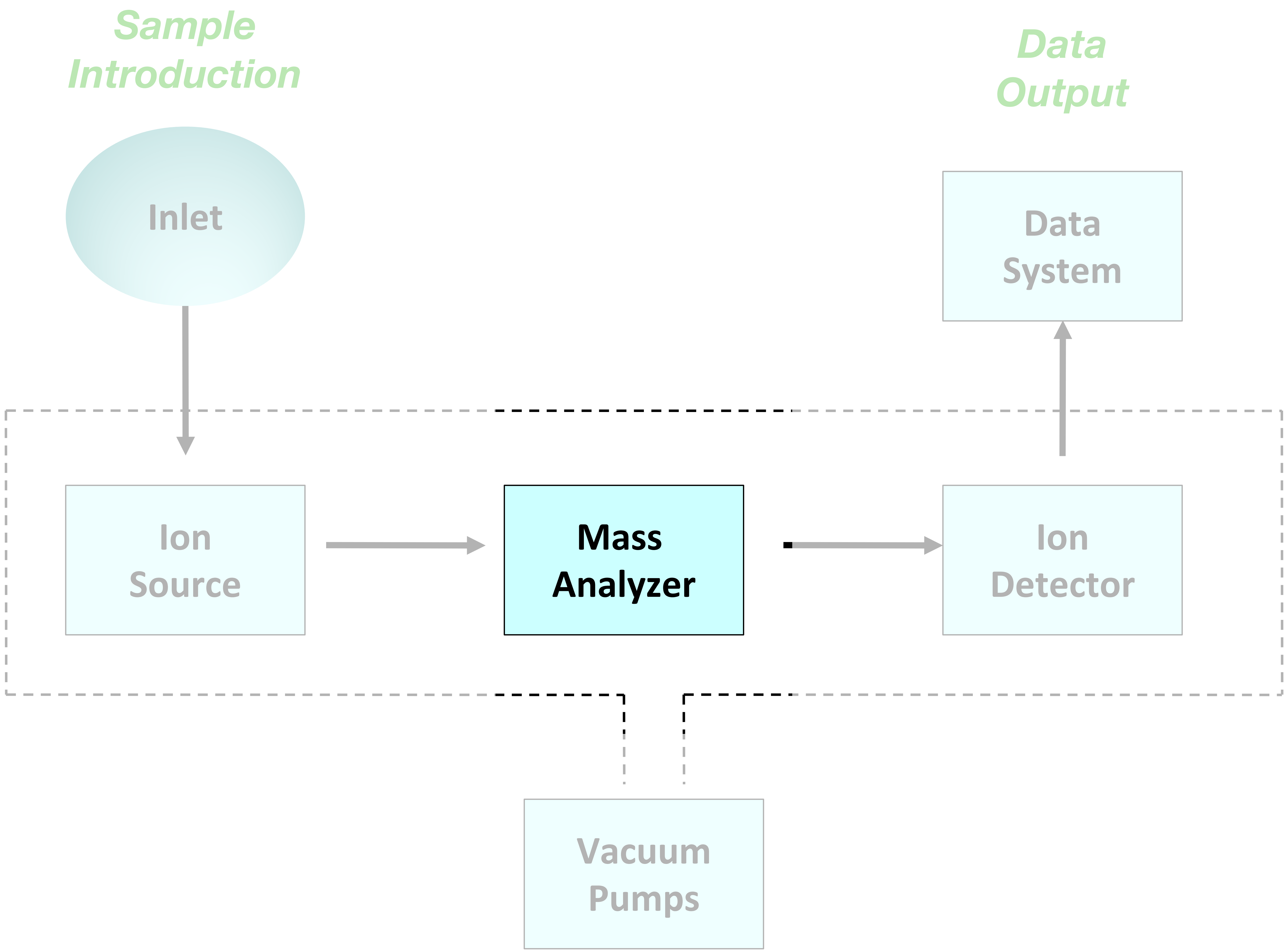
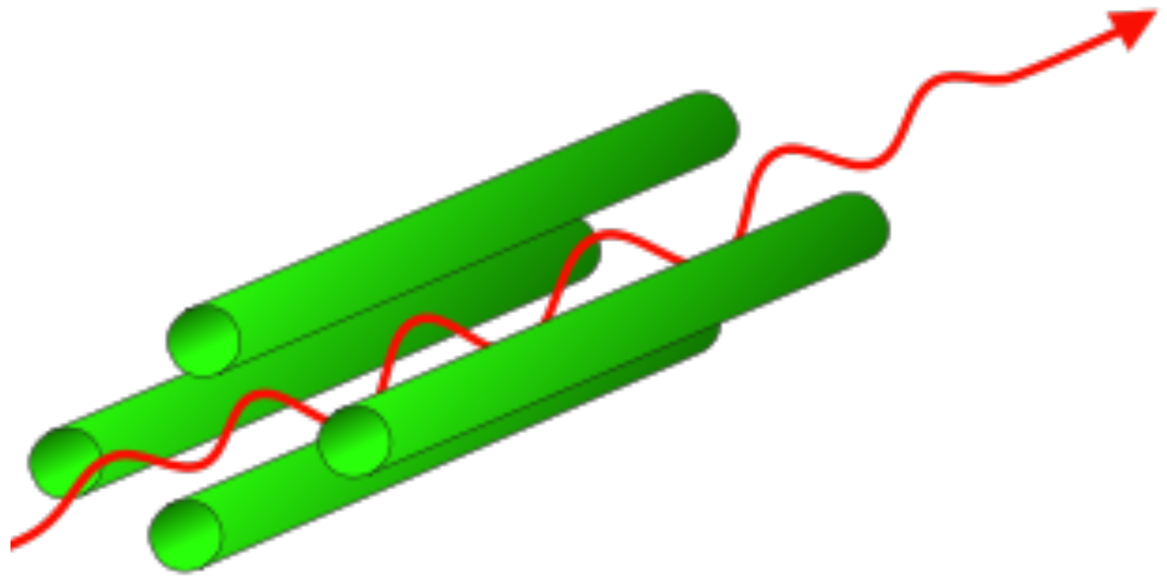
Mass Analyzers

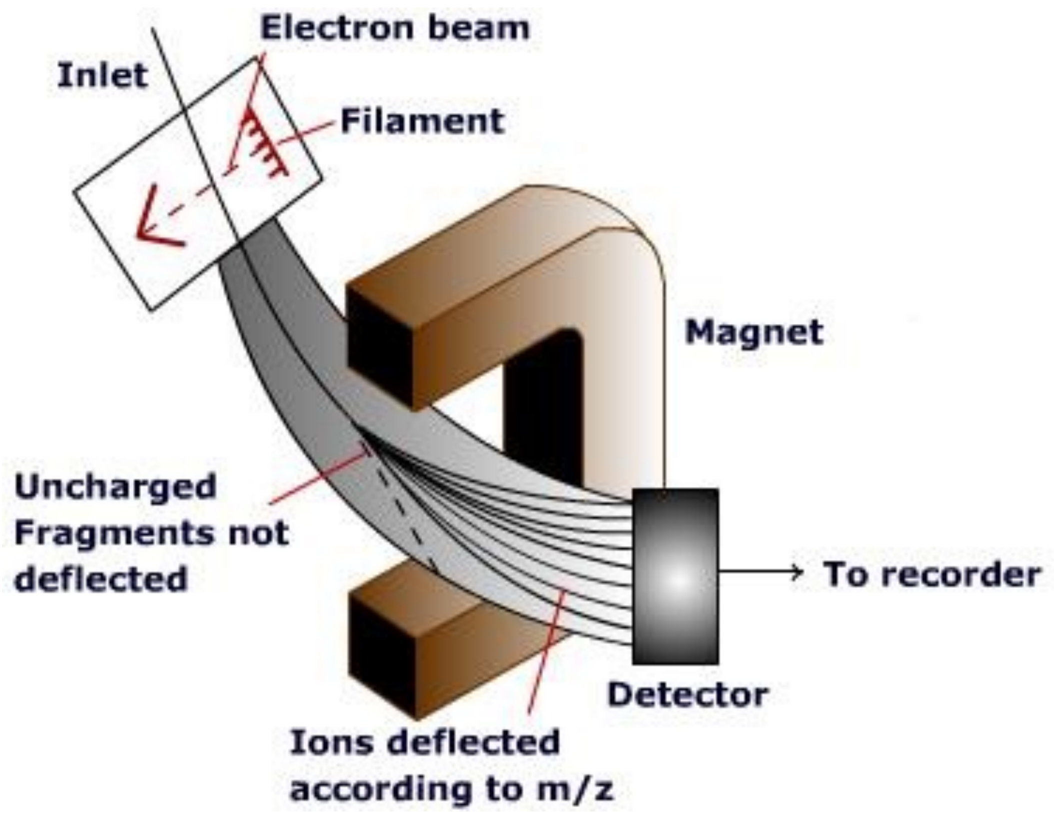


Mass Analyzers

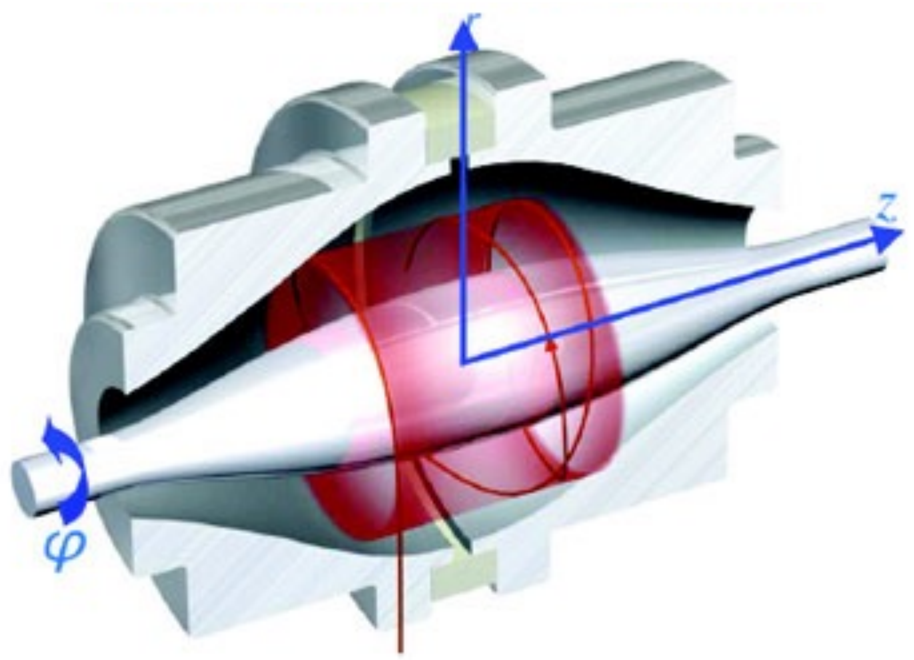


Quadrupole (Q)

Quadrupole ion trap (QIT)

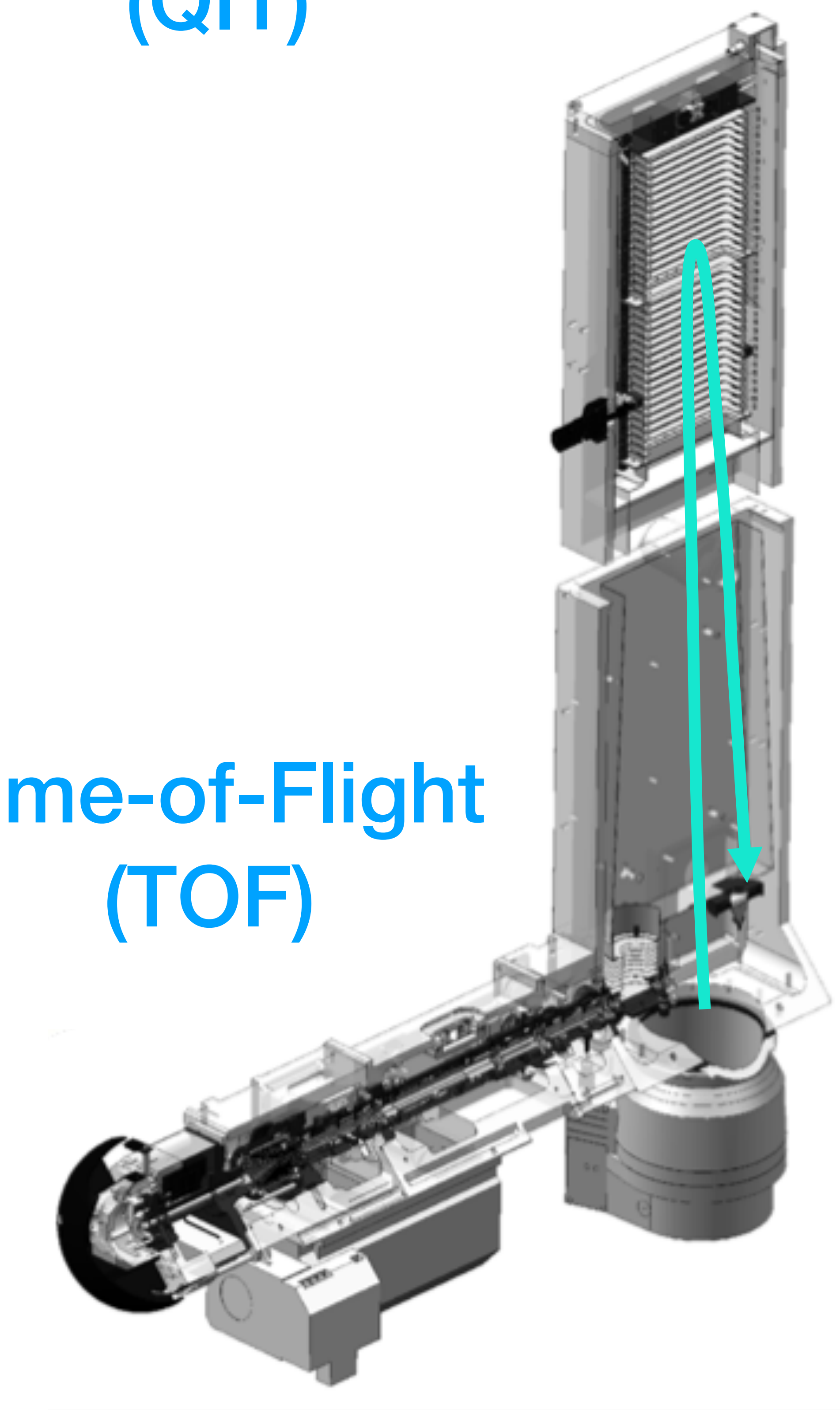


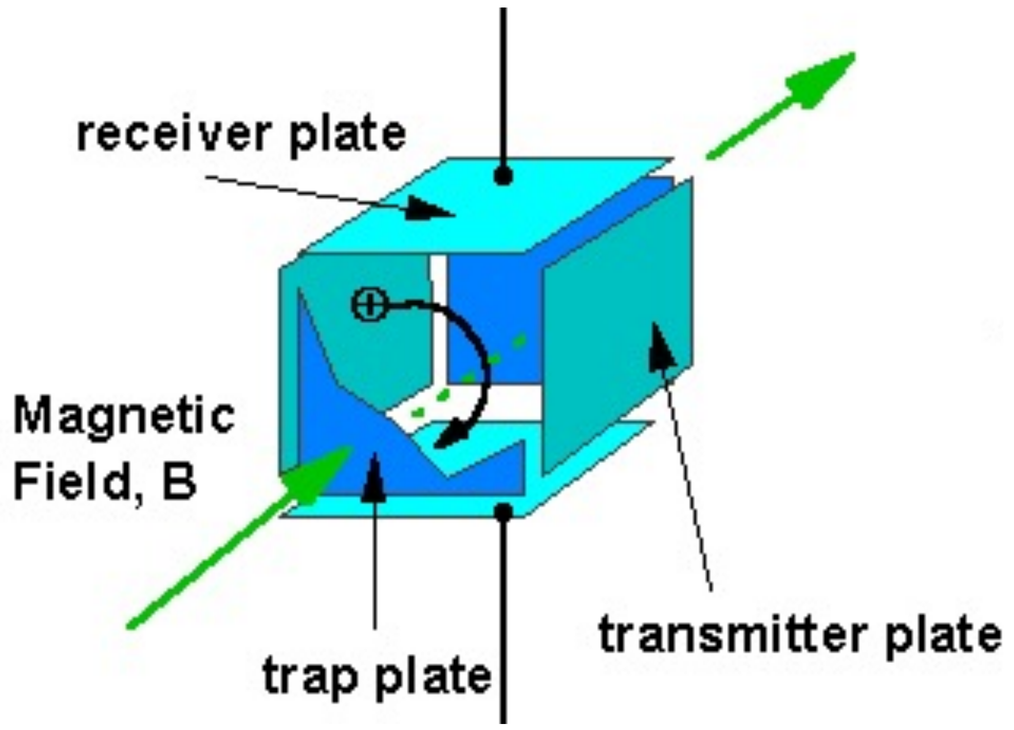
Magnetic sector



Orbitrap

Time-of-Flight (TOF)





Ion cyclotron resonance (ICR)

Principle of mass separation

$$\vec{F} = m \cdot \vec{a} = m \frac{d\vec{v}\left(\vec{r},t\right)}{dt}$$

Newton's second law

The **force on a charged particle** moving through and electric field E and magnetic field B is given by

$$\vec{F} = \underbrace{q\vec{E}\left(\vec{r},t\right)}_{\text{interaction with the electric field}} + \underbrace{q\left[\vec{v}\left(\vec{r},t\right)\times\vec{B}\left(\vec{r}\right)\right]}_{\text{interaction with the magnetic field}}$$

This is called the **Lorentz force**

$$\boxed{\left(\frac{m}{q}\right) = \frac{dt}{dV}[\vec{E} + \vec{V} \times \vec{B}].}$$

We can classify the types of mass analyzers by the type of the field applied to separate ions of different ***m/q***.

Classification of mass analyzers

$$(\frac{m}{q}) = \frac{dt}{dV}[\vec{E} + \vec{V} \times \vec{B}].$$

1. Field-free based analyzers

$$\vec{E} = 0; \quad \vec{B} = 0. \quad \frac{m}{q} d\vec{V} = 0;$$

Give the ions an initial amount of energy, but then let them drift through a field-free region.

➡ **Time-of-Flight (TOF) MS**

2. Electric field based analyzers

$$\vec{F} = m\frac{d\vec{v}(\vec{r},t)}{dt} = q\,\vec{E}(\vec{r},t) \qquad \vec{B}(\vec{r}) = 0$$

➡ **Quadrupole**
Orbitrap

3. Magnetic field based analyzers

$$\vec{F} = m\frac{d\vec{v}(\vec{r},t)}{dt} = q\left[\vec{V}(\vec{r},t) \times \vec{B}(\vec{r})\right] \qquad \vec{E}(\vec{r},t) = 0$$

➡ **Ion cyclotron resonance (ICR)**

Desirable characteristics of mass analyzers

They should:

- be able to sort ions by m/z
- have good transmission (improves sensitivity)
- have appropriate resolution (helps selectivity)
- have appropriate low/upper m/z limit
- be compatible with source output (pulsed or continuous)

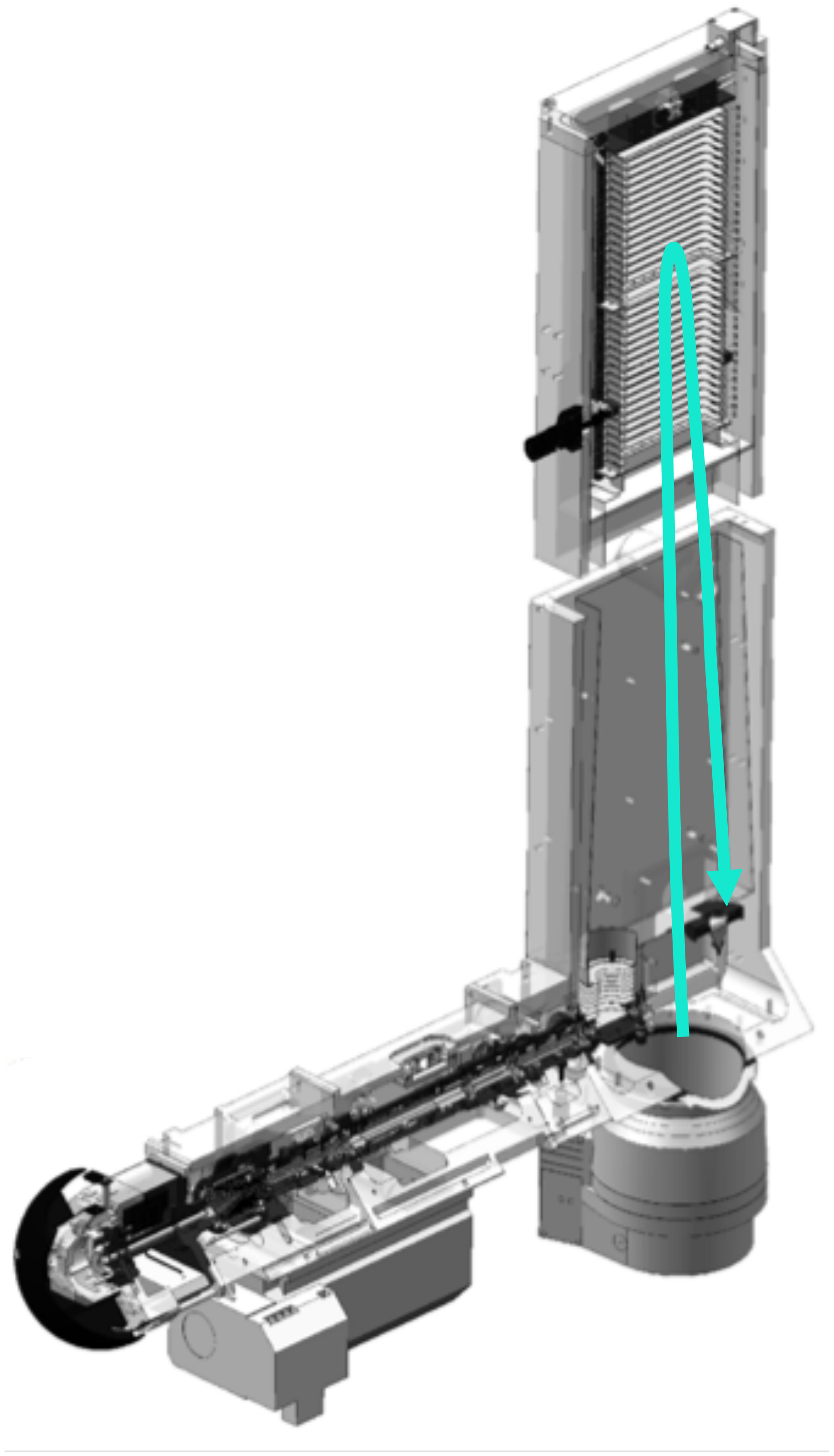
Characteristics of mass analyzers

- **m/z limitation**
  - Depends on the mass analyzer: 100-4000 Th common range for Q
  - 100’000 for TOF, 50000 for Orbitrap
- **Resolution: how it varies across m/z**
  - Q: RP decreases for increasing m/z
  - TOF: RP constant across m/z
  - Orbitrap: RP decreases with increasing m/z
- **Time for achieving high resolution**
  - Should be compatible with LC peaks
- **Costs:** to buy, to own (maintenance, spare parts, etc.)

Comparison of mass analyzers

Type	Resolving Power (RP)	Mass Accuracy (ppm)	Ion sampling	Scan Rate	Cost
Quadrupole	2-5000	100	Continuous	< 1 sec	$
TOF	20-50,000	5	Pulsed	< 0.1 sec	$$
Orbitrap	240,000	< 2	Pulsed	Depends on RP	$$$
ICR	500,000	< 2	Pulsed	Depends on RP	$$$$

Time-of-flight mass spectrometer (TOF MS)



Time-of-flight MS (TOF MS): the basics

- Mass analysis is achieved because at the same kinetic energy, ions of different *m/z* have different velocities and therefore reach the detector at different times

- If 2 ions of different *m/z* starting at the same location, with same kinetic energy and traveling in the same direction:

the ion with the lower m/z will travel faster and reach the detector first

- Requires that ions emerge from **a pulsed ion source** or by **pulsing ion packages** out of a continuous beam

TOF: starting with a pulse

- TOF analyzers need a t_0 starting gate to give a start to the packet of ions

- Pulsed sources (such as MALDI) therefore have an inherent compatibility advantage: laser pulse initiates ion formation in very short time

- For continuous sources (such as ESI), a <u>pusher</u> is used to send packet of ions in the TOF

Time-of-Flight Mass Spectrometer

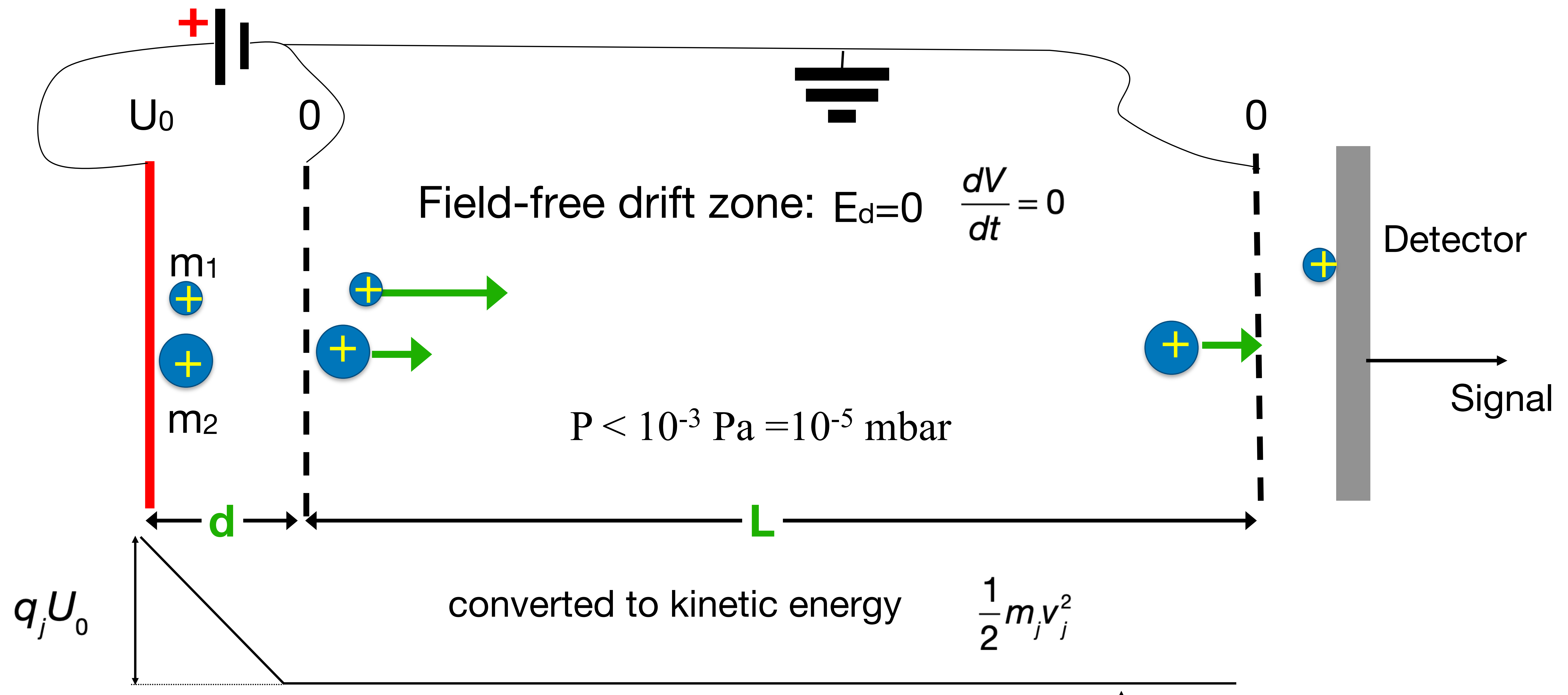
$$KE = q_j U_0 = \frac{1}{2} m_j v_j^2$$

$$\Rightarrow \quad v_j = \sqrt{\frac{2 q_j U_0}{m_j}}$$

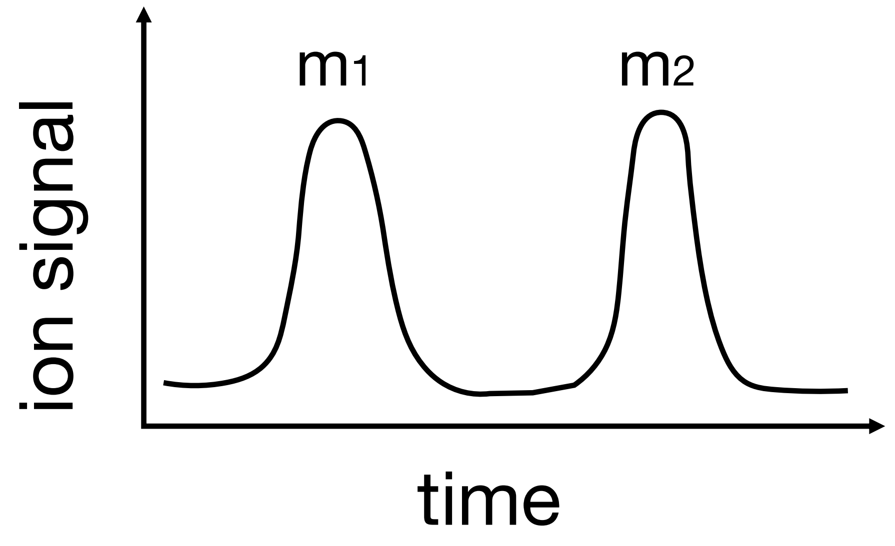
For **d** << **L**:

$$\tau_j = \frac{L}{v_j} = L \sqrt{\frac{m_j}{2 q_j U_0}}$$

$$\boxed{\left(\frac{m}{q}\right)_j = \frac{2U_0}{L^2} \tau_j^2}$$



Ions with larger **m/z** arrive to detector later



Need low pressure: $P[mBar] = \frac{0.066}{L[mm]} \ll \frac{0.07}{10^3} \simeq 7 \cdot 10^{-4}\, mBar;$

Time-of-Flight Mass Spectrometer

Accounting for **d**: $\tau_j = \tau_{0j} + \tau_{1j} = (L + 2d)\sqrt{\dfrac{M_j}{2q_j U_0}} = \left(1 + \dfrac{2d}{L}\right)\tau_{0j}$; $\left(\dfrac{m}{q}\right)_j = \dfrac{2U_0}{L^2}\tau_j^2$

Resolution of *TOF MS*:

Resolution is primarily limited by spatial and thermal distribution of ions in the accelerating region

$$\Delta m \simeq dm = \frac{2\cdot U}{L^2} d(\boldsymbol{\tau}^2) = \frac{4U}{L^2}\boldsymbol{\tau}\cdot d\boldsymbol{\tau}; \quad d\boldsymbol{\tau}_{d,U} = d[L + 2d)\sqrt{\frac{m}{2q\cdot U}}] \approx L\sqrt{\frac{m}{2q}}\cdot d(U^{-1/2}) + 2\sqrt{\frac{m}{2q\cdot U}} d(d)$$

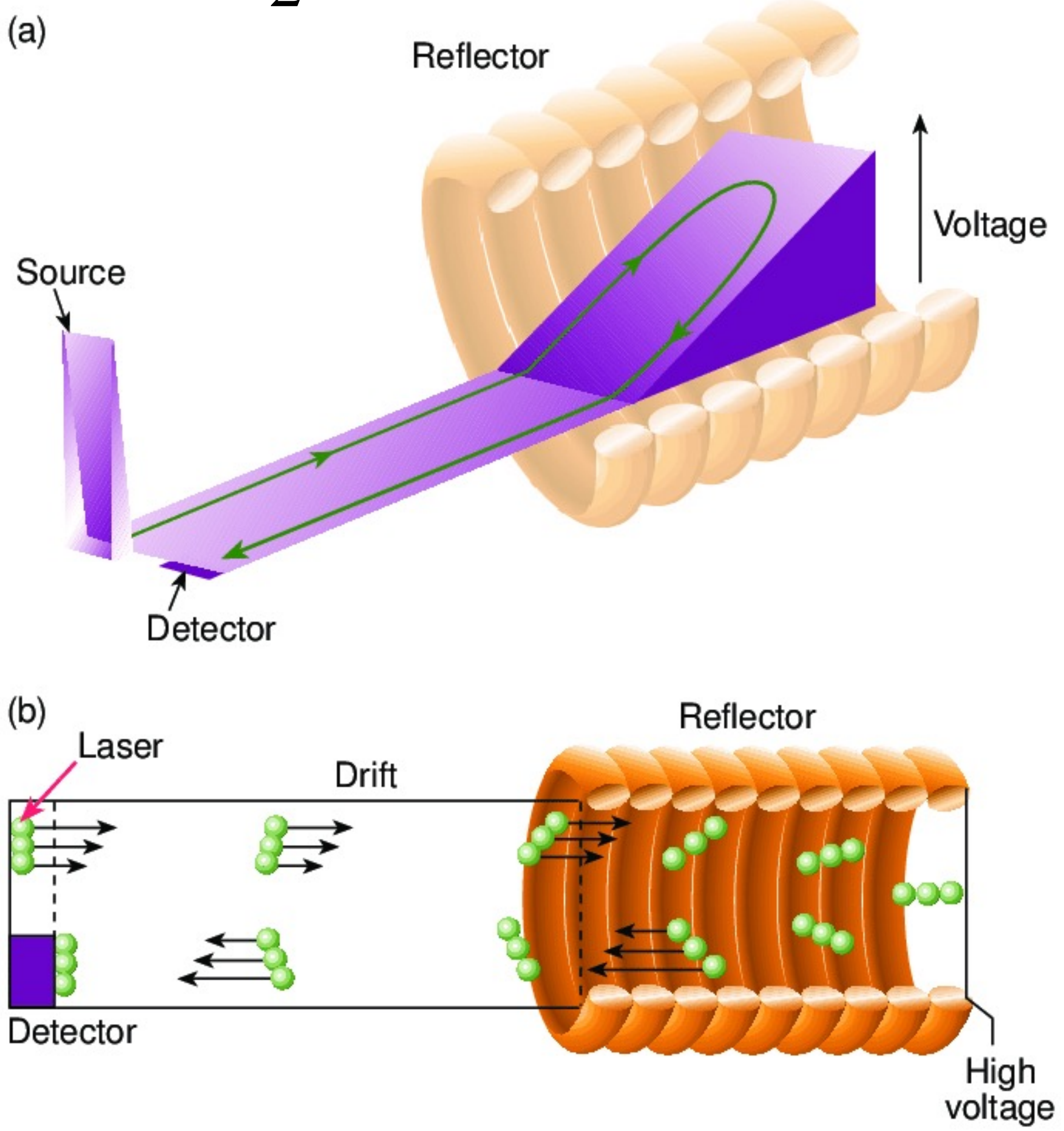
$$d\boldsymbol{\tau}_{d,U} = -L\sqrt{\frac{m}{2q}}\cdot\frac{dU}{2U^{3/2}} + 2\sqrt{\frac{m}{2q\cdot U}} d(d) = \sqrt{\frac{m}{2q\cdot U}}(2d(d) - \frac{L\cdot dU}{2U});$$

$$R = \frac{m}{\Delta m} \simeq \frac{L\sqrt{\dfrac{m}{2q\cdot U}}}{\sqrt{\dfrac{m}{2q\cdot U}}\cdot(2\Delta d - \dfrac{L\cdot\Delta U}{2U})} = \frac{1}{(\dfrac{2\cdot\Delta d}{L} - \dfrac{\Delta U}{2U})}.$$

Resolution of a TOF MS does NOT depend on mass *m*

TOF: Reflectron

$$mgH = \frac{mV^2}{2}$$



- Series of spaced metallic electrodes onto which a positive gradient of potential is applied

- The resulting electric field slows down the ions entering in the mirror: ions stop, reverse course and are reaccelerated

- Higher energy ion penetrates further into the field before reversing, yielding longer flight path

- The detector is positioned off-axis

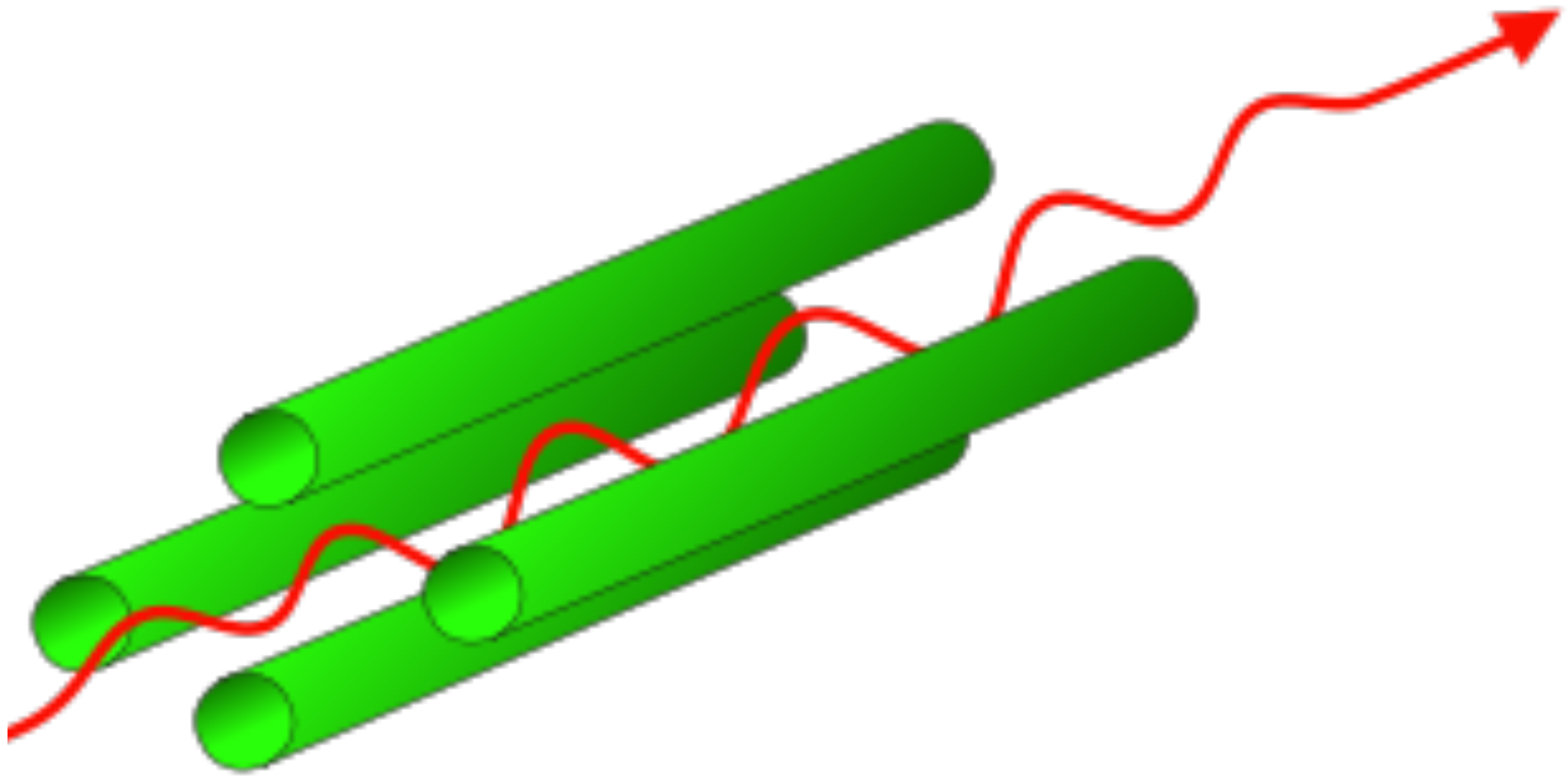
Ions of same *m/z* arrive at detector at the same time

Time-of-Flight Mass Spectrometer (TOF MS)

Advantages

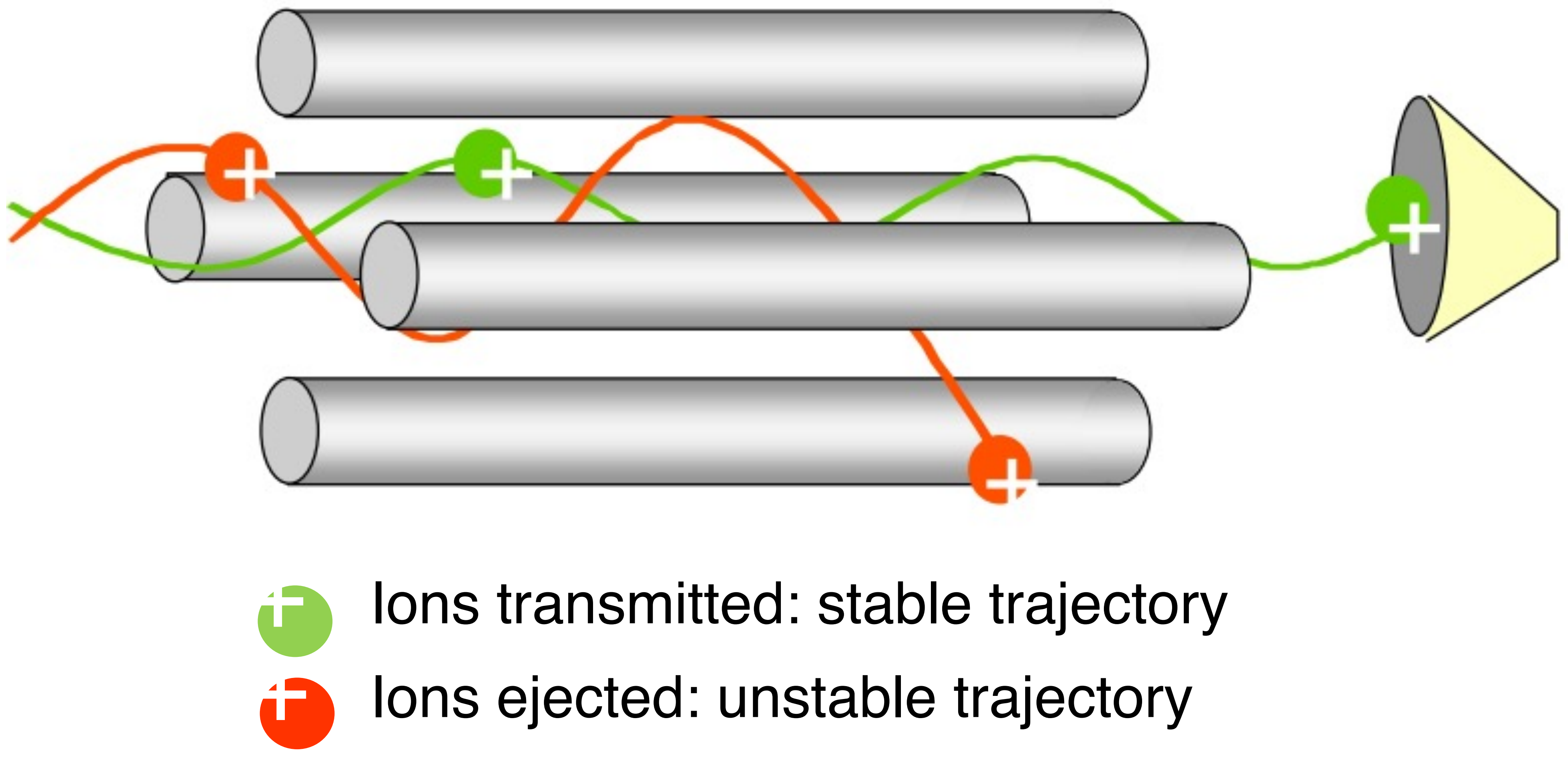
- Good mass accuracy: 5-10 ppm
- High mass resolution: Up to 40’000
- High mass range: $> 10^5$ Da
- Acceptable linearity
- Very good reproducibility
- Very fast acquisition time

Quadrupole mass spectrometer



- Quadrupole is a m/z filter;
- Quad contains 2 pairs of cylindrical metal rods: opposite rods are electrically connected together.

Linear quadrupole mass analyzer

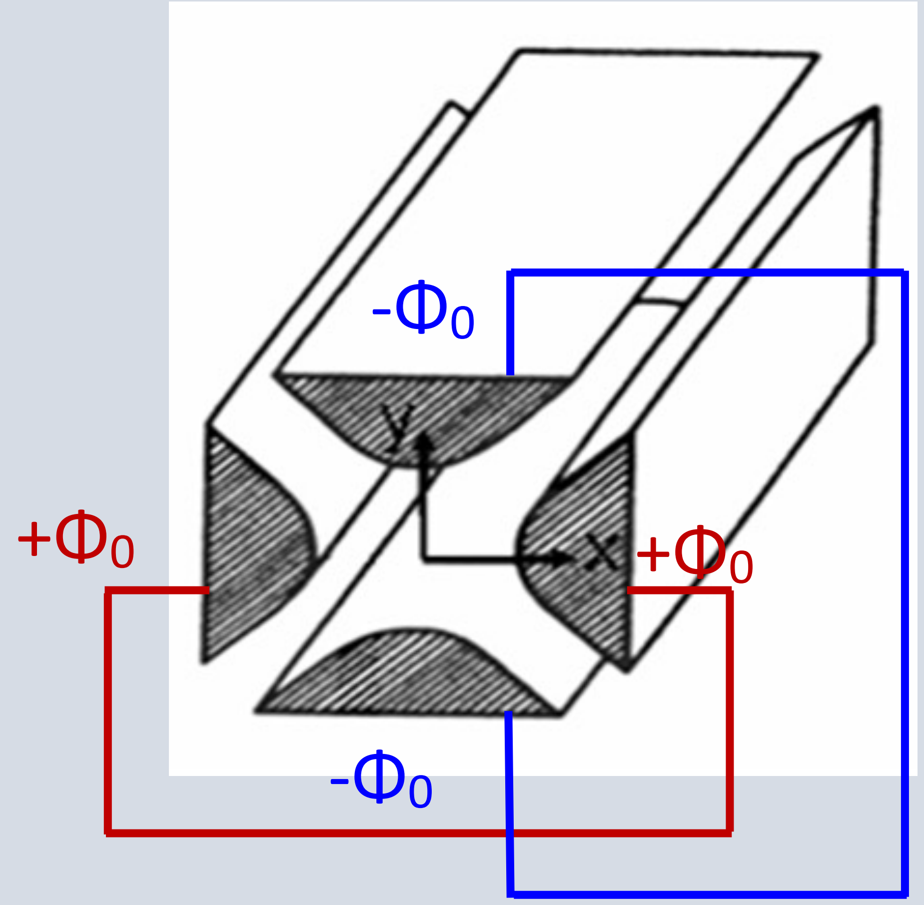


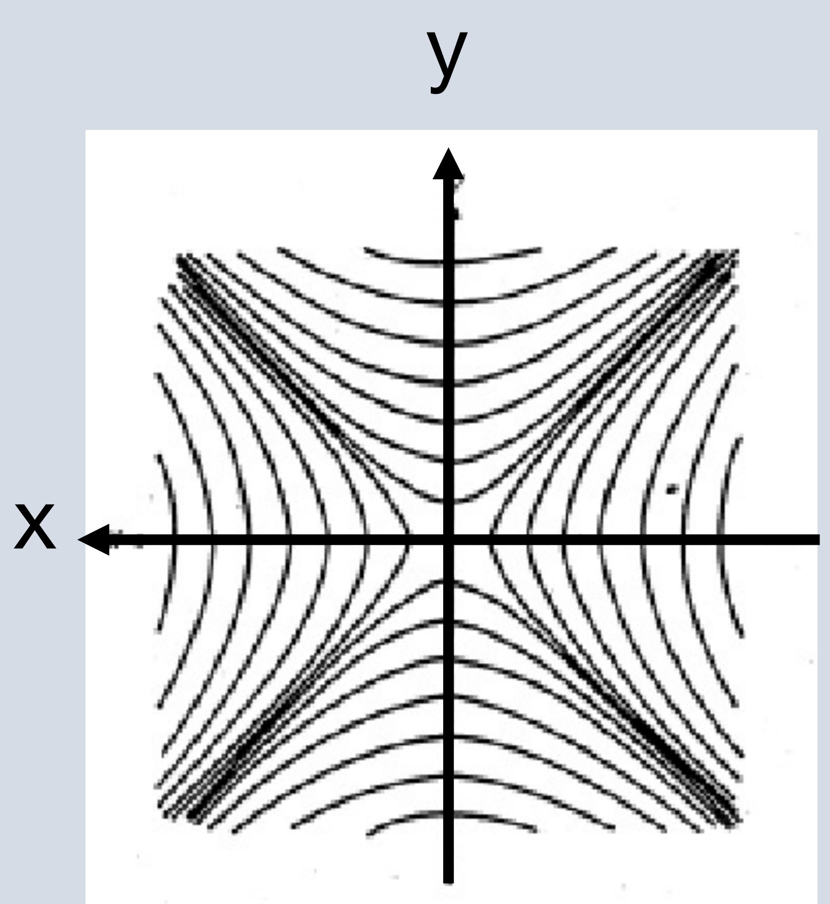
Rods can be cylindric or hyperbolic

- Each pair of rods has a DC (U) + AC(V_0 cosωt) RF voltage applied
- For a given DC and AC amplitude, only ions with a given m/z (or m/z range) have stable oscillations and are transmitted
- By continuously varying the applied voltage, the operator selects an ion with a particular *m/z* or scans for a range of *m/z*
- *Ions with unstable trajectories collide with the rods*
- Ion trajectories are modeled by Mathieu differential equations

Linear quadrupole mass analyzer

Potentials applied on the rods





Equipotential lines

U: Direct potential (DC)

V: RF amplitude (AC)

Typically

U: 500-2000V

V: 0-3000 V

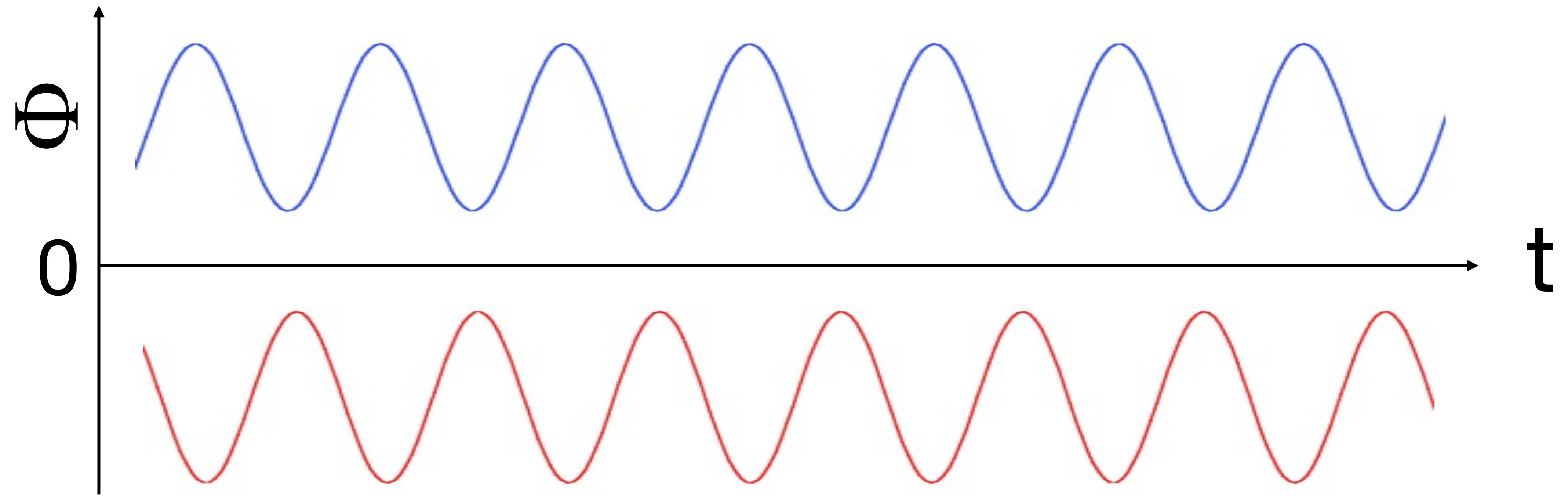
$\omega=2\pi f$ where f is the frequency of the RF field (typically 1 MHz)

Quadrupoles are operated at fixed frequency but variable U & V

X-rods $$\Phi_0 = +(U - V\cos\omega t)$$

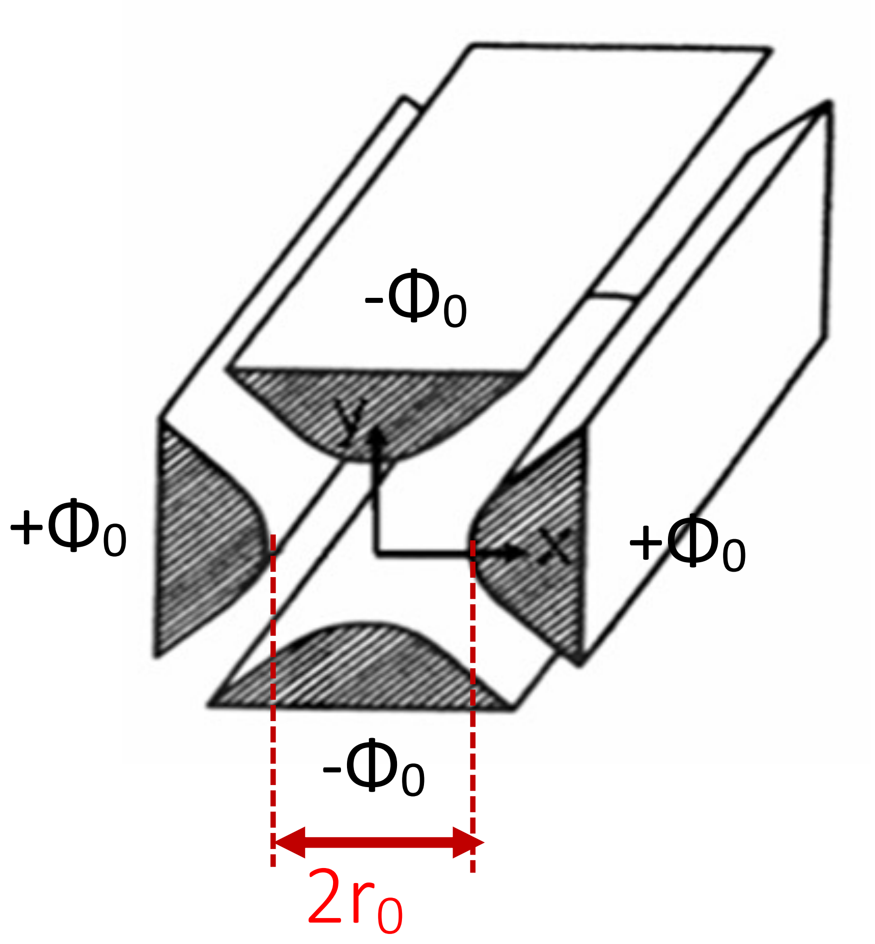
Y-rods $$-\Phi_0 = -(U - V\cos\omega t)$$

(180° out of phase)



Equation of ion motion

The electric potential inside the quadrupole is given by: $$\Phi(x,y)=\frac{\Phi_0(x^2-y^2)}{r_0^2}$$



The force on the ion is given by the gradient of the potential:

$$F_x = m\frac{d^2x}{dt^2} = -ze\frac{\partial\Phi}{\partial x}$$

$$F_y = m\frac{d^2y}{dt^2} = -ze\frac{\partial\Phi}{\partial y}$$

$$F_z = 0$$

which gives rise to:

$$\frac{d^2x}{dt^2} = -\frac{2ze}{mr_0^2}\Phi_0 x$$

$$\frac{d^2y}{dt^2} = -\frac{2ze}{mr_0^2}\Phi_0 y$$

$$\frac{d^2z}{dt^2} = 0$$

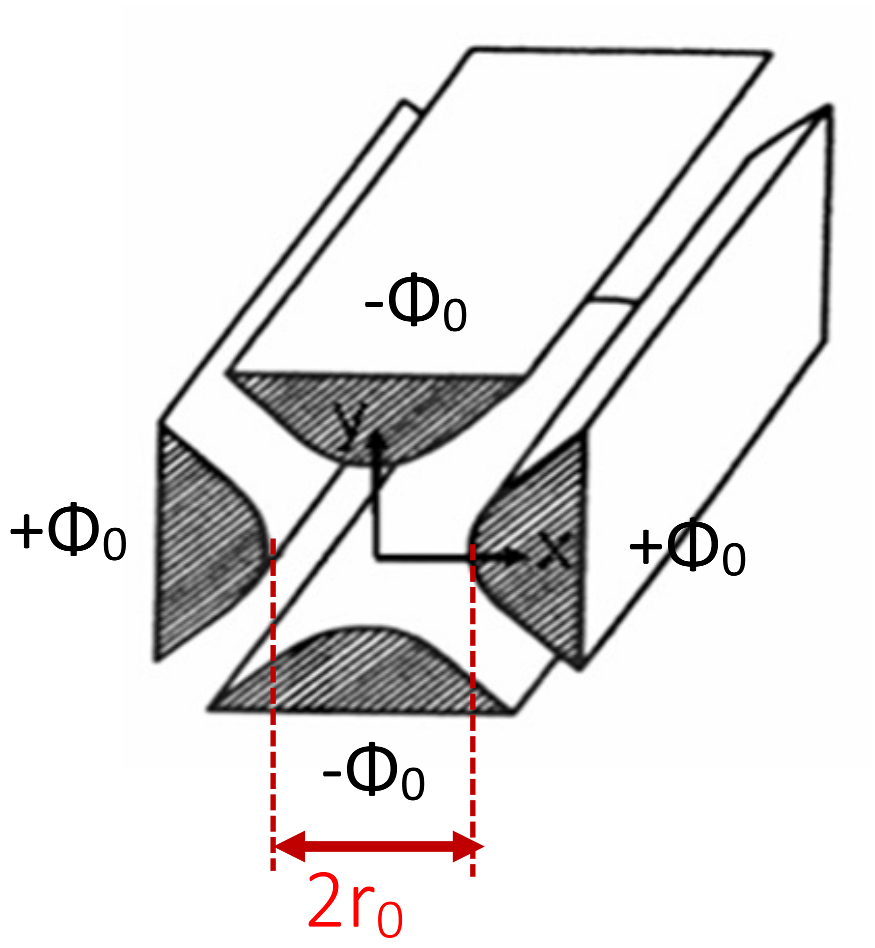
Equation of ion motion

If we now put in the time varying potential:

$$\Phi_0 = +\left(U - V\cos\omega t\right) \quad \text{X-rods}$$

$$-\Phi_0 = -\left(U - V\cos\omega t\right) \quad \text{Y-rods}$$

(180° out of phase)



$$\frac{d^2x}{dt^2} = -\frac{2ze}{mr_0^2}\Phi_0 x$$

$$\frac{d^2y}{dt^2} = -\frac{2ze}{mr_0^2}\Phi_0 y$$

$$\boxed{\begin{aligned}\frac{d^2x}{dt^2} + \frac{2ze}{mr_0^2}\left(U - V\cos\omega t\right)x = 0\\ \frac{d^2y}{dt^2} - \frac{2ze}{mr_0^2}\left(U - V\cos\omega t\right)y = 0\end{aligned}}$$

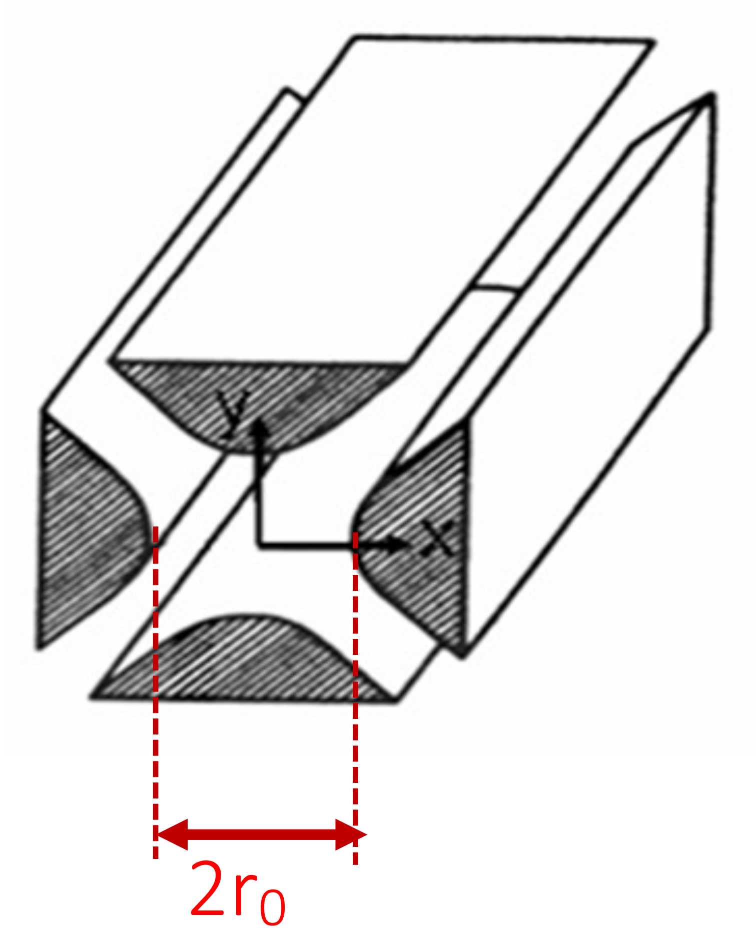
These equations determines ion trajectories: x(t), y(t)

Trajectories will be stable if x, y < r_0

Mathieu Equations

$$\frac{d^2x}{dt^2} + \frac{2ze}{mr_0^2}(U - V\cos\omega t)x = 0$$
$$\frac{d^2y}{dt^2} - \frac{2ze}{mr_0^2}(U - V\cos\omega t)y = 0$$

$$\begin{cases} a_u = a_x = -a_y = \dfrac{8zeU}{m\omega^2 r_0^2} & \text{proportional to DC voltage } U \\ q_u = q_x = -q_y = \dfrac{4zeV}{m\omega^2 r_0^2} & \text{proportional to } V \\ \xi = \dfrac{\omega t}{2} \end{cases}$$



$$\boxed{\frac{d^2u}{d\xi^2} + (a_u - 2q_u\cos 2\xi)u = 0}$$

For u=x; u=y.

Stability condition: $|u| < r_0$

- *a and q are dimensionless*
- *Stability of the solution is governed by relation between a and q*

Variables: U and V; Parameter: m

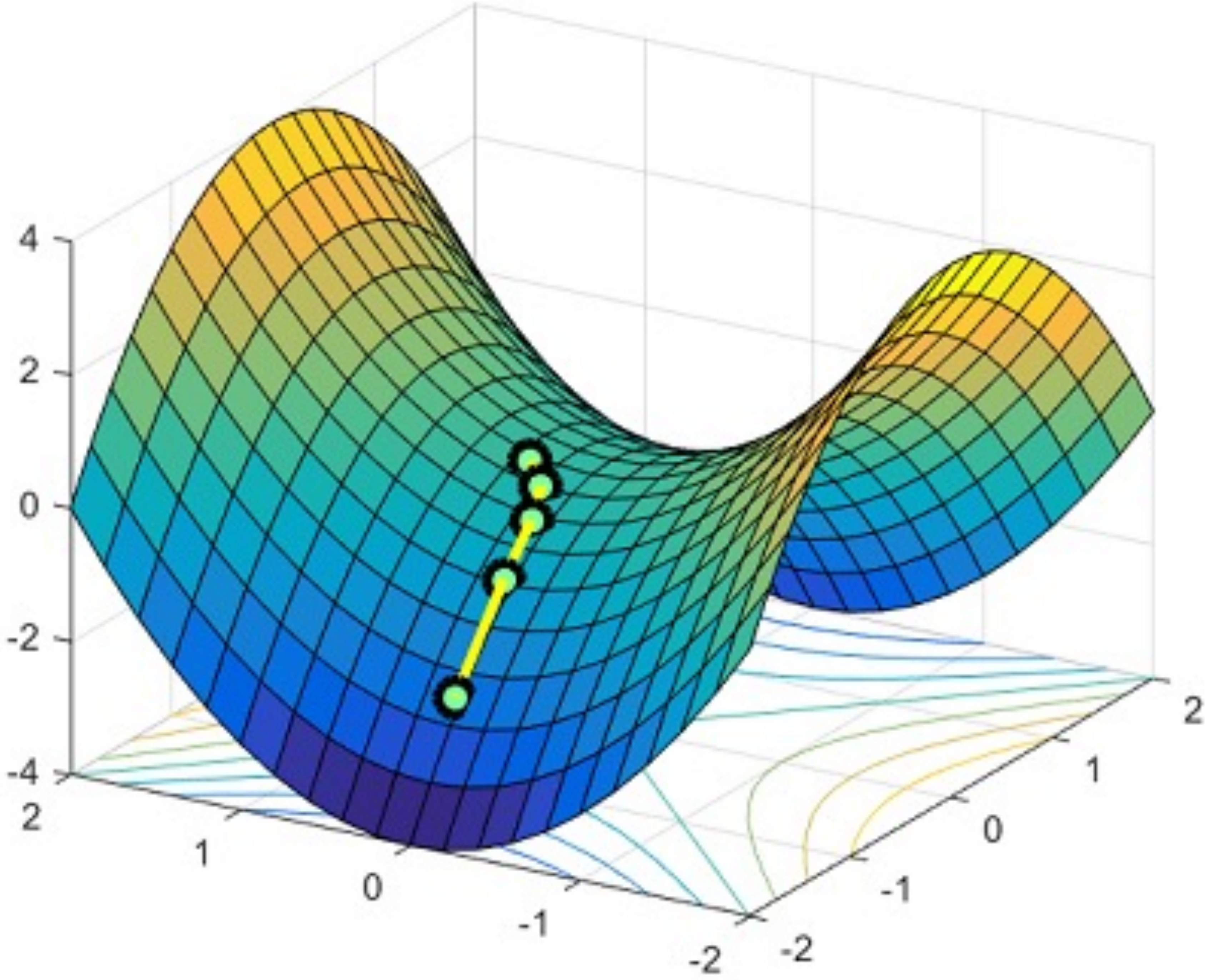
$$a_y = \frac{8zeU}{m\omega^2 r_0^2}$$

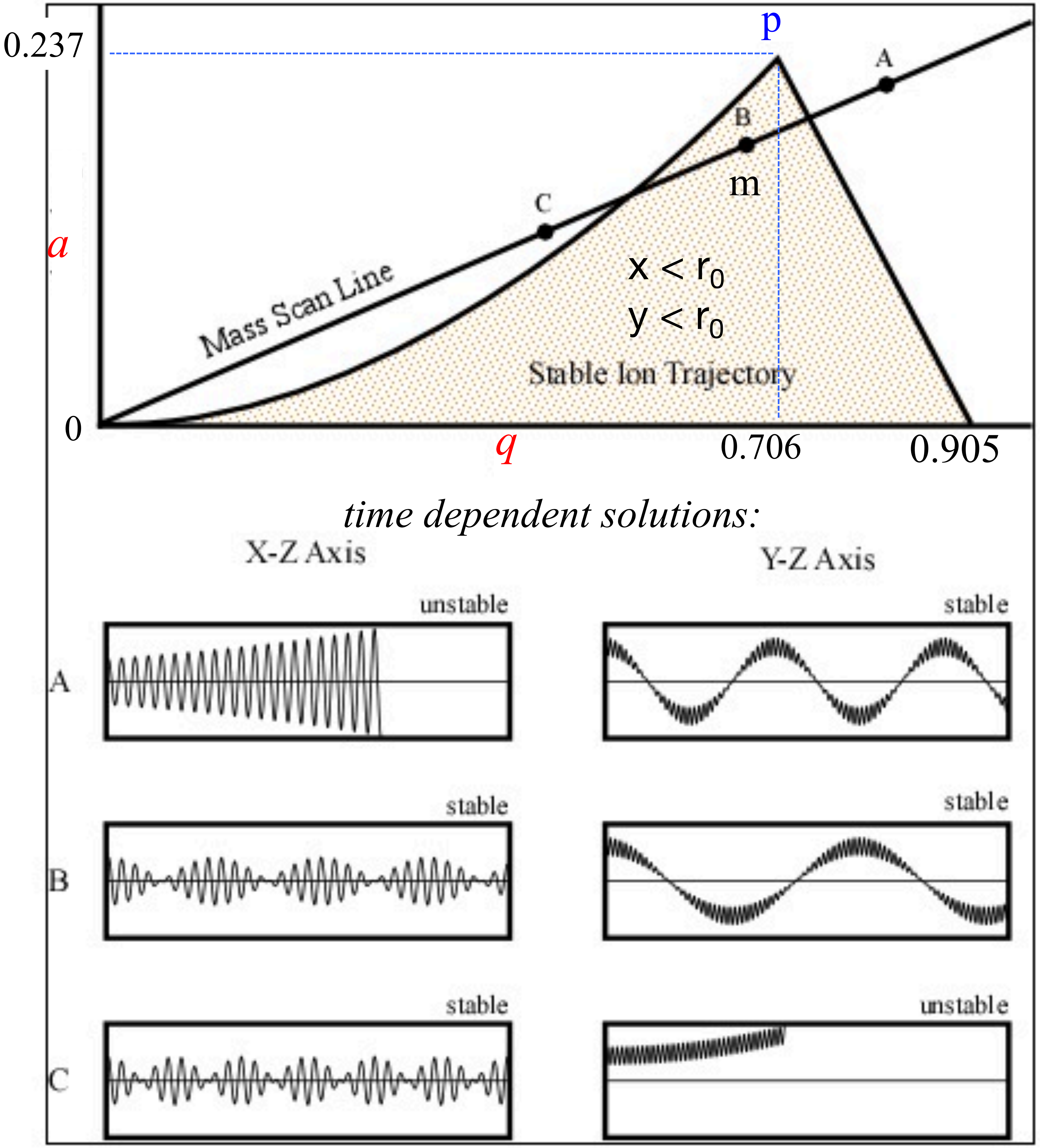
$$q_y = \frac{4zeV}{m\omega^2 r_0^2}$$

a ∝ U/m; q ∝ V/m

$a/q = 2U/V$

P(a, q) = 0.237; 0.706





Variables: U and V; Parameter: m

$$a_y = \frac{8zeU}{m\omega^2 r_0^2}$$

$$q_y = \frac{4zeV}{m\omega^2 r_0^2}$$

$a \propto U/m$; $q \propto V/m$

$a/q = 2U/V$

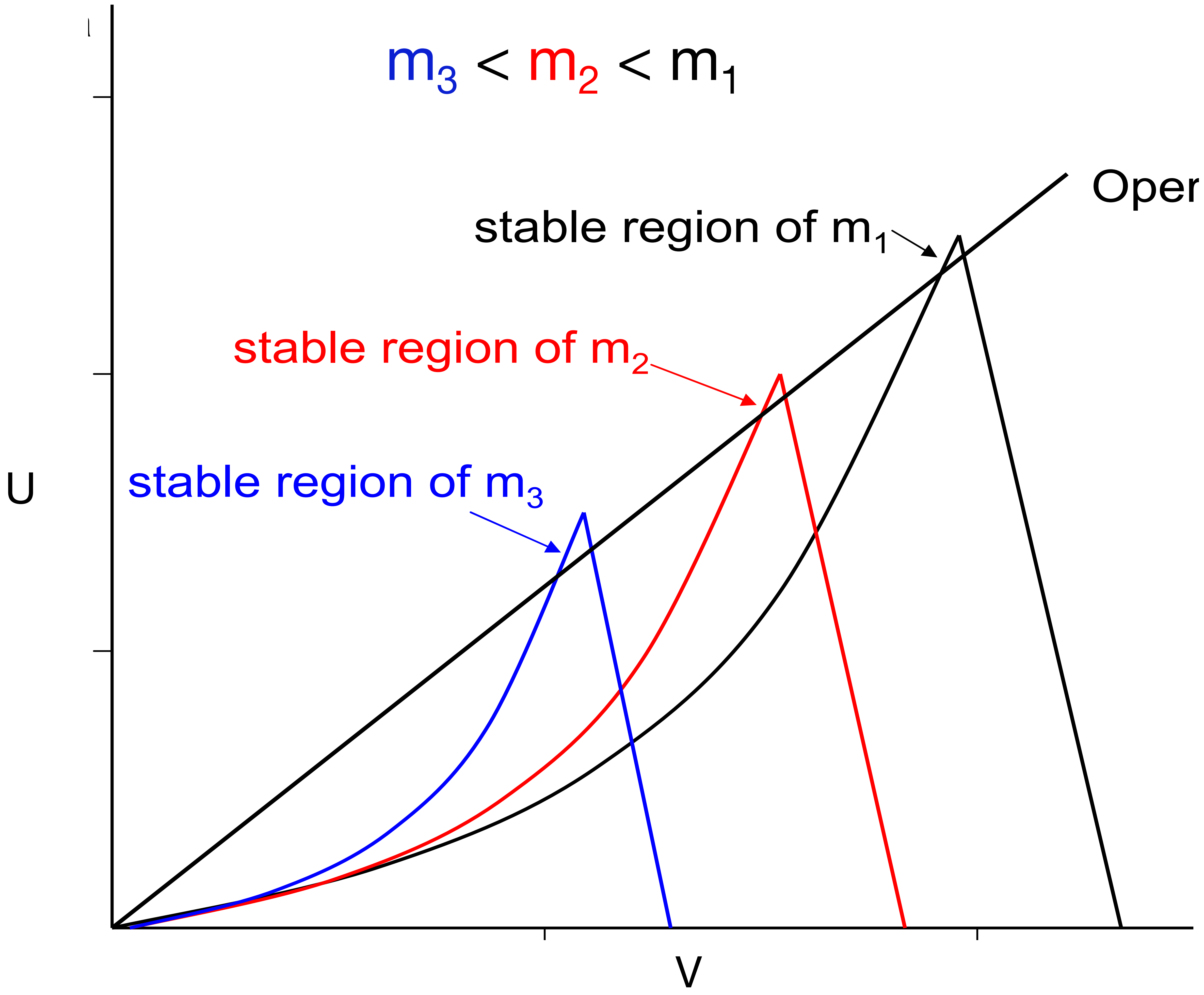
P(a, q) = 0.237; 0.706

The diagram can be easily converted to U, V coordinates

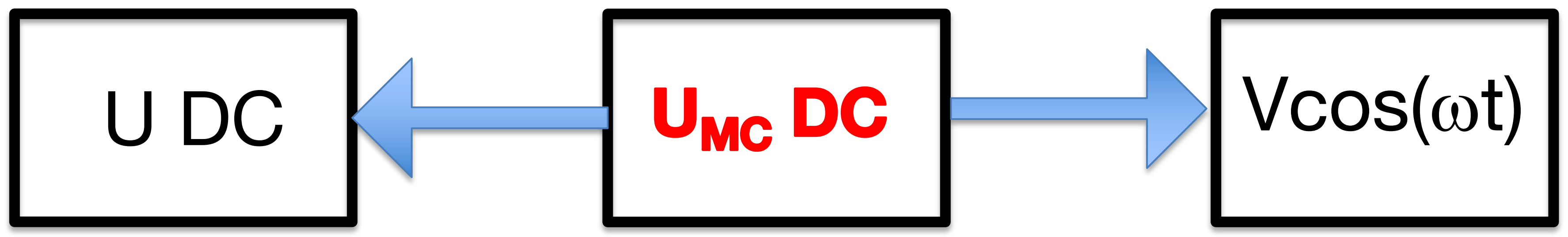
- Each *m* yields its own *"triangle of stability"* in U, V
- The smaller is *m* the smaller are *U* and *V* of the triangle peak
- Trajectories are unstable if:

$$\frac{U}{V} = \frac{a_p}{2 \cdot q_p} > 0.1678$$

For U –> 0 and fixed V light ions do not pass through.

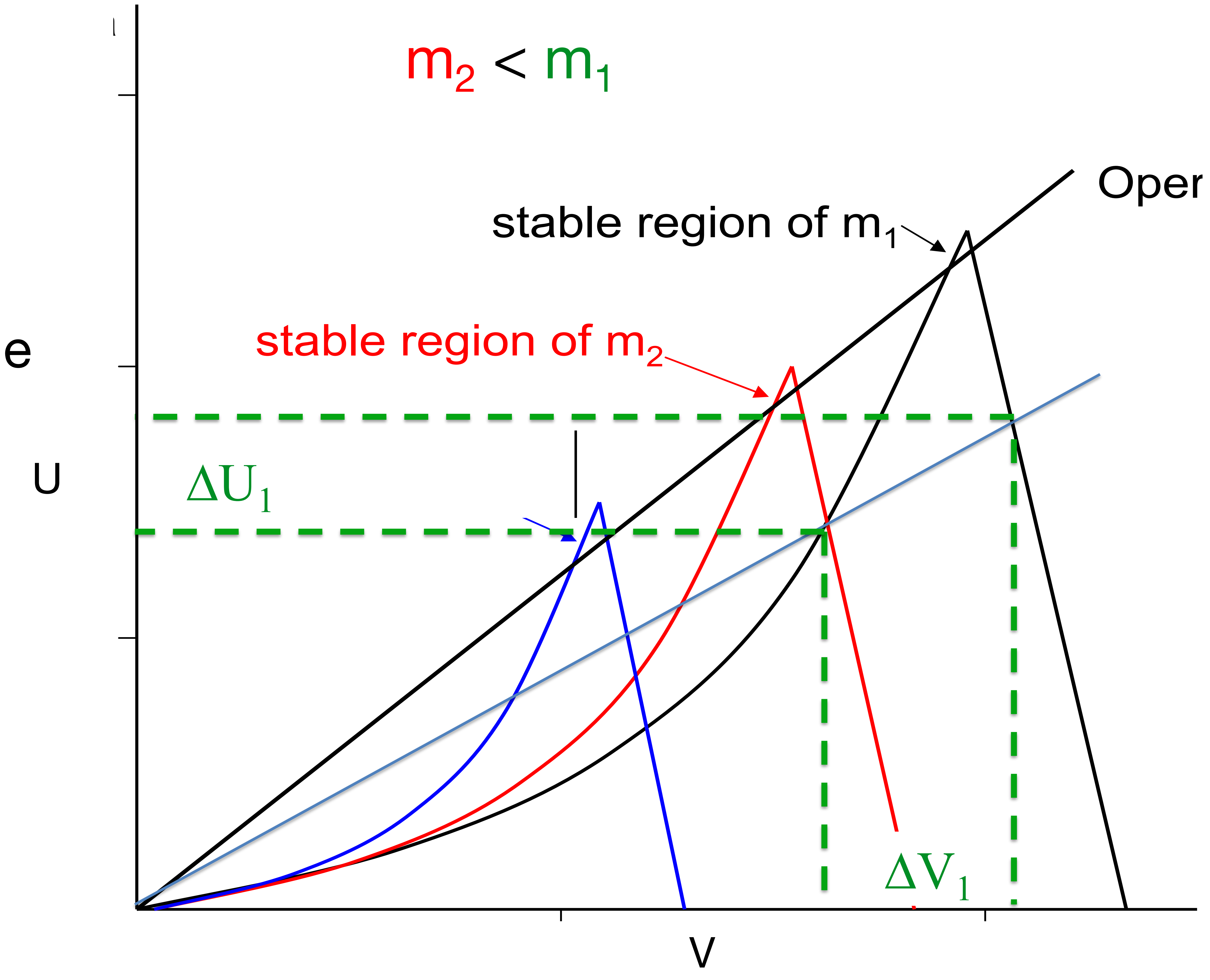


- Scan up U and V <u>simultaneously</u>, such that U/V=const < 0.1678;
- Single Mass-command U_{MC} DC voltage controls U and V:



Resolution of QMS

- MS is the number of ions that pass through in function of U_{MC}: $U \propto V \propto U_{MC}$
- The points where the scan line crosses the triangle of a specific m/z determines the transparency window (ΔU, ΔV, $U/V=\text{const}$) for this m/z. =>
- For ions with m_1/z the width of the mass peak is determined by ΔU_1, ΔV_1:



$$U \propto V \propto m/z; \ \Rightarrow \ \Delta(m/z) \propto m/z \ \Rightarrow$$

$$FWHM \propto \Delta(m/z) \propto m/z$$

$$R = \frac{m}{FWHM} = const$$

- Resolution of quadrupole MS is nearly constant across transmission range;
- Resolution increases (but transmission drops) upon approaching to the (U, V) apex point.

Quiz

To operate a quadrupole in a scanning mode, where individual m/z values are transmitted one after the other (e.g., m/z = 100; 101; 102 …).

A. U is held constant, while V is scanned
B. V is held constant, while U is scanned
C. U and V are held constant, while ω is scanned
D. U and V are both changed
E. A or B

Quiz

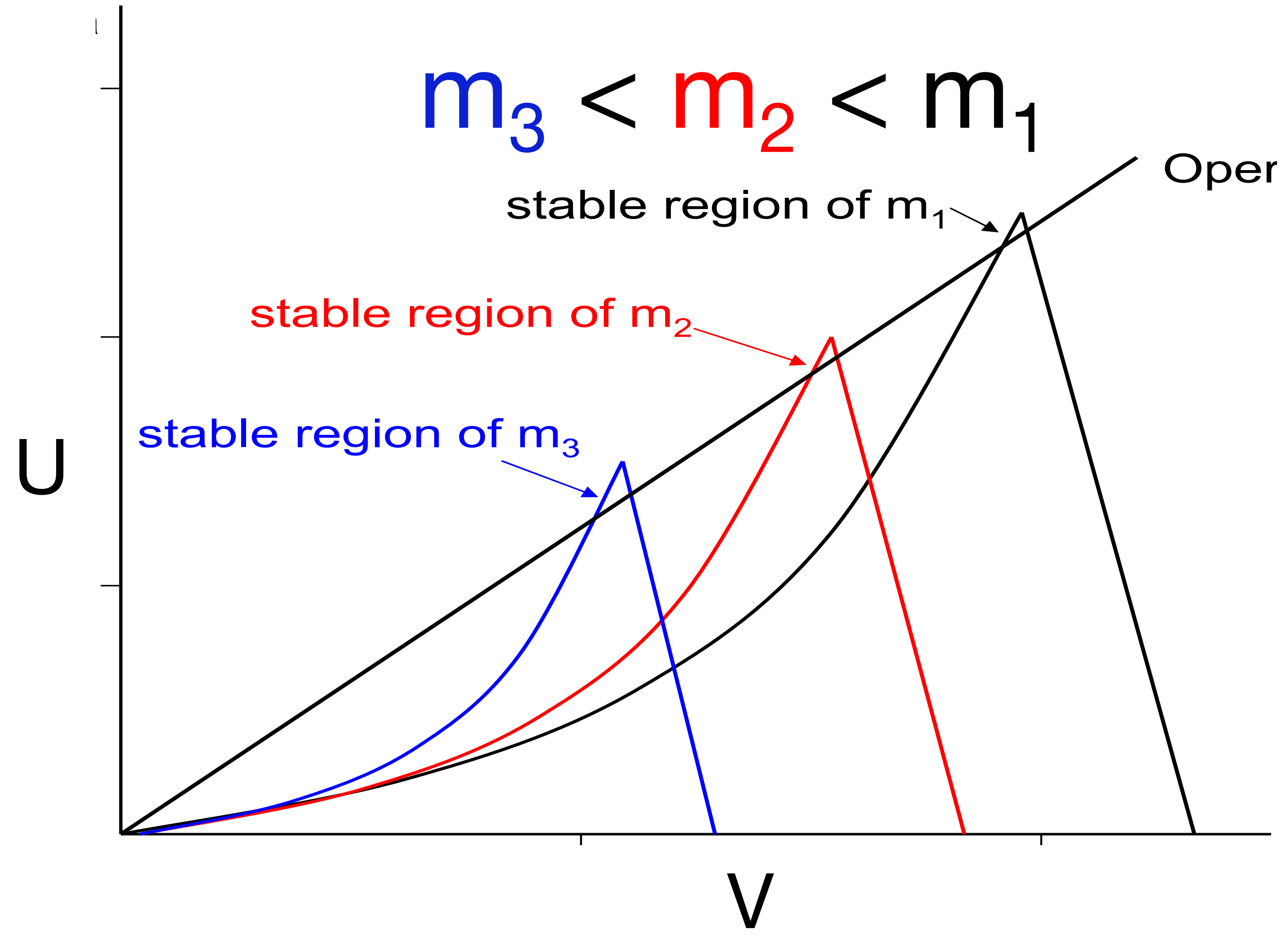
If a quadrupole is operated with a DC potential close to 0 volts, what will be transmitted when the AC potential is fixed:

A. No ions will be transmitted

B. All ions will be transmitted (i.e., all masses)

C. Only the lightest masses will be transmitted.

D. Only the heaviest masses will be transmit



Quiz

The mass resolution in a linear quadrupole:

A. Increases with increasing mass
B. Decreases with increasing mass
C. Is independent of mass
D. Can increase or decrease depending upon the slope U/V

Linear quadrupole MS

Advantages

- Small and lightweight: ~20 cm long
- Inexpensive
- Simple to operate
- Low accelerating voltage can accommodate high source pressures

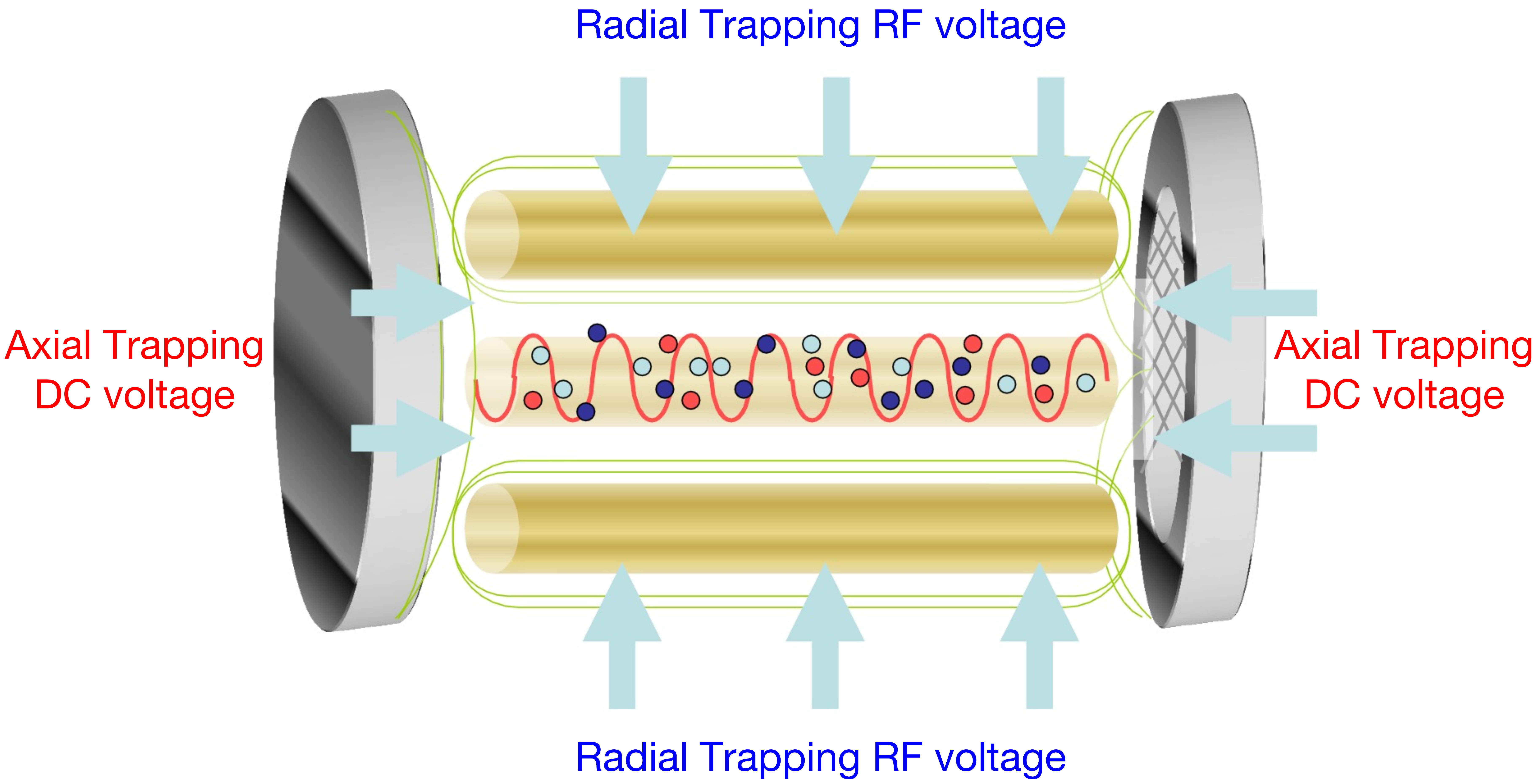
Disadvantages

- Limited mass resolution and mass range
- Contamination of rods can degrade resolution and sensitivity

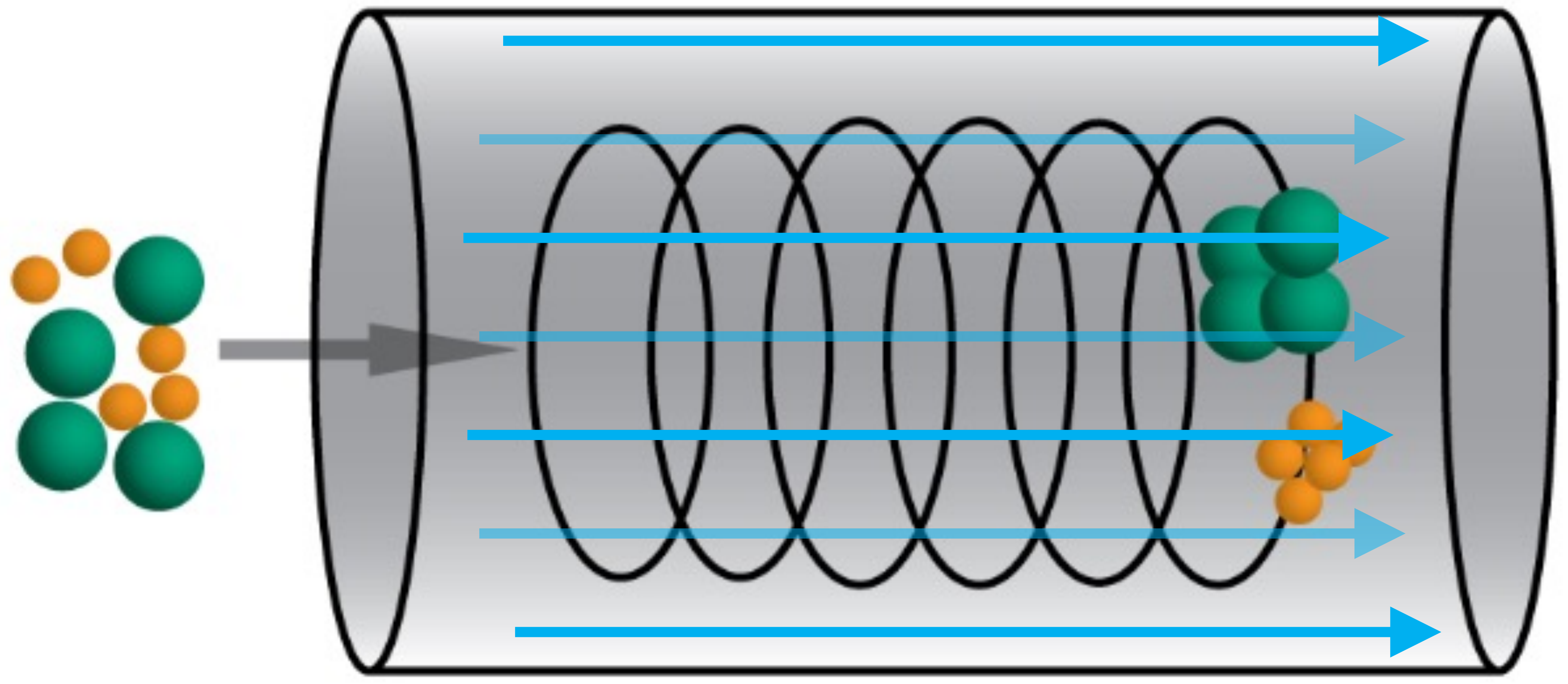
Linear ion trap

Ions are trapped radially by RF potential and axially by DC barriers.

Ions enter radially while the entrance plate is held at low potential. They must have collisions to be trapped.



Ion Cyclotron Resonance (ICR)



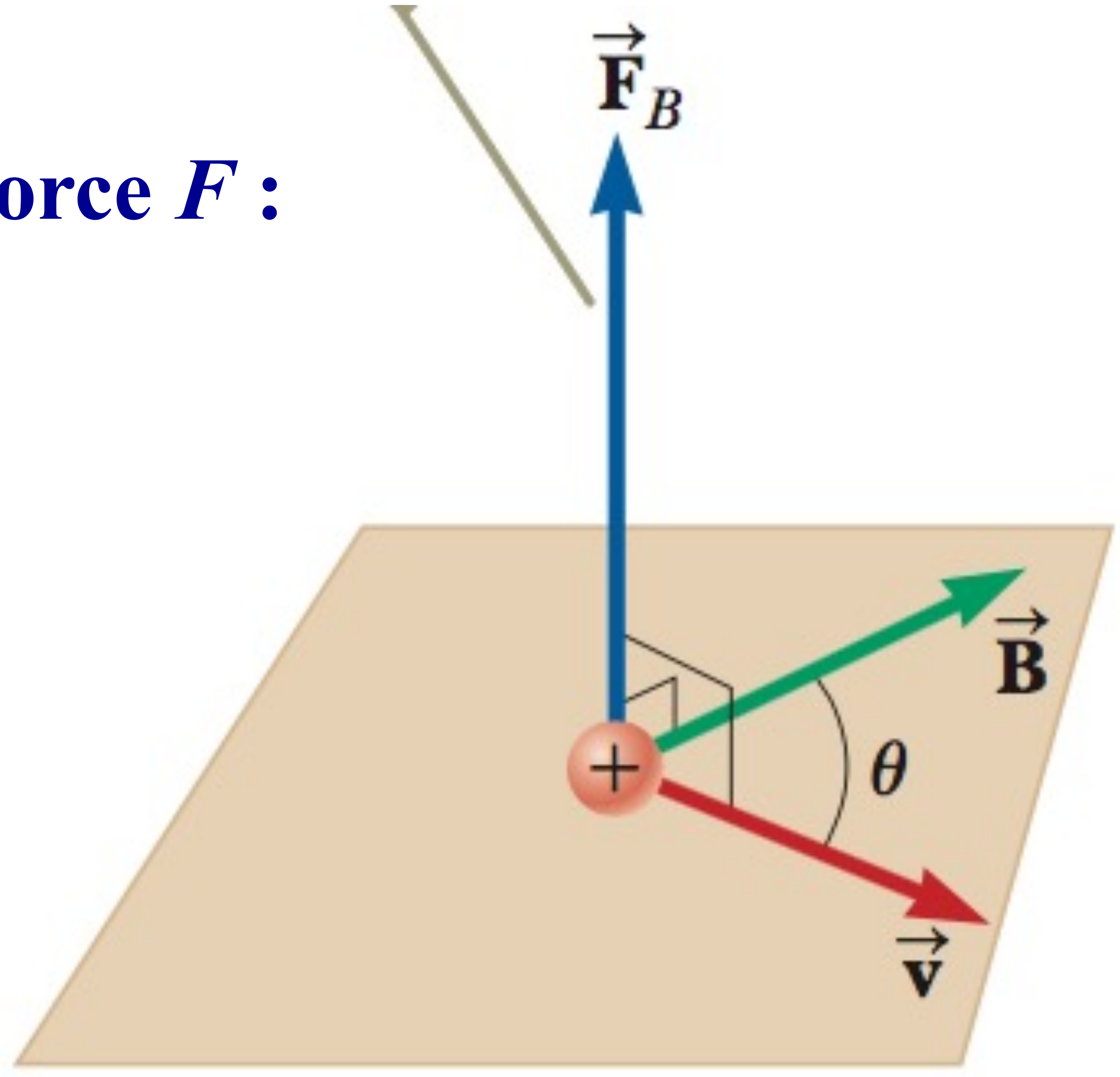
Based on interaction of charges with permanent homogeneous magnetic field

Magnetic force to a charge

A charge q moving with velocity $\vec{V}$ in MF of strength $\vec{B}$ experiences the force F :

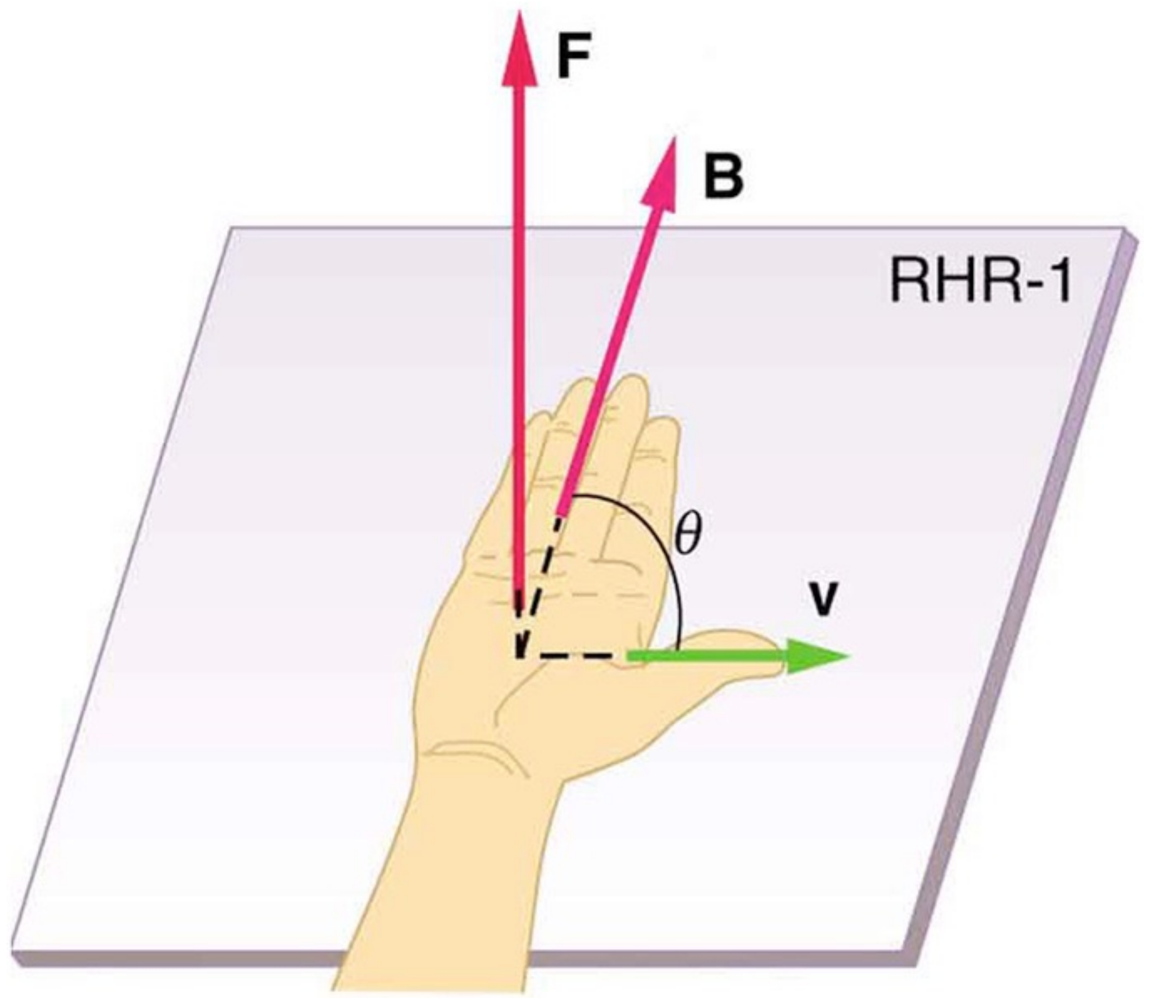
$$\vec{\mathbf{F}}_B = q\vec{\mathbf{v}} \times \vec{\mathbf{B}}$$

called Lorentz force.



- The force is ***orthogonal*** to the velocity and to the field at any time moment;
  Therefore:
- The kinetic energy of the charge does not change;
- The absolute value of $\vec{V}$ remains constant.
- The absolute value of the Lorentz force: $F = q\left|\vec{V} \times \vec{B}\right| = +e \cdot V \cdot B \cdot \sin\theta$

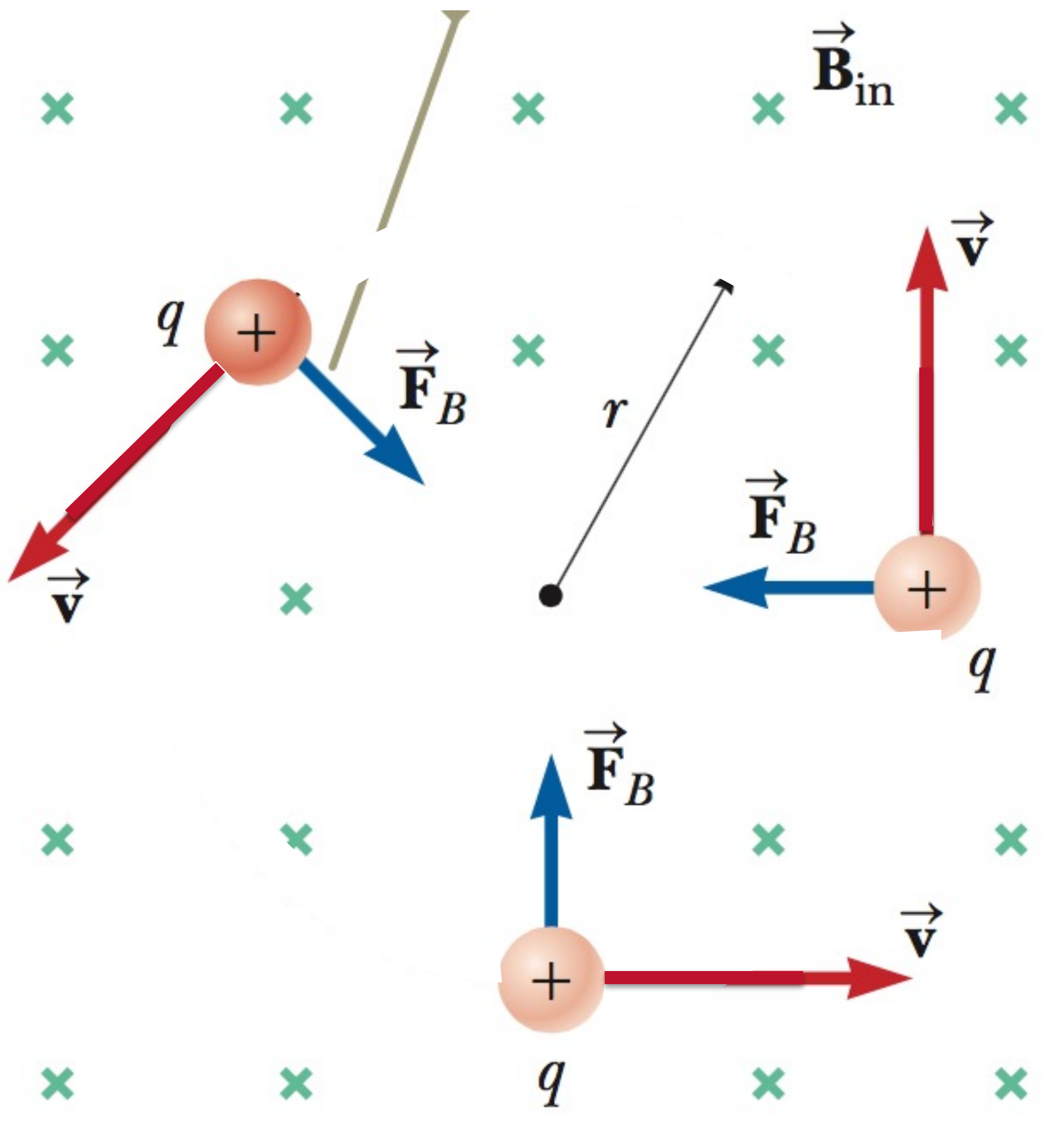
One may determine the direction of Lorentz force for a positive charge using Right Hand Rule:



For a negative charge the direction of the force is opposite !

Motion of a charge in magnetic field

What is the charge trajectory? $\vec{F} = m\frac{d\vec{V}}{dt} = q\vec{V}\times\vec{B}$



In a scalar form this eq. can be written (motion is in x, y plane):

$$\frac{dV_x}{dt} = \frac{qB_z}{m}V_y; \quad \frac{dV_y}{dt} = -\frac{qB_z}{m}V_x$$

Cannot be integrated directly! But sin and cos functions satisfy the eqs.

$$V_x = V_\perp \cos(\frac{qB}{m}t); \quad V_y = V_\perp \sin(\frac{qB}{m}t), \text{ or denoting } \boldsymbol{\omega} = \frac{qB}{m} \text{ and integrating :}$$

$$x = \int V_\perp \cos(\frac{qB}{m}t)dt = V_\perp \frac{1}{\boldsymbol{\omega}}\sin(\boldsymbol{\omega} t); \quad y = \int V_\perp \sin(\boldsymbol{\omega} t)dt = -V_\perp \frac{1}{\boldsymbol{\omega}}\cos(\boldsymbol{\omega} t);$$

What is this periodic motion?

$$|r| = \sqrt{x^2 + y^2} = \frac{V_\perp m}{qB}\sqrt{\sin^2(\boldsymbol{\omega} t) + \cos^2(\boldsymbol{\omega} t)} = \frac{V_\perp m}{qB}.$$

- MF ***B*** is homogeneous and directed away along ***z***
- Charge velocity ***v*** is orthogonal to MF in x-y plane

Charge moves on a circle of radius r
with cyclic frequency ω
around lines of magnetic field

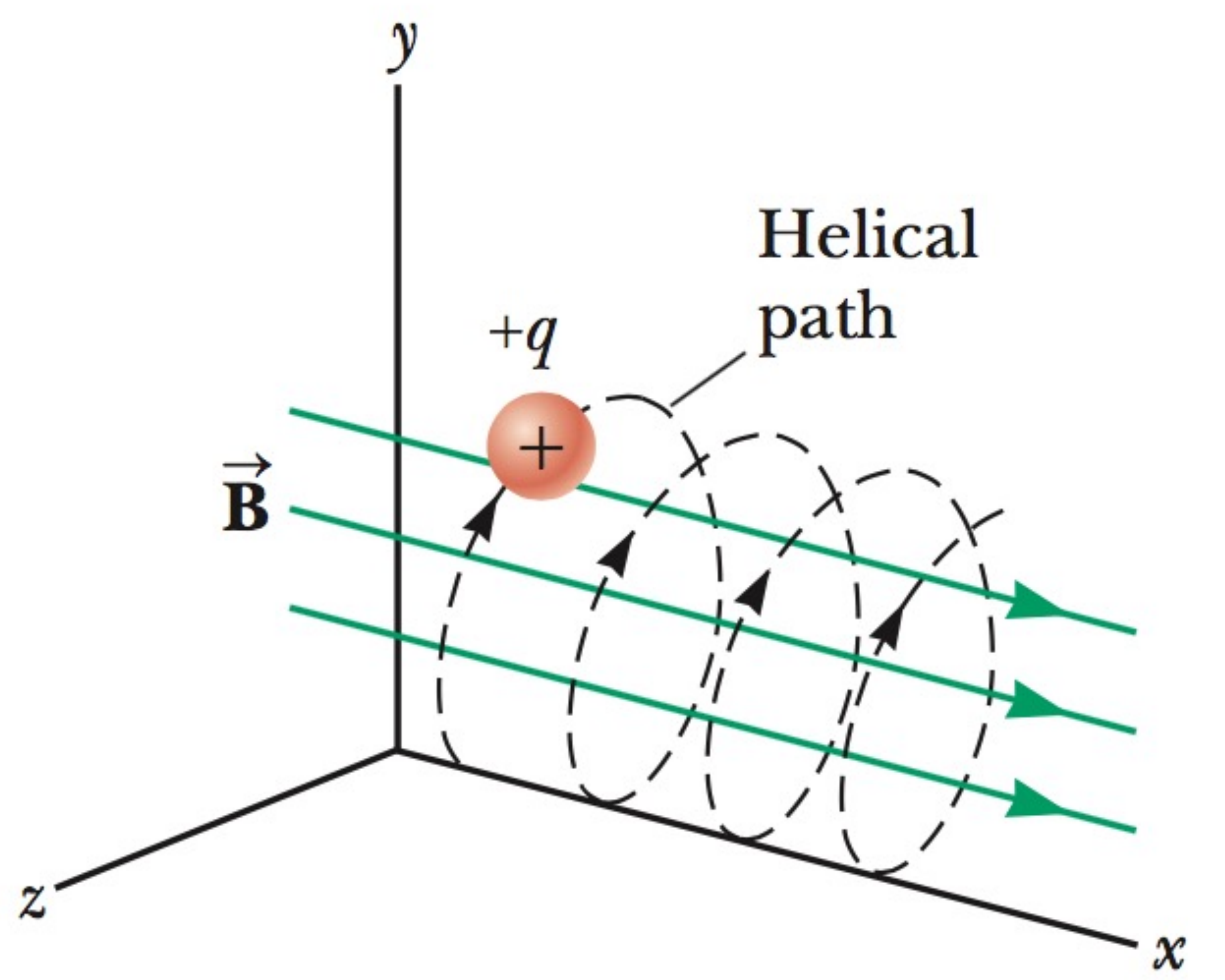
$$\boxed{\boldsymbol{\omega} = \frac{q}{m}B; \quad r = \frac{V_\perp}{\boldsymbol{\omega}}}$$

ω does NOT depends on V !

Motion of ions in magnetic field

When the ion velocity vector is not orthogonal to magnetic field, only the $\vec{V}_{\perp}$ velocity component contributes to cyclotron motion:

$$r = \frac{m \cdot V_{\perp}}{e \cdot Z \cdot B} \qquad \boxed{\omega = \frac{eZ}{m} B}$$



while the $\vec{V}_{||}$ component along the field doesn't change.
The trajectory of the charge then is a helix.

- **In a fixed magnetic field ω_c depends only on q/m;**
- **This fact is used in Ion Cyclotron Resonance mass spectrometers (ICR MS) to determine m/Z of ions by measuring ω_c.**

Calculation of cyclotron frequency

Cyclotron frequency: $$\omega_c = \frac{qB}{m}$$

- Find the cyclotron frequency of an ion of m/z 1000 in a 7.0 Tesla magnetic field.

  q = 1.6022 x 10^{-19} C   coulombs

  B = 7.0 T   Tesla

  m = 1000 x 1.6605 x 10^{-27} kg

$$\omega = \frac{\left(1.6022 \cdot 10^{-19}\ \mathrm{C}\right)\left(7.0\ \mathrm{T}\right)}{1.6605 \cdot 10^{-27}\ \mathrm{kg}} = 6.7542 \cdot 10^{5}\ \mathrm{s}^{-1}\quad \text{(radians/second)}$$

Usually reported in Hz:

$$f = \frac{\omega}{2\pi} = \frac{6.7542 \cdot 10^{5}}{2\pi} = 107450\ \mathrm{Hz}\quad \text{or } 107.450\ \mathrm{kHz}$$

Calculation of cyclotron frequency

Cyclotron frequency: $$\omega_c = \frac{qB}{m}$$

Combine constants to get a general formula:

$$f = 1.53567 \cdot 10^7 \cdot \frac{zB}{m}$$

where:

B is in Tesla***,*** ***m*** is in Da, ***Z*** is the number of charges.

Cyclotron radius

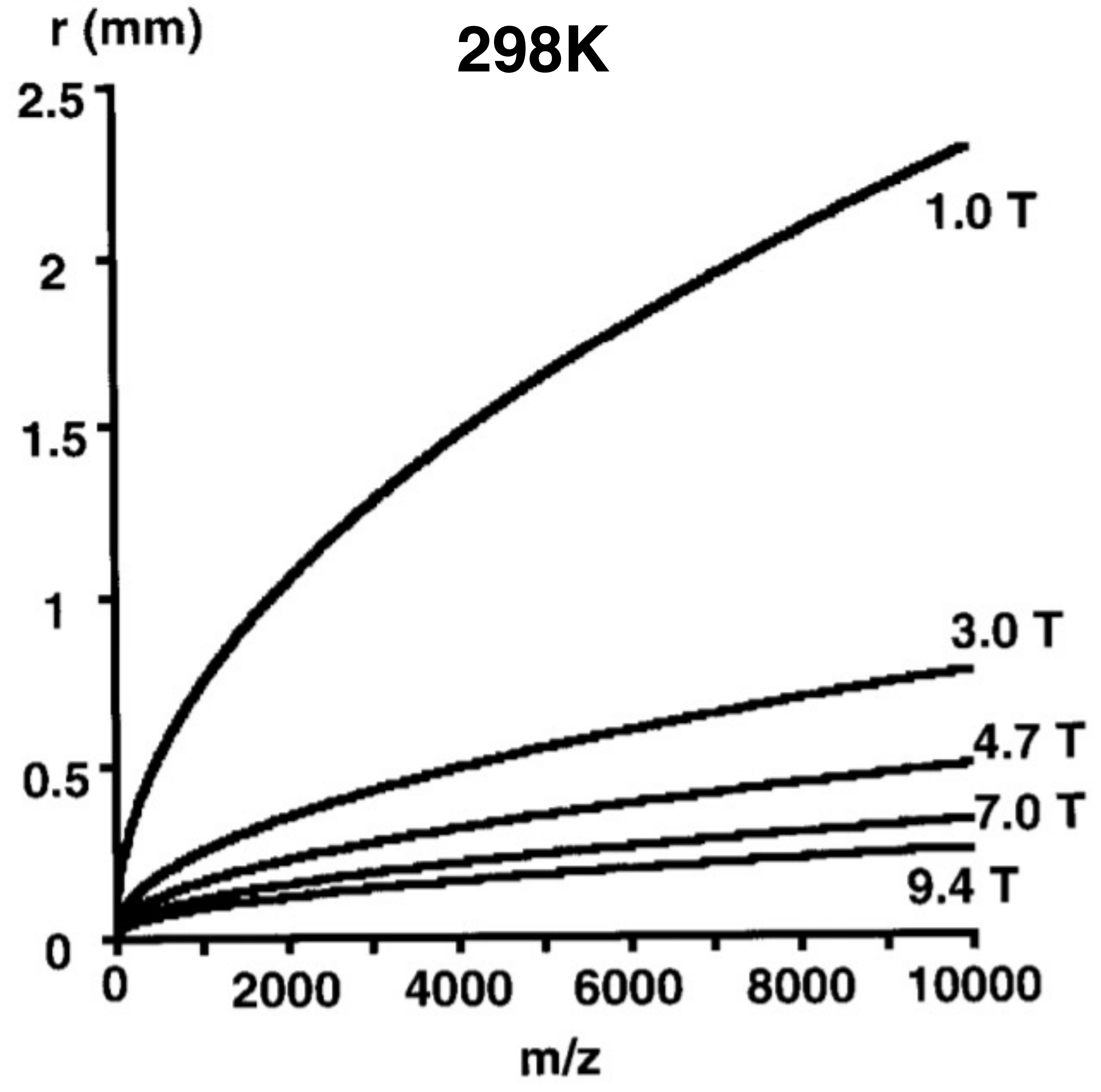
$$qvB = \frac{mv^2}{r} \longrightarrow r = \frac{mv}{zeB}$$

Radius of cyclotron motion

r is proportional to the velocity of ions v, which at equilibrium depends on kT (Boltzmann constant)

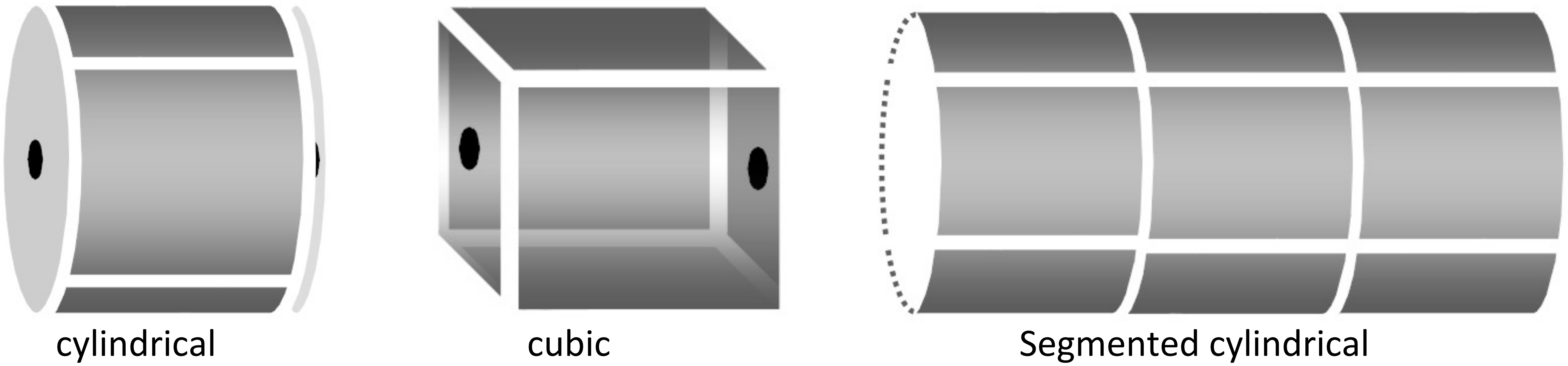
$$\frac{mv^2}{2} = kT$$

$$r = \frac{1.0336510 \cdot 10^{-6}}{zB}\sqrt{mT}$$



Principles of ICR

- Different ICR cell geometries

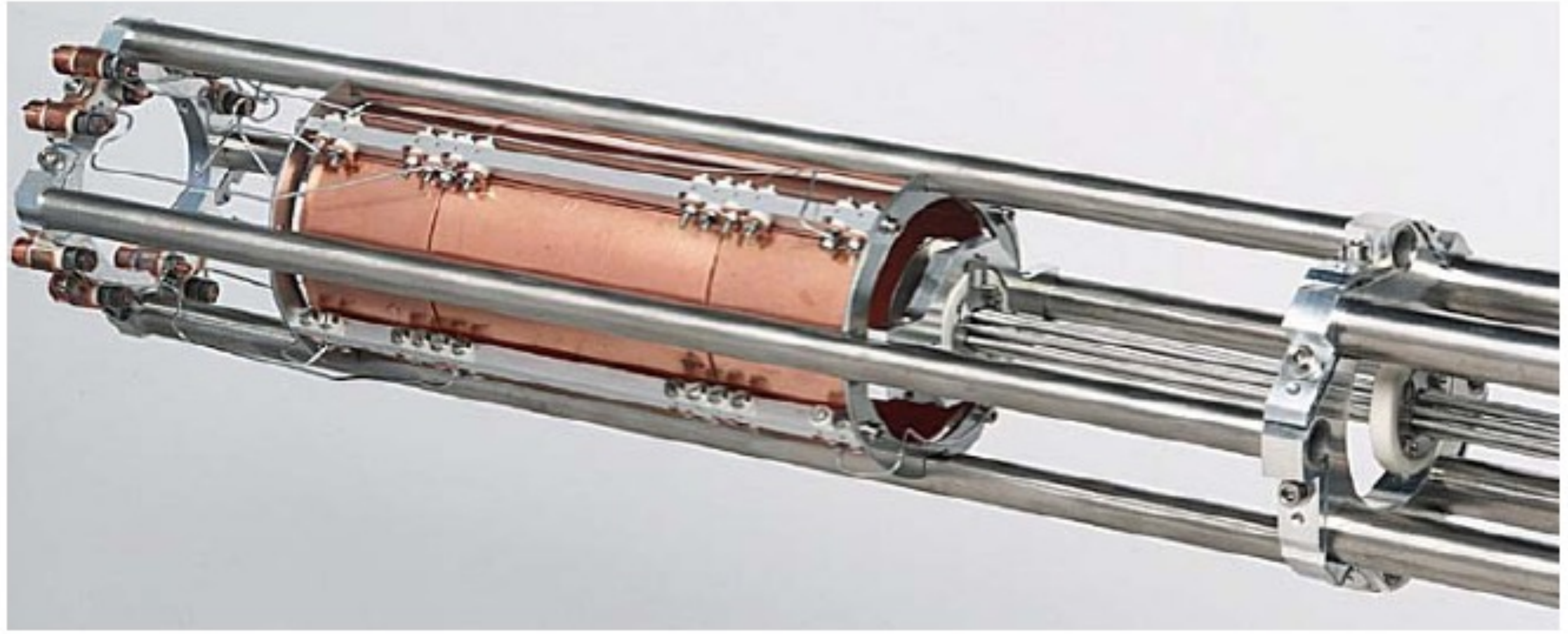


- Discrete packet of ions enter the ICR analyzer

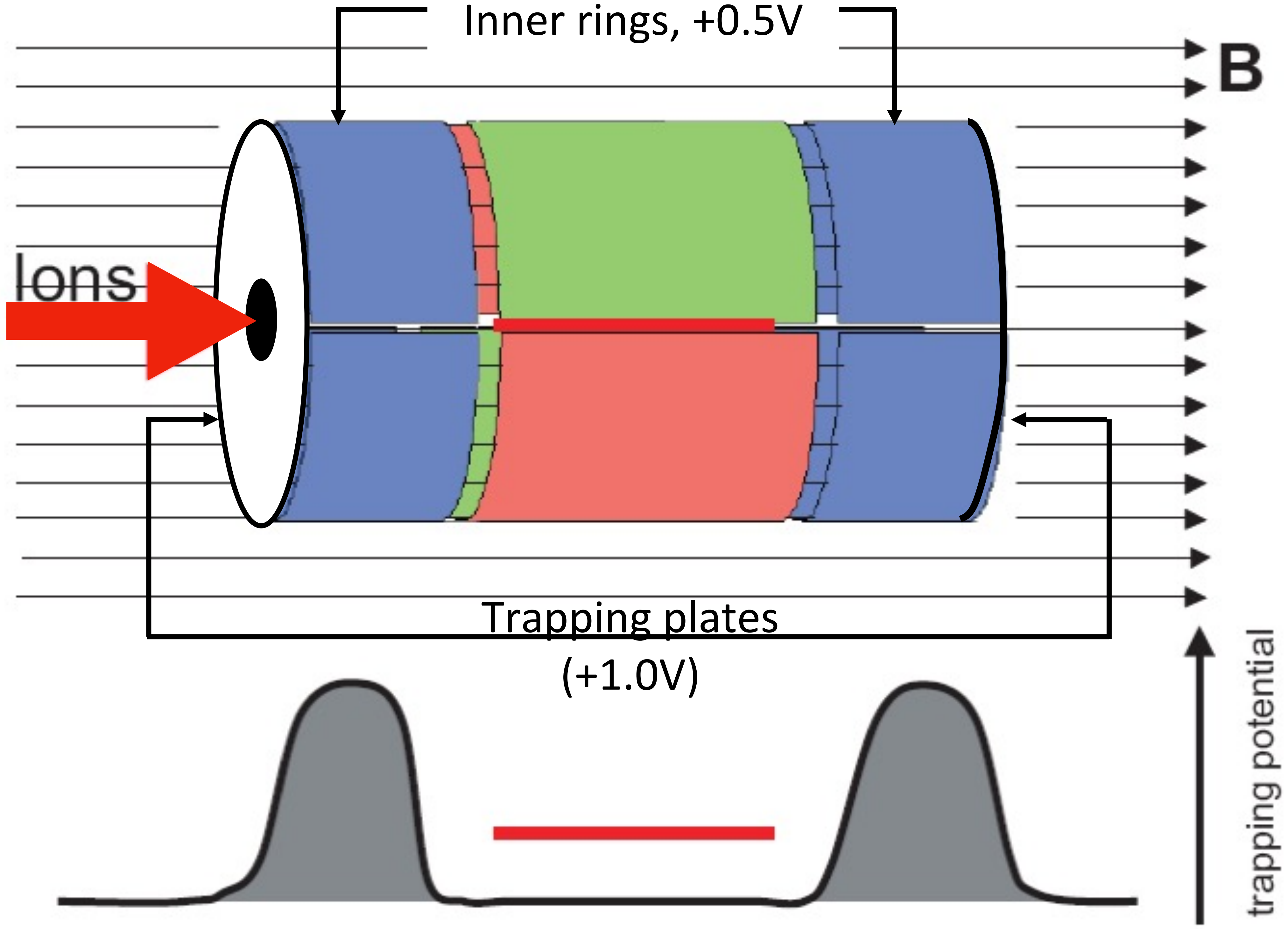
- A homogenous static magnetic field surrounds the cell

- Very high vacuum in the entire analyzer region

ICR cylindrical segmented cells



Superconducting Magnet (3 to 21T)

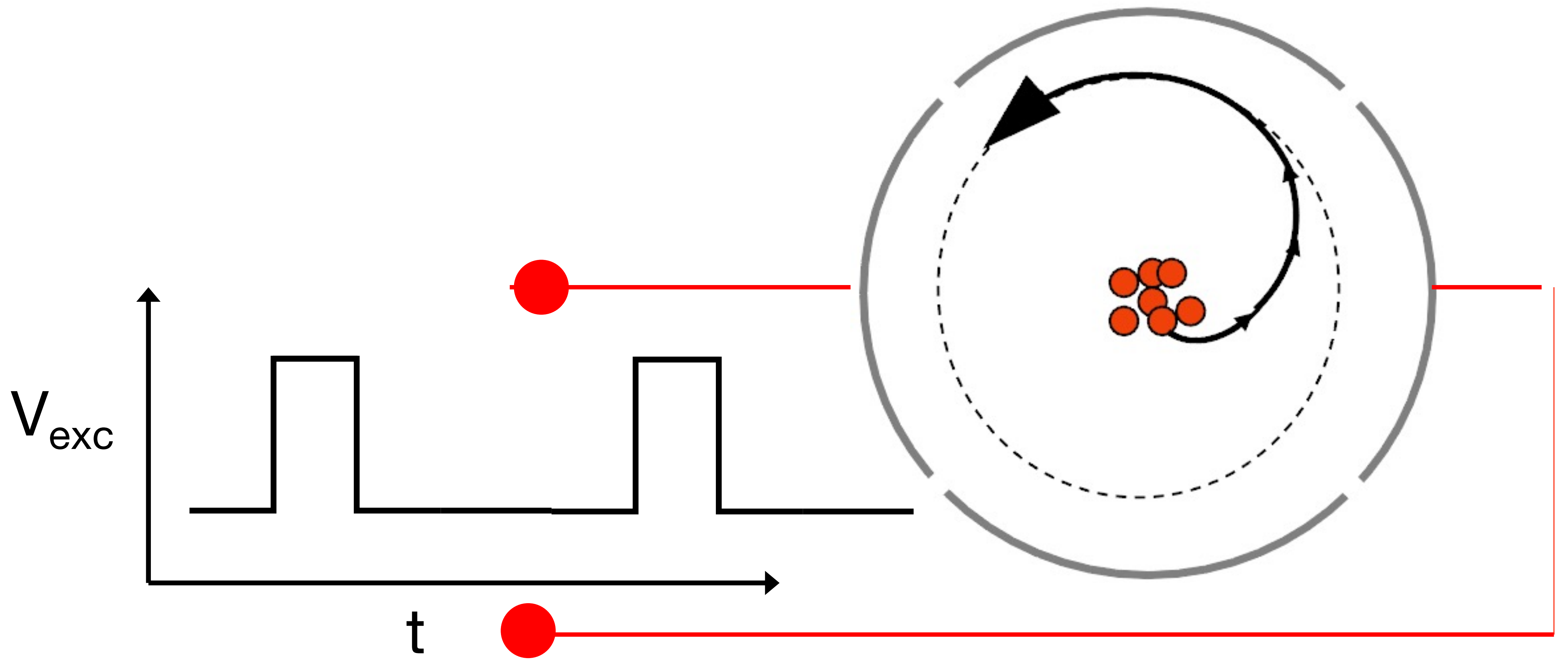


2 excitation electrodes

2 detection electrodes

ICR: ion excitation

- Ions introduced in the ICR cell are not in phase
- Ions turn in an orbit of small radius with random distribution
- Increasing the kinetic energy of ions result in an increase in radius, r
- For broadband m/z detection the excitation is by short (Dt~ 10-6 s) duration) rectangular pulses



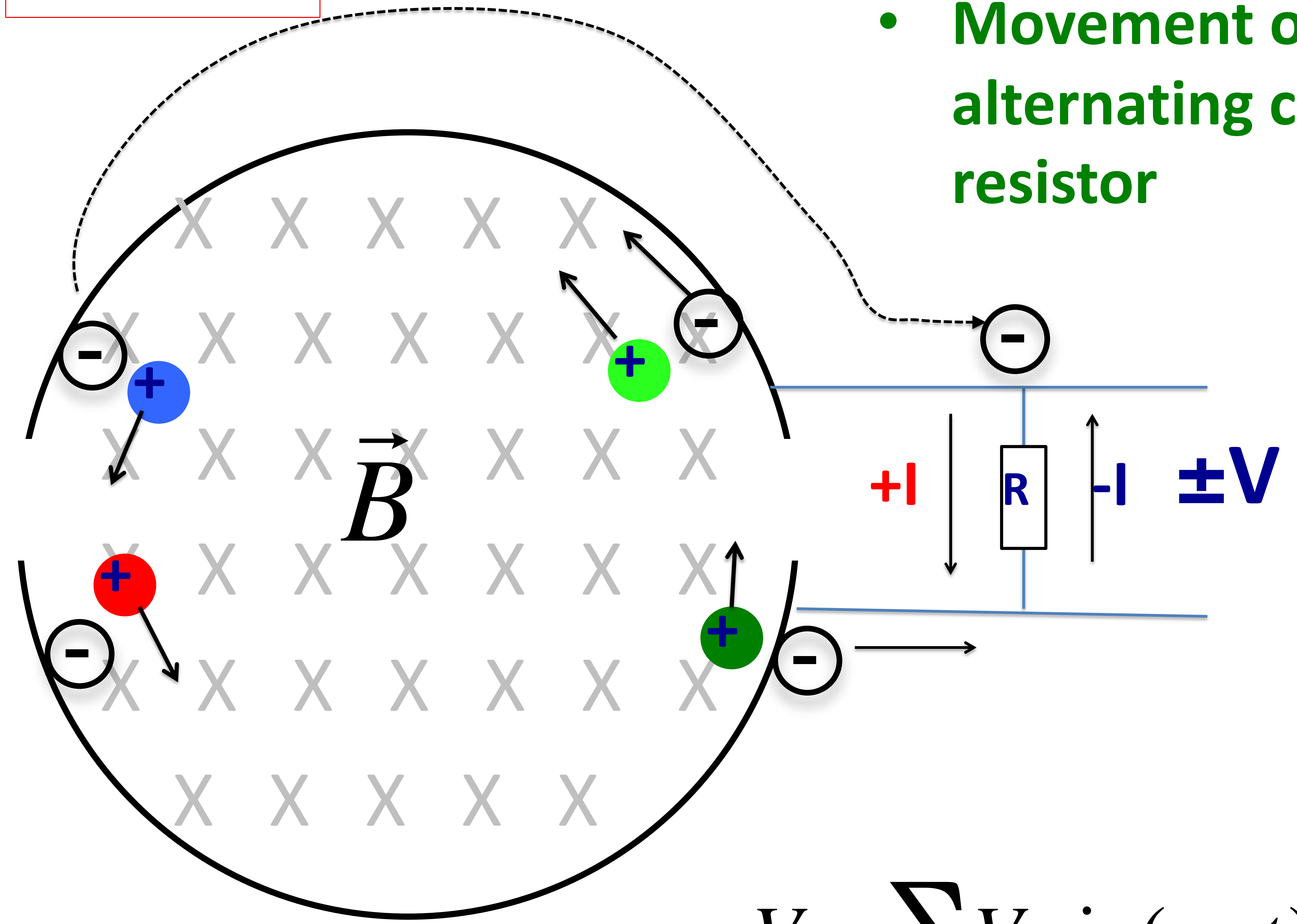
Such a pulse is as a sum of sin(ωt) functions with continuous range of frequencies up to ω_{max} ~1/ Δt (Uncertainty principle: $\Delta t \cdot \Delta\omega \sim 2\pi$)

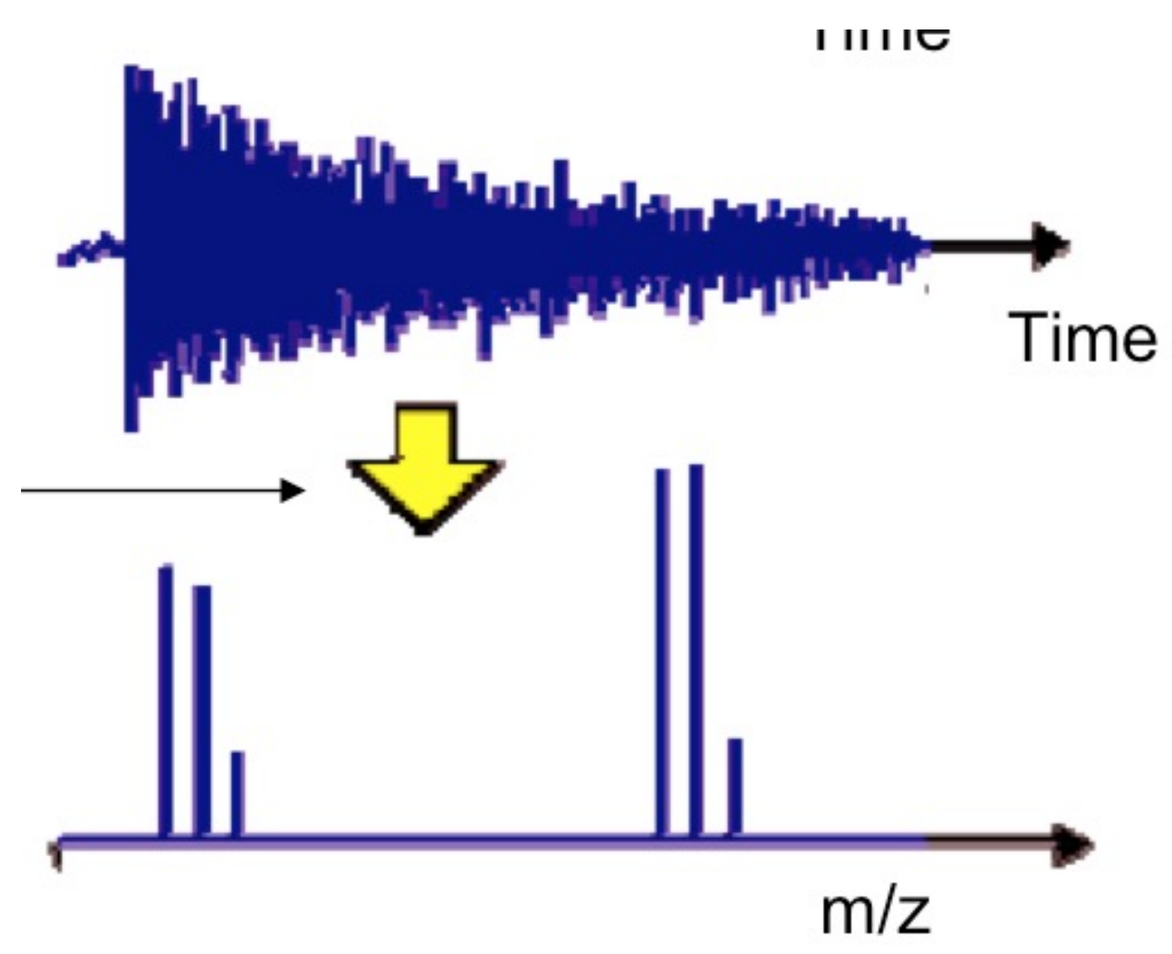
Ion of differen m/z are accelerated by the components of different frequencies.

Ion Cyclotron Resonance mass spectrometer

$$\boxed{\omega = \frac{q}{m} B}$$

- Movement of an ion induces alternating current through resistor





$$V = \sum V_i \sin(\omega_i \cdot t) = \sum V_i \sin(\frac{q}{m_i} B \cdot t)$$

Summary of FTMS Work

Broadband excitation

1. Excitation

RF Sweep

2. Transient

Transient Image current detection

High Resolution (~50,000 FWHM)

High mass accuracy (~1 ppm)

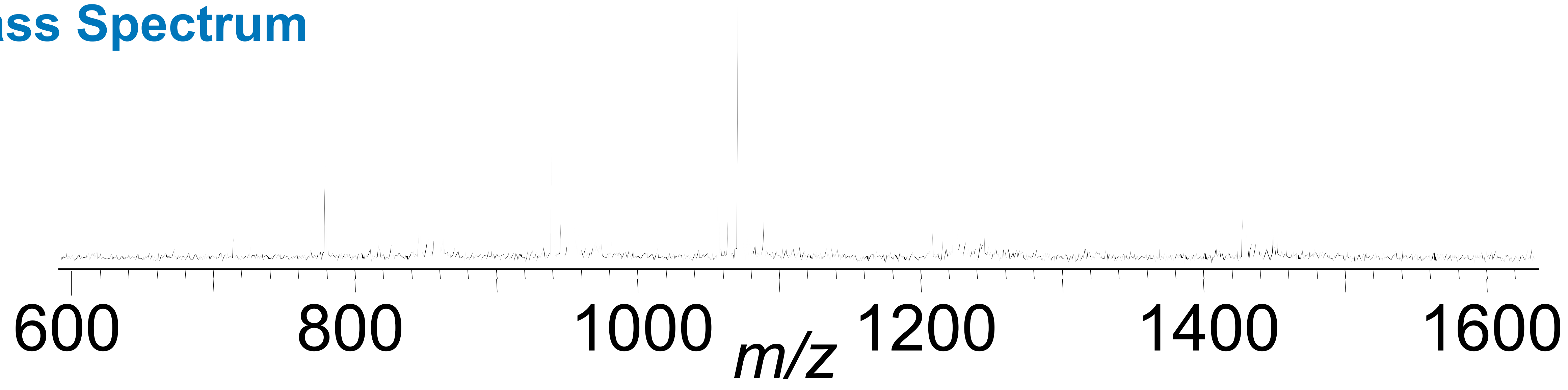
High sensitivity (femtomoles)

3. Fourie-Transform

FFT

Calibrate

Mass Spectrum



Resolution of ICR

Cyclotron frequency: $\omega_c = \frac{qB}{m}$

$$R = \frac{m}{\Delta m}; \quad \frac{m}{q} = \frac{B}{\omega}; \quad \Delta m \simeq dm \propto d\left(\frac{1}{\omega}\right) = -\frac{d\omega}{\omega^2}; \Rightarrow$$

$$R \propto \frac{1}{\omega} \cdot \frac{\omega^2}{\Delta\omega} \propto \frac{\Delta t}{m}.$$

- Resolution of ICR drops linear with 1/*m*
- Resolution of ICR increases with observation time *t*

ICR capabilities

- High-performance mass analyzer
- Resolving power >200’000, typically 500K, drops as 1/m; increases almost linear with time
- High mass accuracy (≈ 1 ppm)
- Requires ultra-high vacuum ($<10^{-10}$ mBar)
- Limited number of ions in the cell (10^6): limited dynamic range
- Expensive (> 1M $)