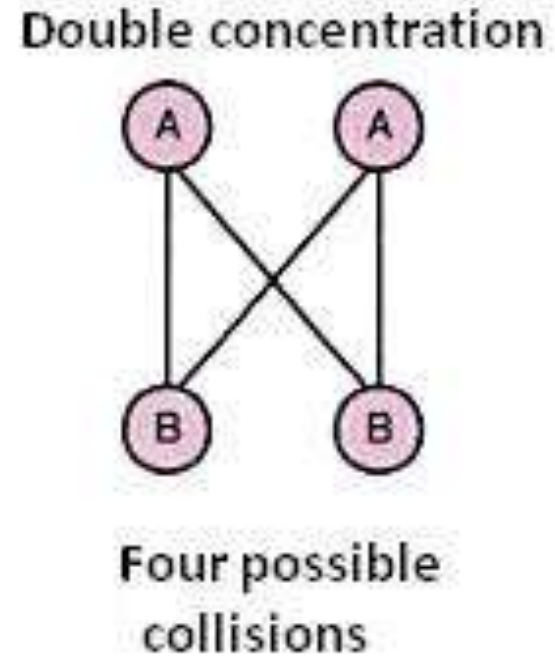
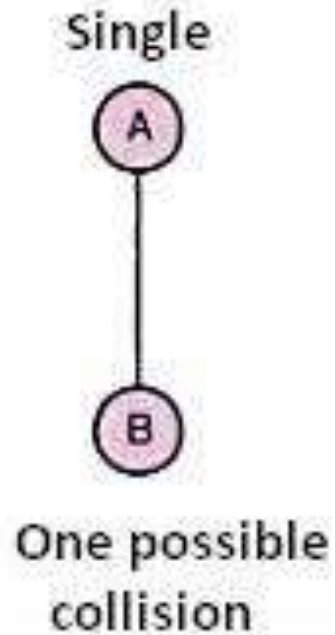
Two fast moving molecules collide



**New product formed**

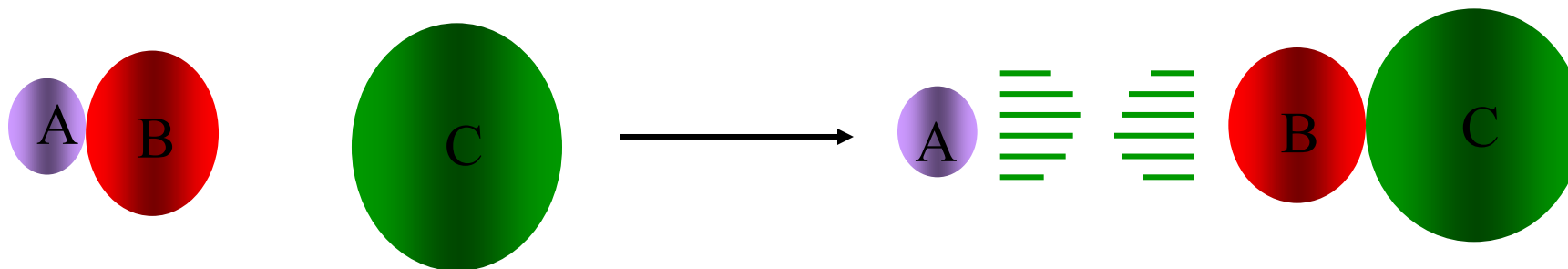
### 3. Frequency of Collisions

Molecules A and B reacting



## Conclusion: Collisions Theory

For a reaction to occur we need an **'effective'** collision



The reacting molecules must react:

- a) in the correct orientation
- b) with sufficient energy
- c) by increasing the **concentration** we increase the chance of **collisions** therefore **increase the chances of a reaction to occur.**

# What is 'Rate of Reaction'?

**Rate of Reaction** measures how fast a reactant is consumed or how fast a product is formed.

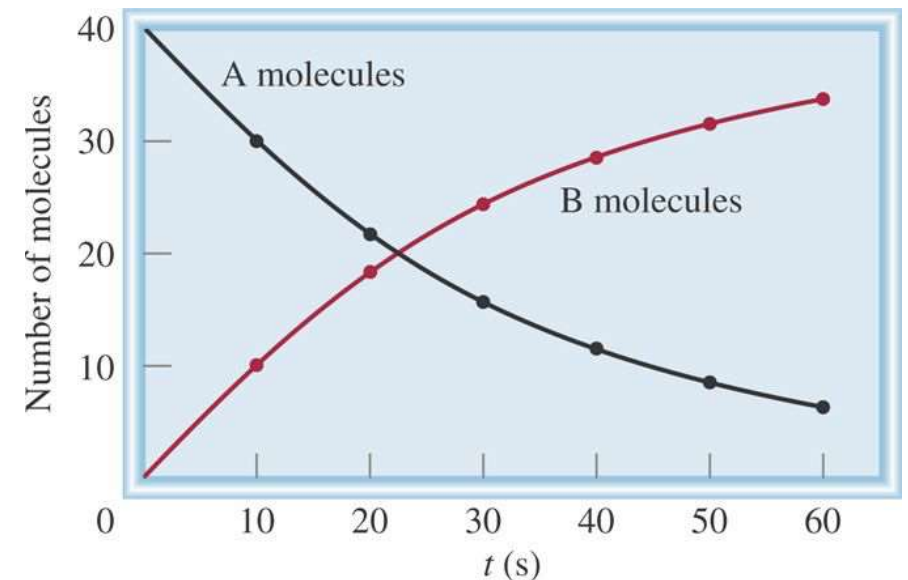
It is expressed as a change in concentration over time.

Unit is “concentration unit” / “time unit” ( $\text{mol/L}\cdot\text{s}$  or  $\text{mol L}^{-1} \text{s}^{-1}$  or  $\text{M s}^{-1}$ )

For a simple reaction:



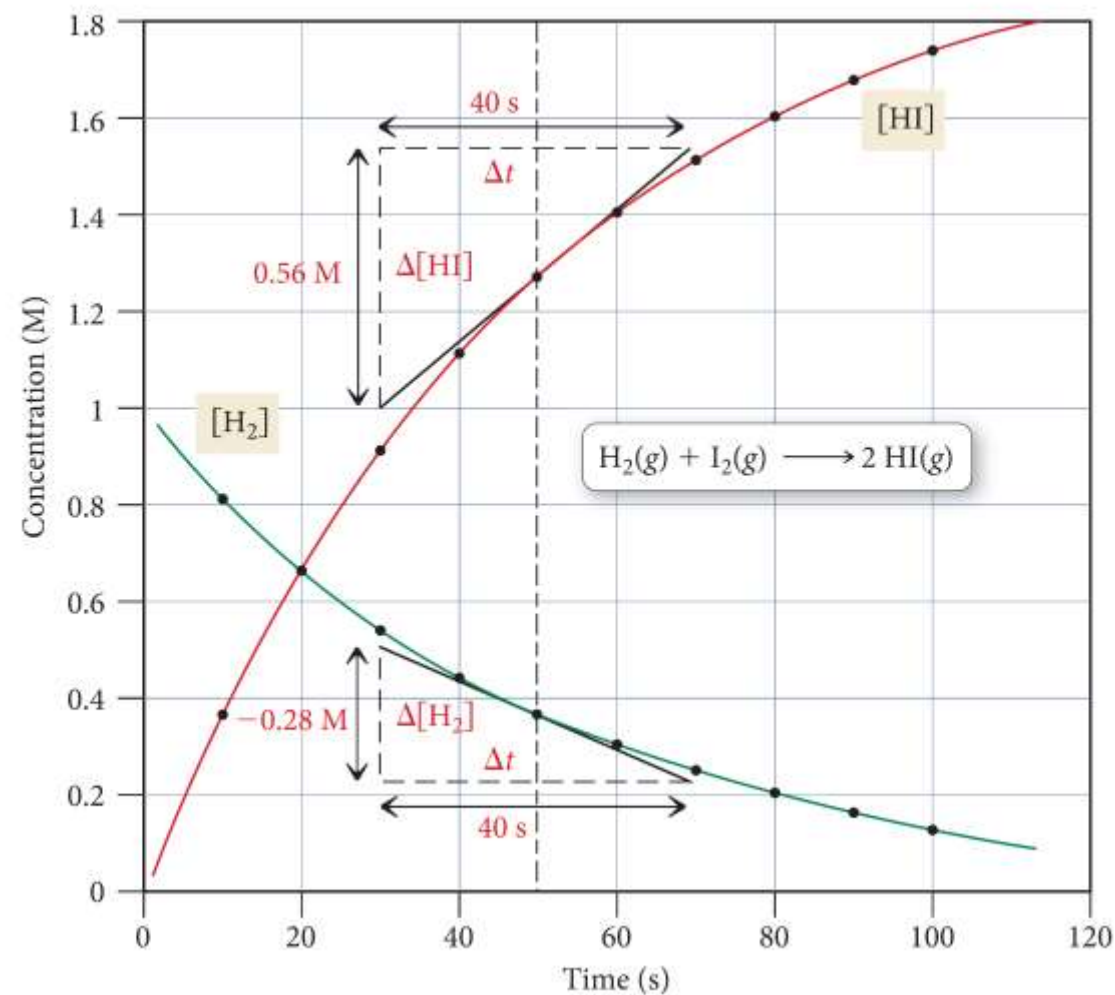
The decrease in number of “A” molecules = the increase in number of “B” molecules.



## How is reaction rate measured?

- The **instantaneous rate** of the reaction is the rate at *any* one point in time and is represented by the instantaneous slope of the curve at that point.

$$\begin{aligned}\text{Instantaneous rate (at 50 s)} &= -\frac{\Delta[\text{H}_2]}{\Delta t} \\ &= -\frac{-0.28 \text{ M}}{40 \text{ s}} \\ &= 0.0070 \text{ M/s}\end{aligned}$$

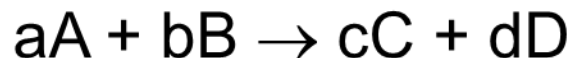


# The rate of a chemical reactions

- The **rate of a chemical reaction** is expressed in terms of the change in the quantity of a reactant or product that takes place in a period of time.

$$\text{Rate of reaction} = \frac{\text{concentration}_{\text{later}} - \text{concentration}_{\text{earlier}}}{\text{time}_{\text{later}} - \text{time}_{\text{earlier}}} = \frac{\Delta[ \quad ]}{\Delta t}$$

- For a general reaction



$$\text{Rate} = -\frac{1}{a} \frac{\Delta[A]}{\Delta t} = -\frac{1}{b} \frac{\Delta[B]}{\Delta t} = +\frac{1}{c} \frac{\Delta[C]}{\Delta t} = +\frac{1}{d} \frac{\Delta[D]}{\Delta t}$$

You must state the temperature at which the reaction takes place



**REACTION RATES VARY WITH TEMPERATURE**



# Rate Laws

**Rate Laws** define the dependence of rate on concentrations - in other words the effect of concentration change on the rate of reaction.

Rate laws are defined through experimental measurements of the reaction rates.

## **Differential Rate Law: Rate versus [Reactant]**

Describes the relationship between reaction rate and reactant(s) concentration.

## **Integrated Rate Law: [Reactant] versus Time**

Describes the relationship between reactant(s) concentration and time.

# The Differential Rate Law

## The Effect Of Concentration On Reaction Rate

- The rate of a reaction often depends on the concentration of one or more of the reactants.
- For a reaction with a single reactant,  $A \rightarrow \text{products}$ , the relationship between the rate of the reaction and the concentration of the reactant, called the **rate law**, can be expressed as

$$\text{Rate} = k[A]^n$$

$k$  is a constant of proportionality called the **rate constant**

**(Note:**  $k$  is only constant when the temperature is constant and, for reactions in solution, the solvent is the same)

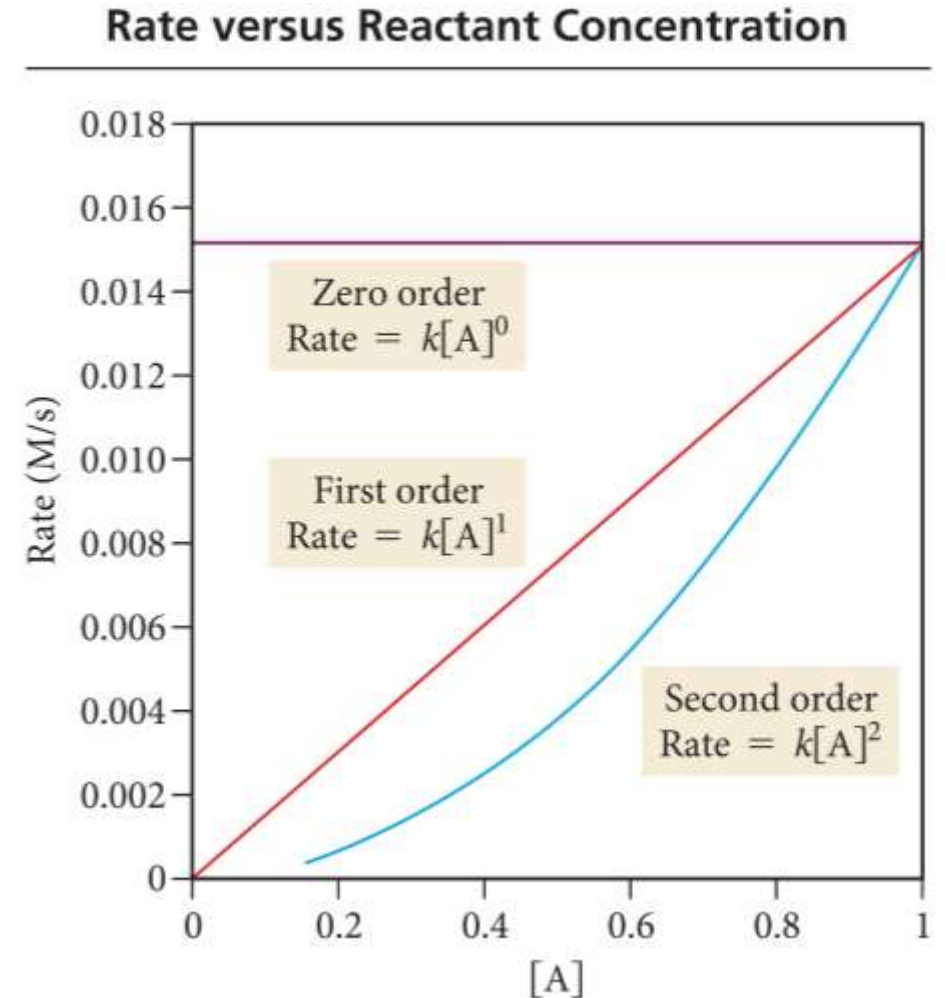
$n$  is the **reaction order**

# The Differential Rate Law

## The Effect Of Concentration On Reaction Rate

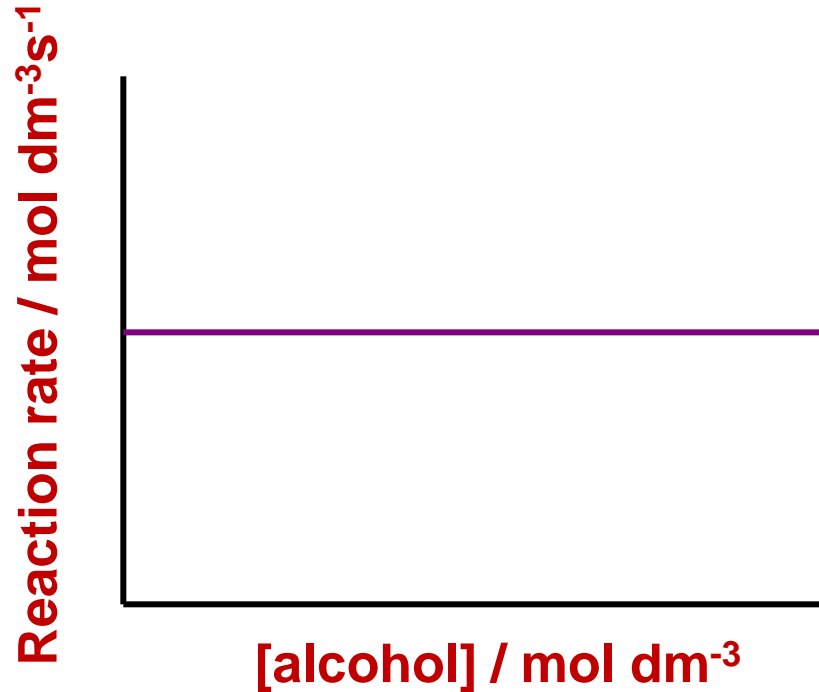
$$\text{Rate} = k[A]^n$$

- If  **$n = 0$** , the reaction is **zero order** and the rate is independent of the concentration of A.
- If  **$n = 1$** , the reaction is **first order** and the rate is directly proportional to the concentration of A.
- If  **$n = 2$** , the reaction is **second order** and the rate is proportional to the square of the concentration of A.



# A zero order reaction

Example: The elimination of alcohol by the body!



$$\text{Rate} = k[\text{alcohol}]^x$$

$$\text{Rate} = k$$

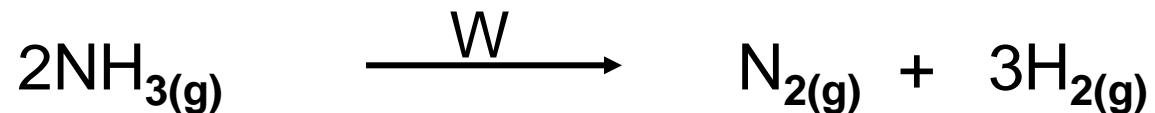
$$\text{Rate} = k[\text{alcohol}]^0$$

$$\text{Rate} = k$$

In zero order reaction the rate is the same no matter what the concentration

## Another example for zero order reaction

Ammonia gas decomposition on a hot tungsten wire



The rate of decomposition does **NOT** depend upon  $[\text{NH}_3]$

$$\frac{-d[\text{NH}_3]}{dt} = k$$

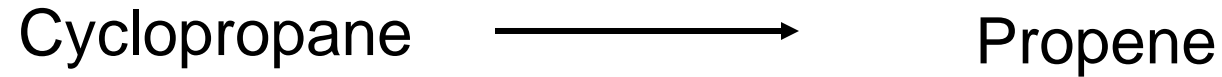
$$\text{Rate} = k[\text{NH}_3]^0$$

OR

$$\frac{-d[\text{NH}_3]}{dt} = k[\text{NH}_3]^0$$

Zero order  
( $x = 0$ )

# First Order Reaction



Rate equation:

$$\text{Rate} = k[\text{Cyclopropane}]^1$$

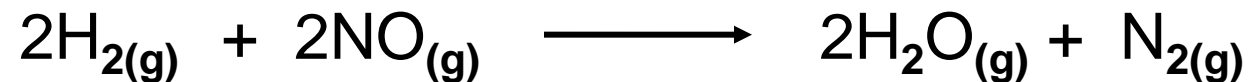
*Rate is directly proportional to the concentration*

if you double the concentration,  
you double the rate  
- first order reaction

**Rate equation is found by experiment**

## Another example

The reaction of nitric oxide with hydrogen at 1280 °C is



Experiment shows that (when [NO] is constant):

If you **double** the  $[\text{H}_2]$ , the rate **doubles**

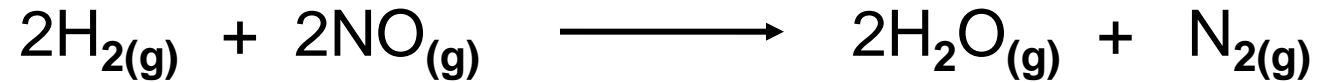
If you **triple** the  $[\text{H}_2]$ , the rate **triples**

**Conclusion**

**Rate  $\propto [\text{H}_2]$**

**Rate =  $k [\text{H}_2]^1$**

Now, the dependence of reaction rate on [NO] is examined



Experiment also shows (when [H<sub>2</sub>] is constant):

If you **double** the [NO] the reaction rate **quadruples** (x 4)

$$\text{Rate} = k [\text{NO}]^x \quad X = ?$$

$$(4) = k(2)^x \quad \text{Rate} = K [\text{NO}]^2$$

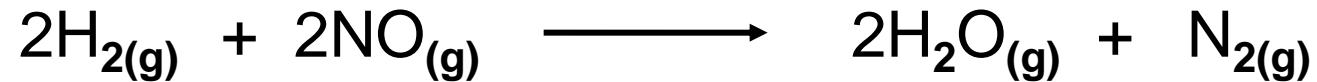
If you **triple** the [NO] reaction rate increases by a **factor of 9**

$$(9) = k (3)^2$$

We call this a **second order reaction** (as the rate is dependent to reactant concentration raised to the power of 2)



## Overall rate law?



Reaction rate dependence was different for each reactant

### EXPERIMENTAL RATE EQUATION

$$\text{Rate} = k [\text{H}_2]^1 [\text{NO}]^2$$

Reaction is '**first order** with respect to **H<sub>2</sub>**'

Reaction is '**second order** with respect to **NO**'

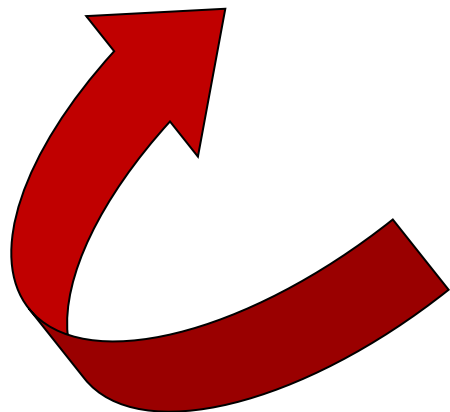
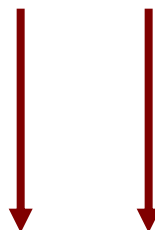
Reaction is '**third order** overall'

Note that: The **order of reaction** is not related to the **stoichiometric coefficient** of the reactant in the overall balanced equation.

# Reaction Order

**The overall reaction order is** the sum of the powers to which all reactant concentrations are raised in the rate law.

Partial orders

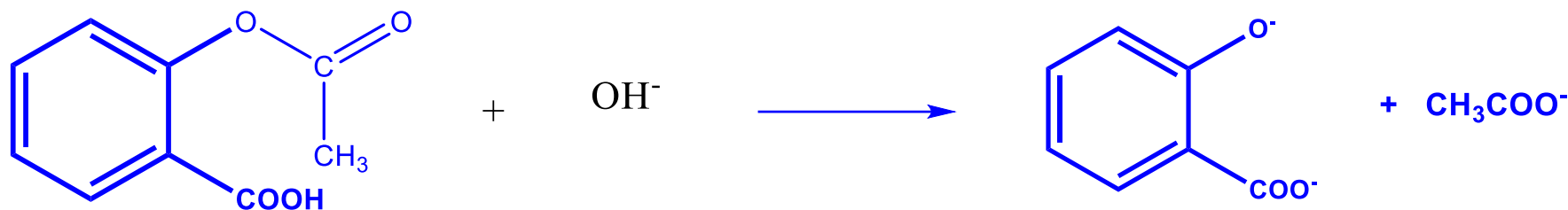


Rate equation or rate law

# Pseudo-First Order Reaction

EXAMPLE:

Hydrolysis of Aspirin



Aspirin

From experimental results:

$$\text{Rate} = k [\text{Aspirin}] [\text{OH}^-]$$

If [OH<sup>-</sup>] present in large excess, its concentration remains virtually constant during reaction

## Pseudo-First Order Reaction

This means that the rate law for Aspirin hydrolysis is:

$$\text{Rate} = k [\text{Aspirin}] [\text{OH}^-]$$

So, it is originally a second order reaction.

But when hydroxide ions are present in large excess, a new constant  $k^1$  can replace  $k [\text{OH}^-]$

$$\text{Rate} = k[\text{Asp}].[\text{OH}^-]$$

$$k.[\text{OH}^-] = k^1$$

 [constant]

Modified rate law →  $\text{Rate} = k^1 [\text{Aspirin}]$

Pseudo-First Order Reaction

**So how does a knowledge of reaction order of a particular drug affect drug dosage?**



# Penicillin and Tonsillitis

The destruction reaction of Penicillin on bacterial cell-wall could be:

Zero-Order reaction:      Rate =  $k$

Regardless of [penicillin] given, **rate of destruction of bacteria will be constant**

First-Order reaction:      Rate =  $k [\text{penicillin}]^1$

Double [penicillin] given, you **double the rate of destruction of bacteria**

Second-Order reaction:      Rate =  $k [\text{penicillin}]^2$

Double [penicillin], you increase the **rate of destruction by a factor of 4**

## Reaction order and drug dosage

- It is also important to know the **half life** of a drug inside the body (half life is the time required for concentration to drop to 50%).
- Knowing a drug's half life allows us to know after how long will there be no enough drug inside the body (to produce its pharmacological effect) and define the dose frequency accordingly.