# Counting individual ions in the air by tagging them with particles

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A R T I C L E   I N F O

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The quantification of ultra-low concentrations of molecules and ions in gases is of fundamental and practical importance for science and technology, for example, the detection of explosives in airports or biomarkers in medical diagnostics. Often the Faraday cup is employed to transfer ion concentrations in an electric current that is then amplified and measured. One of the main challenges is to increase the sensitivity of detection. A novel concept has been developed that enables detection of individual ions in gases by tagging them with neutral nano-objects. The concentration of ionized molecules was measured and a detection limit of 5 cm$^{-3}$ was observed. It is anticipated that this concept opens doors for advances in detection sensitivity for many applications including security, medical diagnostic, trace chemical analysis.

## 1. Introduction

Measurements of ultra-low concentrations of molecules and ions in gases are of great interest in many areas of science and industry. For example, in atmospheric science, very low concentrations of ions and molecules determine nanoparticle formation by nucleation [1,2] and may affect climate change [3]. Phase transitions that include nucleation are important phenomena in physics and chemistry. The homogeneous nucleation and formation of new nanoparticles often occur on ions, e.g. in the Wilson cloud chamber [4] widely employed in high-energy physics. The nucleation is an essential stage in the production of nanomaterials [5]. Another important area of applications is clean room technologies for example microelectronics and pharmaceuticals. Detection of an ultra-low concentration of ionized molecules is crucial for security applications to identify explosives and illicit drugs in airports.

In medical applications and life science the measurement of Volatile Organic Compound (VOC) biomarkers as a diagnostic of cancer and infectious diseases is a rapidly growing area of metabolomics that promises to bring a non-invasive fast diagnostic to points of care [6,7]. An increase in sensitivity will enable diagnosis of earlier stages of diseases and increase patient survival rate. A single cancer cell can generate in the region of circa 10$^3$ biomarker molecules in the headspace [6,8]. This level of concentration is desirable for detection in many applications, e.g. for single cell or bacteria observations and drug development, but it is not achievable with existing technologies. Concentrations of ions and molecules in these cases are very small - often below parts per trillion (ppt) level.

Currently Gas Chromatography (GC) and Mass Spectrometry (MS) [9] based techniques are used to identify and quantify trace level of molecules in the air. To achieve sensitivity below ppt levels requires sample enrichments, e.g. by adsorption. Current techniques are close to their physical detection limits due to the thermal fluctuations in the electron gas of metals [10,11] or losses in the air-vacuum interface as for the MS method. Ion induced nucleation techniques that have emerged since the invention of the Wilson cloud chamber [4] have not evolved into a successful method for trace level detection of molecules because of background noise caused by homogeneous nucleation. It is extremely challenging to measure concentrations below the ppt level (circa 10$^{11}$ molecules per cm$^3$) in the air. This restricts progress in trace concentration measurements in many areas.

A novel concept of measuring the concentration of ionized molecules in gases that enables detection of individual ionized molecules by means of tagging them with readily detectable nano-objects has been discovered. It was found that this method where ions were tagged with electrically neutral objects, e.g. nanoparticles with radius 100 nm, can provide a breakthrough in sensitivity by enabling a single ion or electron to be detected. This provides an increase in sensitivity by three order of magnitude in comparison to existing methods. This concept was termed Individual Ion Tagging (IIT).

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## 1.1. Description of the IIT single ion detection concept

Single ion detection is accomplished by employing a novel detection principle: tagging of ions. Instead of amplification of a weak electric signal from the Faraday cup here we enlarge every ion by attaching to it an electrically neutral tagging object or simply tag. This creates a mixture of electrically charged (by ions) tags and neutral tags. Charged tags containing ions then separated from the neutral tags with an electric field and counted individually by an Optical Particle Counter (OPC).

It is important that tagging objects should be considerably larger than molecular ions to be individually detectable by an OPC. This implies a size limit on the tag radius $R_t > 100$ nm. In principle, tags can be detected also by a Condensation Particle Counter (CPC) [12]. This enables the reduction of tag size down to several nm but leads to low tagging efficiency due to reduction in the collision probability of ions with tags [13]. The optimal radius range for tags therefore is 100–300 nm.

In addition, tags should be electrically neutral. This excluded tag formation methods based upon dispersion of bulk material into nano-objects, e.g. nebulization of liquids. Homogeneous nucleation of liquid or solid particles from a gas phase is a preferable method of generating tags [14]. In practice multi-component nucleation is employed to generate neutral tags because it is more efficient [15].

Molecular ions are tagged in a tagging chamber. Collisions of ions with tags are mainly controlled by the Brownian diffusion that can be enhanced by turbulent diffusion [12,13]. The concentration of tags in the tagging chamber should be much greater than the sample ion concentration to sustain tagging probability ($P_t$) close to 1. For the volume of the tagging chamber ($V_{tc}$) should be sufficiently high to satisfy inequality (1)

$$e^{-f_c \frac{V_{tc}}{Q}} \ll 1 \qquad (1)$$

Here $f_c$ is the ion-tag collision frequency [12,13] and $Q$ is the flow rate through the tagging chamber. Expression (1) is derived from the definition of ionization rate $dN_{it}/dt$ where $N_{it}$ is the number of tagged ions at time $t$

$$\frac{dN_{it}}{dt} = f_c(N_i - N_{it})$$

Integration of this equation at initial condition $N_{it} = 0$ at $t = 0$ leads us to the expression

$$\frac{N_{it}}{N_i} = 1 - e^{f_c t_r}$$

Here $t_r$ is the residence time in the chamber ($t_r = V_{tc}/Q$). For desirable $P_t$ ($P_t = N_{it}/N_i$) to be close to 1 the exponent should be much less than 1. Thus in the tagging chamber a mixture of charged tags that collided with ions and neutral tags is formed.

Charging probabilities were calculated assuming uniform concentrations of neutral tags and charged tags for different $V_{tc}$ and flow rates, Fig. 1. The ion-tag collision frequency was calculated from the collision theory [12] assuming that ion - surface collisions are negligible. The charging probability is influenced by the volume of the tagging chamber and the flow rate. An increase in the volume $V_{tc}$ and a decrease in the flow rate result in charging efficiencies to be close to 100% ($P \sim 1$). To achieve high charging probability at $Q = 1$ cm$^3$/s

Each charged tag has the same properties as the original neutral tag except for electrical mobility. Therefore, electrically charged tags can be separated from the neutral tags in an electric field. For this two parallel adjacent laminar flows are formed in the extraction chamber: the sample flow from the tagging chamber and a clean air flow without ions and tags generated by a separate pump. When a suitable strength electric field [12] across the flows
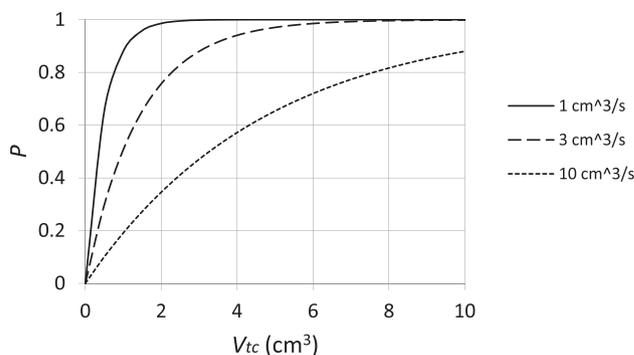


**Fig. 1.** Charging probability ($P$) of 300 nm spherical tags density 1200 kg/m$^3$ vs. volume of the tagging chamber ($V_{tc}$) at various flow rates by N$^+$ ions.

is applied charged tags from the sample flow are moved into the clean air flow. Therefore, the clean air flow coming out of the extraction chamber contains only charged tags. These tags are individually counted with an OPC. The number of charged tags is equal to the number of ions (subject to expression 1) hence readings from the OPC delivers number of ions in the sample flow. Thus number of ions is counted without employing the Faraday cup and measuring an electric current.

The number of ions in a sample is equal to the OPC tag counts only if each tag is charged with a single elementary charge. For this the number of tags should be much greater than the number of ions in a sample.

## 1.2. IIT ion counting device

This concept was realized in a set-up containing 4 modules: a tag generator, a tagging chamber, a tagged ion extraction chamber and an OPC (Fig. 2a). The first module is the tag generator where spherical particles of $R_t = 300$ nm are formed by homogeneous nucleation from dimethyl phthalate. It comprises a stainless steel condenser and a glass saturator with a heater [16].

The second module (the tagging chamber) is a stainless steel cylinder of 20 cm$^3$ volume with two inlets and an outlet (Fig. 2a). A sample flow (0.2 L/min) containing ions enters the tagging chamber through one inlet and the flow of tags (0.3 L/min) enters the chamber through the other inlet. Under these conditions, the number concentration of tagging objects ($N = 3 \cdot 10^6$ cm$^3$) was much greater than the number of ions and
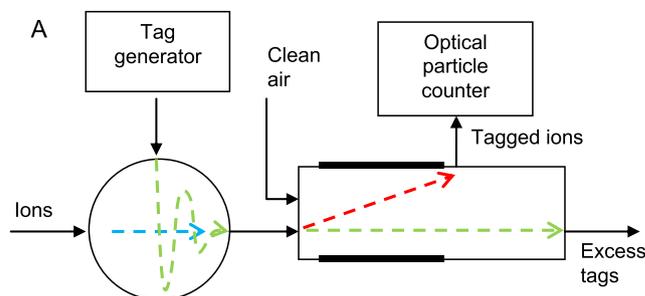


**Fig. 2a.** Schematic of the ion counting set-up. The tagging object trajectories are shown with dashed green lines. The tagging chamber is shown with a circle. The blue dashed line schematically shows ion trajectories in the tagging chamber. The red dashed line indicates the direction of the tagged ions, and the green horizontal line shows trajectories of neutral tags in the extraction chamber (two bold horizontal lines show electrodes in the extraction chamber). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

the ion tagging efficiency was 98%. The mixture of charged tagging objects and neutral unchanged tags is directed to a charged tag extractor through the tagging chamber outlet.

The rectangular charged tag extractor (third module) is formed by two copper plates (4 cm x 10 cm) spaced by a 0.5 cm spacer [16,17]. Inside the extractor two parallel laminar flows are formed. The mixture flow inlet (delivering charged and neutral tags) is shown at the bottom of the extractor on the left and a clean air flow above it (Fig. 2a). Without an electric field in the gap between the electrode plates the mixture of charged and neutral tags moves horizontally in the lower flow to the excess tag outlet. When a sufficient strength electric field [12,17] is formed between the stainless steel electrodes charged tags (tagged ions) are separated from the rest of the neutral tags and moved into the adjacent clean laminar gas flow that is directed then to an OPC (MetOne, Pacific Scientific Instruments).

Finally, the tagged ions are counted in the OPC individually [16,17]. Because the number of charged tags is equal to the number of ions the OPC reading provides the ion number.

## 2. Results and discussion

The IIT method potentially enables a single ion in a sample to be detected. However, in the set-up there might be some losses of ions, for example due to $P_t < 1$ or the tagged ion extraction efficiency being less than 100%. The total losses of ions in the set-up described here were found to be less than 20%. Therefore, at least 80% of ions could be detected with the first IIT set-up built. In the second optimized version of the set-up the losses were considerably reduced enabling detection up to 96% of ions in a sample mainly due to optimization of the tagging chamber volume. The losses were evaluated by directing to the tagging chamber a known number ions taken from the outlet OPC.

To evaluate the lower detection limit of the IIT the set-up (Fig. 1a) it was tested with clean air where airborne particles and all ions were removed by employing an ion trap [12] and an aerosol filter (Fig. 2b). In these tests ion counts measured were $5 \pm 1$-counts per $cm^3$.

The origin of these background counts was investigated using external metal flasks that were placed between the ion trap and the inlet of the tagging chamber, Fig. 2b. Several external flasks of volume from 20 $cm^3$ to 3000 $cm^3$ were tested. For example, with an 80 $cm^3$ external flask the average number of counts measured was 44 counts per $cm^3$. Also sharp peaks up to 1500 ions per $cm^3$ were observed (Fig. 3).

It was found that the material of the external flask does not affect the counts. In addition, removal of radon from the air using clean nitrogen from a high-pressure cylinder does not affect the number of counts either. On the contrary, peaks and average background counts were influenced by the volume of the external flask. Therefore, it might be suggested that the counts observed in the
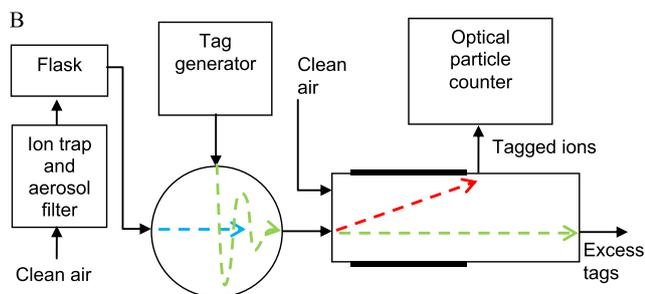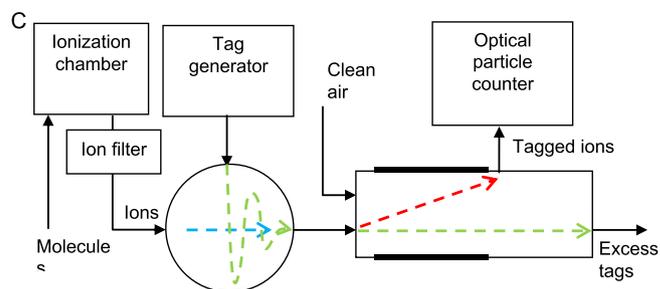


**Fig. 2c.** Schematic of the molecular counting set-up with an ionization chamber and an ion filter. The rest is the same as in Fig. 2a.
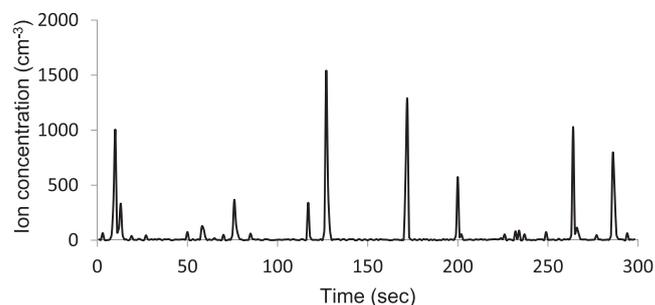


**Fig. 3.** An IIT counts vs. time for a stainless steel external chamber of 80 $cm^3$ internal volume.

clean air were associated with ions generated by cosmic rays ionizing air molecules in the external flask. The total volume of air conduits in the IIT without an external flask was less than 20 $cm^2$. This volume-effect shows that the background ion count level found for the set-up (Fig. 2a) is influenced by the geometry of the set-up and it is not defined by the physical limit of the IIT method. Therefore, potentially the background count level can be reduced.

The IIT method enables the counting of molecules as well as ions. For this an ionization means should be added to the IIT set-up. A $^{241}$Am ionization chamber [17] was added in front of the set-up (Fig. 2c). Any ionizing source generates in the air a number of different ions, e.g. $^{241}$Am $\alpha$-emitter produces $O_2^-$ and $H_3O^+$ based ions. To count molecules an ion filter is required to select ions of interests. A Differential Mobility Spectrometer (DMS) ion filter [12,18] was placed between the ionization chamber and the tagging chamber (Fig. 2c). The filter enables one to scan the ion mobility parameter and record mobility spectra as a function of the compensation voltage (CV). Therefore, only ions of chosen mobility could pass through the ion filter to the IIT set-up. With the ionization chamber and the ion filter, several molecules have been detected including cocaine, trinitrotoluene, iso-propanol and acetone. The latter two are typical VOC metabolites often found as *in vivo* and also *in vitro* samples and identified as possible biomarkers of some pathological conditions.

To confirm the detection capability of the method a reference method is needed. Unfortunately, there are no methods available to generate and to quantify such low concentrations of ionized molecules in the air at which the IIT is capable of measuring (down to hundreds and tens of molecules per $cm^3$). The detection capability of the IIT method was evaluated assuming that for ultra-low concentrations the ion losses are equal to losses for larger concentrations. The concentration measured in tests was down to hundreds of ionized molecules per $cm^3$, e.g. 560 per $cm^3$ for acetone (Fig. 4). A signal of 15 molecules per $cm^3$ could be reliably detected with 3:1 signal noise ratio. The minimal detection level for this sig-



**Fig. 2b.** Schematic of the set-up with an ion trap and a flask. The rest is the same as in Fig. 2a.
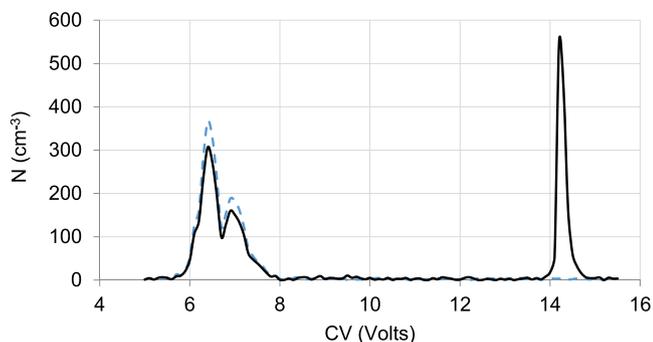
**Fig. 4.** IIT counts vs. compensation voltage of the ion filter. Clean air containing traces of acetone was introduced into the set-up according to Fig. 2c. The background signal from the clean air is indicated with a dashed line, while the signal from air with acetone is shown with solid line.

nal/noise level would be 15 molecules per $cm^3$. This is equivalent to measuring an electric current of the order of atto-amps that is practically impossible (or very difficult) at room temperatures with conventional methods.

The IIT method is confirmed to be able to count individual ionized molecules. This is also sufficient to monitor VOC metabolites emitted by single cells and single cell bacteria making it potentially possible to detect cancer and other biomarkers at earlier stages.

The IIT breakthrough in sensitivity of charge detection opens new horizons in many areas. For example, one such application of IIT could be detection of high energy cosmic ray particles with energy above $10^{16}$ eV. The cosmic ray flux for these energies is below 1 $m^{-2}$ $yr^{-1}$. It is a challenge to detect these particles with conventional means. However, there are no physical limitations to building an IIT detector with the sensor area much greater than 1 $m^2$, e.g. up to $10^4$ $m^2$ or even greater. This may help in finding the maximal energy of cosmic ray particles: the Greisen–Zatsepin–Kuzmin limit [19]. There is no reason why IIT could not be applied for detection of weakly interacting massive particles in environments where cosmic rays are not present such as deep underground mine laboratories.

The origin of peaks of different height in cosmic ray tests (Fig. 3) is likely to be associated with the different energies of particles perhaps protons ionizing air molecules in the flask. Also it can be expected that different particles, e.g. protons, muons, electrons can generate different number of ions. Therefore, IIT can be employed to detect and possibly identify ionizing radiation for security and other applications. It is anticipated that this concept opens doors for advances in detection sensitivity in chemistry, biology, medicine and physics.

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