

High resolution mass spectrometry using a linear electrostatic ion beam trap

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Abstract

We describe a new mass spectrometric technique that is based on the use of a linear electrostatic ion trap and a newly discovered self-bunching phenomenon. Ions are stored in the trap and their oscillation frequencies are determined by Fourier transform of their oscillation times. Using this system, we demonstrate that it is possible to simultaneously trap several masses and obtain their mass spectra with high resolution. The instrument is compared to time-of-flight mass, as well as to ion cyclotron resonance mass spectrometers.

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1. Introduction

Mass spectrometry is one of the most common analytical techniques in modern physical and biological sciences. It is used for detection and characterization of matter in almost any field ranging from biology, material sciences, and clinical studies to space, environmental, and climate research. One of the earliest types of mass spectrometers is the time-of-flight mass spectrometer (TOFMS) [1,2]. Although initially considered inferior to the dispersive mass spectrometric techniques, such as magnetic sector and quadrupole mass spectrometry, TOFMS has recently seen a revival due to its enormous advantages in the field of biological applications. TOFMS can be coupled to almost any type of pulsed or continuous ion source, it has a very high duty cycle, which increases with the mass-to-charge ratio of the analyte, high resolving power to fairly large molecules, and it is not experimentally complicated. The ability to couple TOFMS to matrix-assisted laser desorption ionization (MALDI) and electrospray sources made it the tool of choice for many bio-

logical applications. TOFMS can readily reach mass resolving power of 10^3 – 10^4 with very high efficiency. In general, TOFMS detection sensitivity and mass resolution decreases with increasing mass. This loss of sensitivity results from the decreasing efficiency for secondary electron production of the microchannel plates (MCP), which are usually used for detection of the impinging ions. The mass resolution in a TOFMS is proportional to the inverse of the square root of the mass and therefore diminishes with increasing mass-to-charge ratio. These two properties of TOFMS have limited its application in certain biological and material sciences, such as structural biology and characterization of nanoparticles, where large masses are studied.

Increase of the mass resolving power of TOFMS to about 4000 was achieved by introducing several methods for ion extraction, such as delayed extraction (often used in combination with MALDI ion sources) [3] and orthogonal injection (often used in conjunction with electrospray ion sources) [4]. The introduction of the reflectron TOFMS, in which the ion beam is reflected at least once, in order to compensate for the spread in the initial ion velocity distribution, also contributed to the improvement of TOFMS mass resolving power [5,6]. Since the resolution of TOFMS depends to a large extent on the length of the flight tube, other approaches

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to improve the resolving power were the use of a multi-turn or multi-pass design [7,8].

Excellent mass resolving power and mass accuracies combined with high efficiencies, even at the high mass ranges, are the characteristics of the Fourier-transform ion cyclotron resonance mass spectrometer (FTICR-MS) [9,10]. Coupled with an electrospray source that produces multiply charged molecular ions, FTICR-MS has proven to be an excellent tool for high mass biomolecule spectrometry as well as for inorganic analysis. The FTICR-MS can readily reach mass resolving powers of up to 10^5 with high efficiency [11]. However, in order to reach the high resolving powers needed for advanced mass spectrometry of massive biomolecules and nanoparticles, large superconducting magnets with magnetic fields higher than 10 T are required. This requirement makes the FTICR-MS an expensive and large tool, which limits its applicability. The mass range in modern FTICR-MS instruments exceeds 10^4 (but not 10^5) with high resolution, which makes FTICR increasingly attractive for MALDI and electrospray applications [12]. Ion–ion interactions, however, tend to limit the dynamic range and abundance sensitivity, particularly when the ions of interest are only a small fraction of the total ions present. Finally, the need to obtain high accuracies leads to long measurement times, rendering FTICR-MS a rather slow mass spectrometric technique.

In this paper, we describe a new type of mass spectrometer [13–16] that combines many of the properties of the FTICR-MS with a small and simple TOFMS-like instrument. The new Fourier-transform time-of-flight mass spectrometer (FT-TOFMS) is a linear ion trap in which a bunch of ions is trapped in a linear flight tube for an extended period of time (approximately in seconds). Using a non-destructive detection method, the oscillation times of trapped ions are recorded and their oscillation frequencies are translated to mass measurement using a Fourier transform with very high (10^5 – 10^6) resolving power, very similar to that of the FTICR-MS. One property of the system, which is the key to its high resolution is that ions remain bunched for a time that is much longer than the expected typical dispersion time which would lead to loss of bunch coherence. This bunching is not achieved through the usual kinematic compensation as in reflectrons, but rather through the Coulombic interaction between the trapped particles [15,17]. Since the trap employs only electrostatic fields, its operation is not mass limited and therefore its high mass resolving power can be sustained for very high molecular weights.

2. Experimental setup

A schematic drawing of the electrostatic ion trap is shown in Fig. 1. The mechanical design of the ion trap and its operation have been described previously [13,14,18]. Briefly, the ion trap consists of two coaxial electrostatic mirrors, each composed of a stack of eight cylindrical electrodes. The con-

figuration of the trap is characterized by the potentials on five of these electrodes: V_1 , V_2 , V_3 , V_4 , and V_z (see Fig. 1), the other three being grounded. The distance between the innermost grounded electrodes of each mirror is 227 mm, so that the region between the mirrors is practically field free.

The ions are injected into the trap by momentarily reducing the potential of one (or more) electrode of the entrance side so that the maximum potential on the mirror axis is lower than the kinetic energy of the incoming ions (for singly charged ions). The electrodes on the other side are kept at high potential so that the ions are reflected back toward the entrance lenses. To trap the ions, the potentials of the electrodes are chosen in such a way that they obey two stability conditions: The first one, which is trivial and relates to longitudinal confinement, requires that the maximum potential on the mirror axis be higher than the kinetic energy of the ions divided by their charges. The condition for transverse confinement is not obvious, and is obtained from considerations similar to those leading to the stability criterion for an optical resonator [13,14,18]:

$$\frac{L}{4} < f < \infty \quad (1)$$

where L is the effective distance between the mirrors and f is their focal lengths, assuming that the mirrors are symmetric. For ions with keV energies, the typical oscillation time is of the order of 10 μ s, scaling with the square root of the mass.

$$T = \frac{1}{f} \propto \sqrt{\frac{M}{q}} \quad (2)$$

where f is the oscillation frequency and M and q are the mass and charge, respectively. The stored beam radius depends very much on the voltages applied on the mirror electrodes, and is usually in the range of 1–2 mm.

At a background pressure of 3×10^{-10} Torr, the typical lifetime of ions in the trap is ~ 5 s. This lifetime is determined by measuring the rate of leakage of neutral particles from the trap, using a MCP detector located after the trap. These neutral particles are formed by the electron capture collisions between the stored ions and atoms of the residual gas in the trap. As mentioned earlier, since the trap is purely electrostatic, there is (in principle) no limitation as far as the mass-to-charge ratio is concerned, which enables trapping of very heavy ions.

The evolution of the ion bunch during storage is monitored by a cylindrical pickup electrode located at the center of the trap. The electrode length is 7 mm, and its inside diameter is 18 mm. The total capacitance of the pickup electrode, its support rod, and vacuum feed-through is $C_p \sim 10$ pF. The pickup is connected to the gate of a junction field effect transistor (JFET) whose drain is fed to a charge sensitive amplifier [19]. The amplified signal is recorded with a digital oscilloscope and a fast Fourier transform (FFT) of the data gives the frequency spectrum. This detection scheme is mass independent, in contrast to the commonly used MCP which has lower amplification for larger masses [20].

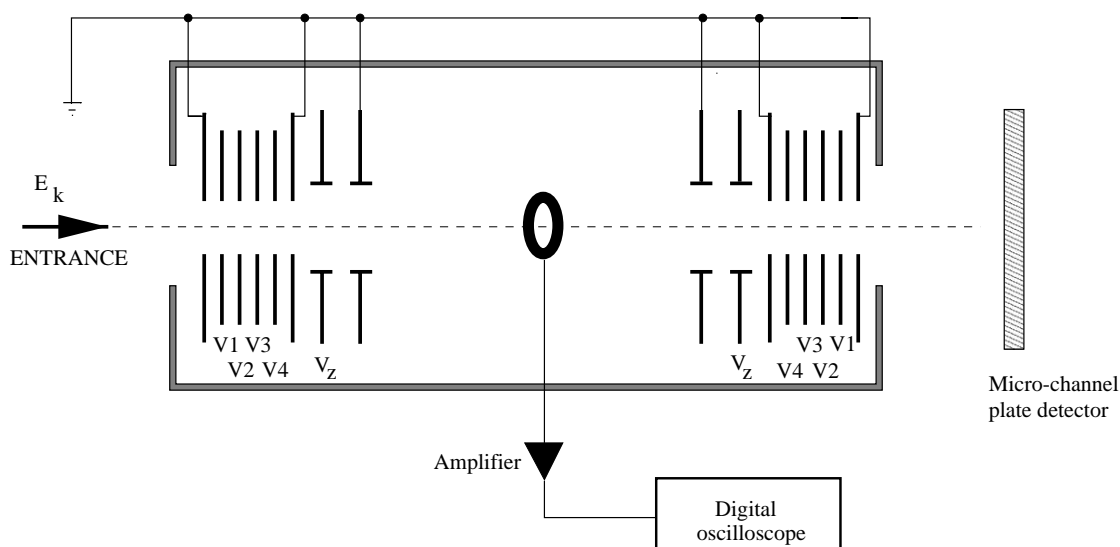


Fig. 1. Schematic view of the ion beam trap. The bunch is injected through the left side of the trap. The central ring is the pickup electrode. Note that the section between the innermost electrodes of the two mirrors is essentially field free.

Depending on the electrode potentials V_1 – V_4 , the trap can operate either in a dispersive or self-bunching mode [21]. In the following, we describe the properties of these modes, and show examples of experimental results.

3. Experimental results

3.1. Dispersive mode

A typical experiment is performed by injecting a short (~ 200 ns) bunch of ions into the trap. In principle, the

bunch can be produced by a MALDI source [16], but in this study, we present results for ions produced using a standard electron impact ionization source. The source produces a constant current of ions, which is chopped by applying a fast electric pulse to a pair of steering plates located downstream, effectively producing an ion bunch with a width as short as 200 ns.

The left panels in Fig. 2 show a typical signal measured for a 4.2 keV Ar^+ bunch during a window of 15 μs , for three different times after the injection. The negative pulses indicate the sign of the image charge on the ring detector, and each pulse represents the passage of about 10^6 ions through

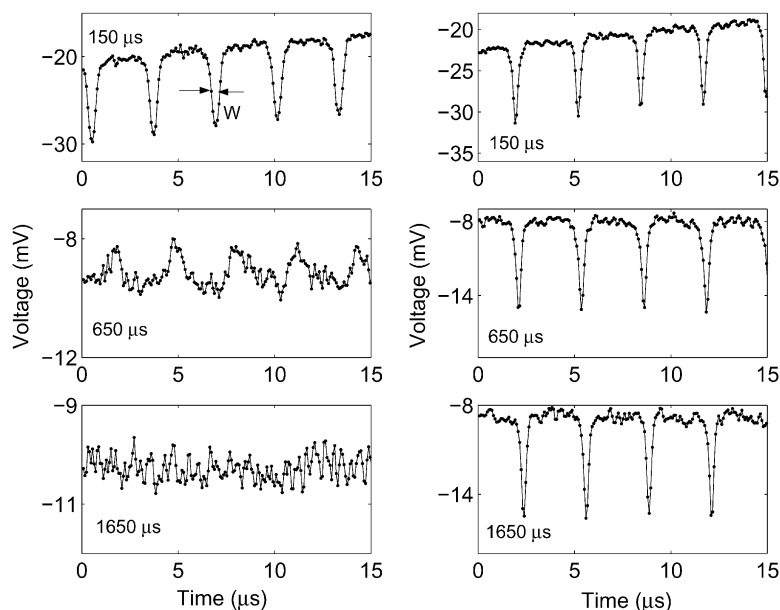


Fig. 2. The signal observed with the pickup electrode for an initially short bunch of Ar^+ at 4.2 keV for three different time windows of 15 μs after injection: The three left panels are in the dispersive mode, while the three right panels are in the self-bunching mode. The initial value of the time window is written in each plot.

the pickup electrode. The oscillation time of the ions was measured to be $\sim 3 \mu\text{s}$. The development of the ion bunch width W can be followed as a function of storage time, and as can be seen in the left panel of Fig. 2, debunching (i.e., broadening of the measured pulses) occurs on a time scale of ~ 1 ms. It is important to point out that the fact that the signal vanishes does not mean that the ions are lost from the trap, but rather that the ions move in the trap in a non-correlated way. Debunching occurs because: (1) not all ions have the same exact initial velocity, (2) not all ions are moving exactly on the same trajectories, and (3) the Coulomb repulsive force between the ions in the bunch pushes them apart, increasing their relative velocities and thus widening the bunch. We call this mode “dispersive”.

3.2. Self-bunching mode

As previously demonstrated in refs. [15,21], it is possible to dramatically alter the behavior of the ion bunch by using a different set of potentials on the mirror electrodes, thereby changing the slope of the potential barrier. The right panels in Fig. 2 show again the bunch width for the same three time windows as in the dispersive mode. However, in this case, the ion bunch is stable, and broadening does not occur. In fact, ion bunches in this mode can be observed for times which are as long as several hundreds of milliseconds, corresponding to tens of thousands of oscillations, without any discernible change in their width [15,21]. We call this the “self-bunching” mode.

The only difference in the ion trap setup between the two modes presented in Fig. 2 is the slope of the potential in the mirrors region [21]. In the first case (left panels of Fig. 2), the ions experience a steeper gradient than in the second case (right panels of Fig. 2). Why does the bunch stay together in the latter case? The reason lies in the special dynamics which is taking place in a periodic system with interacting particles. A systematic study of this phenomenon was performed [18] and it was found that a necessary, but not sufficient condition, for self-bunching to occur is that the dispersion of the trap, i.e., the derivative of the oscillation period (T) by the kinetic energy (E), had to be positive: $dT/dE > 0$, and that the particles have to interact with a *repulsive* force. Although the fact that a repulsive force leads to bunching might seem counter-intuitive, it is possible to explain this in a relatively simple physical picture: For particles oscillating in a potential where $dT/dE > 0$, the fastest particles have the longest oscillation times. Thus, for a bunch in such a potential well, the fastest ions will tend to localize in the rear of the bunch, while the slowest ones will tend to be located at the front. This correlation is the inverse of the one for the dispersive mode (when $dT/dE < 0$), and the effect of the Coulomb interaction (which is dominant at the turning points) is accordingly different: The fast particles, located at the back, will have their velocities reduced by the Coulomb force, while the slow ions, located at the front, will be pushed further ahead, thereby increasing their velocities.

The combined effect is to move the rearward particles toward the front of the bunch, and the leading particles toward the back, hence keeping the size of the bunch constant. The minimum density of ions needed in order for self-bunching to occur depends on the initial energy distribution of the beam [17]. For an ion source as used in the present work, where the energy spread is ~ 1 eV, and the bunch width ~ 200 ns, the minimum number of ions is about 100 [17].

A complete explanation of this phenomenon, in the framework of the electrostatic ion trap, has been published recently [17] and a good understanding of the conditions under which such self-bunching occurs has been achieved. It was also shown that the phenomenon is similar to the one existing for the onset of the so-called negative mass instability in relativistic storage rings [17]. In the present manuscript, we concentrate on the potential of using the ion trap in the self-bunching mode as a high resolution mass spectrometer.

3.3. Application of the electrostatic trap for mass spectrometric applications

Since the trap is purely electrostatic, the oscillation time of an ion depends on its mass-to-charge ratio (Eq. (2)). Hence, by measuring the oscillation time or frequency and the charge, the mass-to-charge ratio can be determined. In the self-bunching mode, T can be measured with an accuracy limited only by the trapping time, since, as was shown above, the negative mass instability prevents broadening of the peak, i.e., dephasing of the ions [17]. This is much like the situation in the so-called Fourier-transform mass spectrometry (FTICR-MS). In the standard version of FT-MS [22], the ions are trapped under the influence of magnetic and electric fields, and undergo cyclotron motion. As in our case, high resolution is achieved because the ion motion is detected for many cycles, while the packet of ions does not lose its coherence.

From the data shown in Fig. 2, it is easy to demonstrate that a mass spectrum with high resolution can be achieved in the self-bunching mode for a single mass. However, and in the same manner as in a FTICR-MS [22], coalescence of the motion of two different ions with very close masses could occur. In fact, since it is the Coulomb interaction which keeps the ions together in a bunch, the same interaction could make two separate bunches composed of two different species coalesce into a single bunch. In such cases, only one frequency would be measured.

A preliminary test was performed with a singly charged ion beam of several isotopes of Xe, produced by electron impact ionization. Because the ions injected into the trap pass through a magnetic steerer, the beam is initially defocused in order to compensate for the mass selectivity of the magnet. This enables injection of the five most prominent isotopes of Xe into the trap. However, the defocusing and magnetic steering results in a distortion in their relative abundance (the natural relative abundance is: $m = 129$, 26.44%; $m = 130$, 4.08%; $m = 131$, 21.18%; $m = 132$,

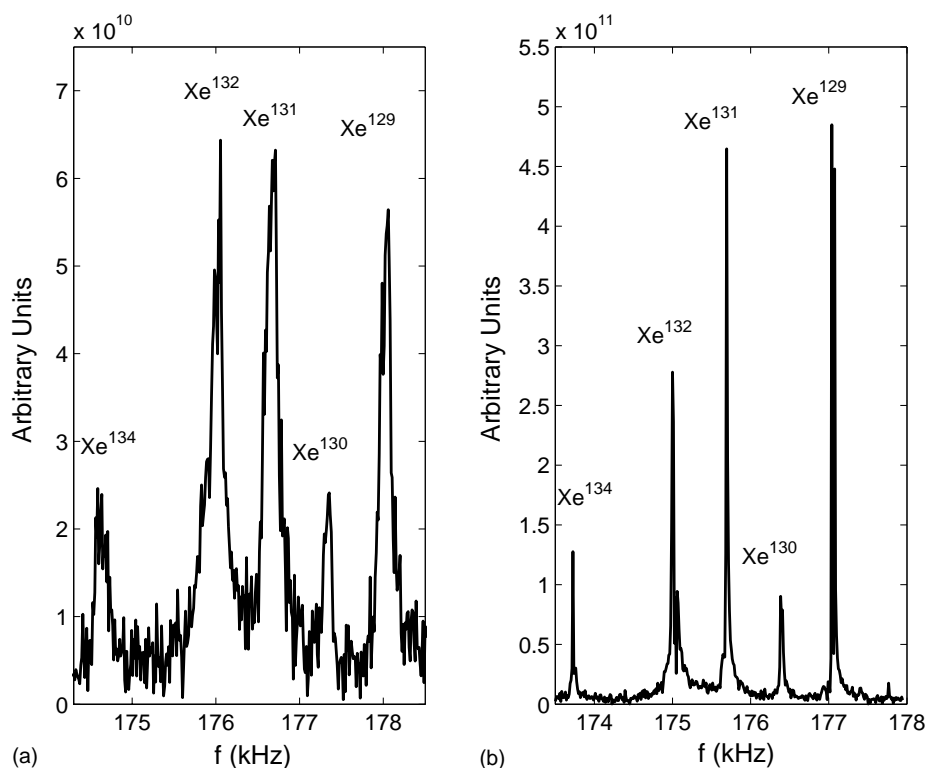


Fig. 3. Fast Fourier transform of the signal for five different isotopes of Xe^+ injected in the trap at 4.2 keV. (a) Dispersive mode and (b) self-bunching mode. The relative height between the peaks does not represent exactly the expected natural abundance of Xe, as the steering and focusing of the beam before injection in the trap is performed with a magnetic (mass dependent) steerer.

26.89%; $m = 134$, 10.44%). The ion beam energy was set to 4.2 keV, and about 10^6 ions were injected. The pickup signal was digitized for 100 ms and Fourier transformed. The FFT results are shown in Fig. 3a and b, both for the dispersive and for the self-bunching mode. The five peaks are well separated in both cases, demonstrating that peak coalescence does not occur. However, while the frequency resolution is about 90 Hz (σ) in the dispersive mode (Fig. 3a), it is of the order of 9 Hz (σ) in the self-bunching mode (Fig. 3b), yielding a frequency resolution of $\Delta f/f \sim 5 \times 10^{-5}$, corresponding to a mass resolution of $\Delta m/m \sim 10^{-4}$. As the storage time (and measurement time) was only 100 ms, the measured width corresponds to the resolution limit, and the peaks in Fig. 3b are mostly made of a single data point. Also, the signal-to-noise ratio is improved in the self-bunching mode by more than a factor of three. Data with better resolution ($\Delta m/m = 7 \times 10^{-6}$), taken after 300 ms of measuring time, and analyzed at a higher harmonic frequency, have been presented elsewhere [17]. Due to the similarities of the present technique to FTICR-MS and TOFMS, we refer to it as FT-TOFMS technique.

4. Discussion

The results above demonstrate that it is possible to store several masses in the trap and to use Fourier analysis to ob-

tain a mass spectrum. A system nearly identical to the one described here has been designed by Benner [19], but has been used for mass measurement of highly charged molecular ions only, produced by electrospray, one molecule at a time. The possibility of using self-bunching for a cloud of ions in order to avoid dephasing was not investigated in that case.

At this point, it is interesting to evaluate the advantages and disadvantages of using the electrostatic trap as a mass spectrometer, compared to the commonly used TOFMS or FTICR mass spectrometric methods. It is well known that mass resolution and separation improves in a TOFMS when the time-of-flight increases. However, due to practical limitations, the field-free region in conventional TOFMS cannot be longer than a few meters. The present ion trap effectively extends the length of the field-free region to about 10 km (after 100 ms), while keeping the bunch confined in space and time. Another point of comparison is the detection limit of the MCP detectors which are used in standard TOFMS. Although the detection efficiency of these detectors is quite high ($\sim 40\%$) for light masses, it decreases rapidly with increasing particle mass up to tens of kDa, where the detection efficiency is, for all practical purposes, negligible. In the present system, the pickup electrode has a detection efficiency which is in fact improving with mass, as it can be shown [21] that the area under a single pulse (such as the one shown in Fig. 1) is proportional to qN/v , where q and

N are the charge and number of ions in the bunch, respectively, and v is the beam velocity. Practically, this allows also to work with smaller acceleration voltages, making the ion source easier and cheaper to design. The main disadvantage of the ion trap system, when compared to the TOFMS, is the lack of single particle detection sensitivity and the long measurement time needed for high mass resolution. For average masses, about 100 singly charged ions are needed to overcome the thermal noise of a good amplifier [19].

The principles of mass analysis by the FT-TOFMS are very similar to those of the FTICR-MS, and similar issues determine its application as a mass spectrometer. Very high resolving power (up to 10^8) have been obtained with these instruments, when the magnetic field is produced by a superconducting magnet [23]. However, when compared to the FTICR-MS, the FT-TOFMS technique presents several advantages, such as simplicity and much lower cost. Similarly to FTICR-MS, the present method uses the measurement of a time-dependent image charge to extract from the periodicity of the motion the charge-to-mass ratio. The coherence of the cloud of ions which is moving in the Penning trap inside a FTICR system is based on the lack of velocity dependence for the cyclotron oscillation, together with a highly homogeneous magnetic field. The interaction between the particles (space charge) is actually a nuisance which leads to dephasing of the cloud of ions in the trap.

In the FT-TOFMS, the coherence is achieved through the repulsive interaction between the ions, while there are no special requirements for the static electric field except that the potential well formed by these fields has to produce a positive dispersion ($dT/dE > 0$) for the motion of the ions. The maximal resolving power that can be obtained with the present instrument is still unclear, but mass resolution of the order of 10^{-6} has already been obtained [17].

5. Conclusions

We have presented a new technique for mass spectrometry that is based on an “ion resonator” very similar in principle to “optical resonators”. Working in a self-bunching mode, the system has the advantages of being intrinsically stable, and can avoid the debunching of the ion clouds oscillating between the two mirrors. The FT-TOFMS shares many principles and characteristics with the FTICR-MS, i.e., the ability to achieve high resolving powers for heavy masses.

The results presented here are preliminary, and the system is now being coupled to a new MALDI ion source, which will allow characterization of the spectrometer under typical working conditions. Additional experiments will be carried out in order to observe the onset of coalescence,

which is likely to occur between heavy, closely spaced masses. The instrument is simple enough to be added to an existing TOFMS in order to improve its mass resolution and sensitivity for heavy masses. The development of this new mass spectrometer will enable the detection and analysis of, among others, large physiological biological complexes.

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