

# IONIZATION CLUSTERS AT DNA LEVEL-EXPERIMENTAL MODELING

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**ABSTRACT** The importance of initial clustered damage to DNA is a hypothesis, which has to be approached also from physical modeling of the initial products of interacting single charged particle at DNA. A new tool for such studies, presented here, is based on modeling of the ionisation patterns resulted due to single charged particle crossing a nitrogen cavity of nanometre size. The nanometer size sites equivalent in unit density to DNA and nucleosome, have been modeled in a device, called Jet Counter, consisting of a pulse operated valve which injects nitrogen in the form of expansion jet into an interaction chamber. The distributions of the number of ions in a cluster created by single alpha particle of 4.6 MeV along 0.15 nm to 13 nm size tracks in nitrogen have been measured. The new descriptors of radiation action at DNA level is proposed.

## INTRODUCTION

The cell endpoints such as inactivation, mutation and neoplastic transformations are initiated by a clustered damage to DNA. These, are produced by a charged particle traversed through single DNA helix and nucleosome. To date, the basic pattern on energy deposition (also cluster formation) at the nanometre level are solely based on track structure calculations. A few attempts to date for elaborating an experimental method for studying the ionization cluster formation at nanometre levels were reported (1-6). Among these the solution known as Jet Counter (7), proved to be very suitable for experimental modeling of the frequency distribution of ion cluster sizes formed in DNA size volume due to single track of charged particles. The stochastic quantity measure by this technique is cluster size and its frequency distribution. The main difference between microdosimetry technique (at cell size) and technique developed for nanometer sizes is that first measure stochastic quantities which are energy deposition related while the later fluency related. The area of application of Jet Counter technique is discussed.

## MATERIAL AND METHODS.

### Modeling of nanometre size.

Similarly to the microdosimetry technique (where a mammalian cell is modelled as a gas cavity filled with tissue equivalent gas) it has been assumed that the first approach for studying ionization processes at nanometer level can be modeled in gas cavity with an appropriate size. A gas cavity which simulates a nanometric volume (in unit density scale) is created by method explained in Fig 1A. A simulated nanometre size, SNS, is obtained by pulse expanding of nitrogen (jet) to a volume of interaction chamber, IC. The IC volume, has cylindrical form 10 mm diameter and by 15 mm height, with stainless steel walls (TE material can be used as well). The nitrogen jet is created due to pulse operated valve, PZ, which injects nitrogen from a volume, R, over a valve, through a nozzle with a 1 mm diameter orifice to IC below a nozzle. At lower part of the IC, a cavity between grid S and the edge of IC is a simulated nanometre size, SNS, site, i.e. a cavity from which ions are collected with known efficiency. The SNS

cavity is schematically shown in Fig 1B as an enlargement. It forms a cylinder with height of half of its diameter, shown in Fig.1C. The timing chart of nitrogen flow through the SNS, seen in Fig.1 (bottom), has been established based on transmission of monoenergetic electrons through a layer of nitrogen, across the diameter of SNS cavity. The minimum at a transmission curve means maximum density of nitrogen. The maximum instant density of nitrogen lasts around 200 us and for this time window the SNS site is defined. The instant density within interaction chamber is controlled by nitrogen pressure inside the reservoir R. The position of an electron gun, EG, and an electron detector CH1, with respect to alpha source and Si detector is shown in Fig. 1D.

### Method for measuring of ion cluster size spectra.

There are two modes of operation of Jet Counter, namely, first – in coincidence with incoming single particle, especially suitable for the experiments with heavy charged particles (microbeam experiments) and second, without coincidence, for photons, neutrons and low energy electrons. The coincidence mode is applied for measuring of the spectra of ion clusters for alpha particles from a source of  $^{241}\text{Am}$ , shown in Fig.1A. The collimated alpha particles, 4.6 MeV, from a source (gold plated AMM2 type Amersham) intersect a SNS chamber (alongside of its diameter) at half of its height and are registered by a Si detector. The ions created, by single alpha particle along its path (as well as the delta electrons) within the SNS, are removed by an electric field of a grid, G, then guided through G1 to DM205IG detector. The pulses from this detector are amplified by fast preamplifier VT 120 and enter the 10 ns resolution multiscaler, MCS, type 914T ORTEC. The associated electronic set up as well as the timing chart of the experiment for registering the signal clusters is shown in Fig.1A. The channel on the MCS is advanced after each pulse from Si detector. In this way a signal cluster spectrum, for a given thickness of SNS is recorded. From the recorded data, the signal cluster distribution as a function of cluster size is derived. One of the important feature of this method is ability to measure the “zero size” event rate. The measured spectra are deconvoluted to the true number of ion spectra (8).

## RESULTS

The results of the measurements of signal cluster spectra for the cylinders with the following dimensions in nm (diameter by height) 0.15 x 0.075, 1 x 0.5, 2.2 x 1.1, 4.9 x 2.45, 8.8 x 4.4 and 13 x 6.5 of the sensitive volume irradiated by narrow beam of 4.6 MeV alpha particles, (<sup>241</sup>Am gold plated source), are seen in Fig.2. Results for 300 eV electrons for a sensitive volume 2 nm by 1 nm are seen in Figures 2 (bottom right).

## INTERPRETATION OF THE RESULTS

The results of measurements with Jet Counter are in form of probability distribution of size of ion cluster for a given geometry of irradiation. The ionisation cluster size was defined here as the number of ionizations produced by charged particle across its full track within this volume. The shape of the cluster probability was compared with Poisson distribution. For this purpose, the first moment of the experimental distribution was calculated and used as the mean value of a Poisson-like distribution. The results are presented in Fig. 2 as the solid lines. It must be added that no normalization procedure was applied to experimental results. As seen (Fig.2) the general assumption that ionization cluster probabilities produced by heavy charged particles are governed by the Poisson law is completely confirmed experimentally, at least, in the case of 4.6 MeV  $\alpha$ -particles in nitrogen.

## CLUSTER MODELING AT DNA

The ionization pattern at DNA can be studied in simulated nitrogen volume 2 nm diameter 1 nm height. **The frequency distribution of cluster size for a given charged particle versus ion cluster size derived experimentally for 2nm x 1nm site can be assumed as new descriptor of radiation action at nanometre level (in unit density scale).**

Based on this distribution the following quantities can be derived, namely:

**Cumulative frequency** of obtaining cluster size  $F_k$

$$(\geq k) = \sum_k^{\infty} f(n) \quad \text{for } k = 1, 2, 3, 4$$

**First moment of frequency distribution** i.e. the mean number of ions (ionizations) in a cluster for a given geometry of irradiation as well as for a given simulated nanometre size.

## Example of application of Jet Counter

Radiation Physics: - direct comparison of the experimental data with Monte Carlo calculations (Grosswendt and Pszona (9) this symposium) as the method for verification of ionisation theory for charged particles. The experimental results for alpha particles were compared with Monte Carlo results done by B. Grosswendt (this conference) and excellent agreement has been found.

Radiobiology: i/ Modeling of ion cluster distribution at DNA and nucleosome levels for single

beam experiments. ii/ As an approach for interpretation of yield of ssb and dsb per charged particle using cumulative distribution for cluster size not less than two. The cumulative distribution  $F_2(\geq 2)$  per unit fluence, derived from results for 300 eV electrons and 4,6 MeV alpha particles (shown in Figures 2) are in qualitative agreement with data on yield of dsb by Kampf and Eichorn (10 fig. 4).

Radiological Protection – new approach for deriving risk parameters based on bio- effectiveness concept by Watt (11).

## CONCLUSIONS

It has been confirmed that the JET COUNTER is an unique setup with ability to simulate the cylindrical sensitive volumes variable between 0.15 x 0.075 to 13 x 6.5 nm in unit density scale for nitrogen gas. It is evident that with more dense gas (e.g. propane) the simulated range can be extended to 20 nm.

i The frequency distributions of ion cluster size created by 4.6 MeV alpha particles for 0.15nm to 13 nm tracks in nitrogen have been measured for the first time. These distributions follow Poisson rule.

ii Ion cluster spectra for sub 300 eV electrons interacting with 2nm by 1nm nitrogen site have been determined experimentally. This experiment is the first ever conducted.

iii. The frequency distribution of ionisation clusters measured for 2 nm by 1 nm simulated volume is the new basic descriptor for radiation damage at DNA level.

## ACKNOWLEDGEMENTS

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## References

1. Pszona S. *Studies for nanometer microdosimetry*. Annual report on research project COO 3243-2. USAEC, New York, pp 102-107 (1973)
2. Chmelewski D, Parmentier N, Le Grand J. *Dispositive experimental en vu d'étude dosimetriques au niveau du nanometre*. In: Proc 4<sup>th</sup> Symp on Microdosimetry. (Report EUR 5122) Commission of the European Communities, Luxembourg, pp 869-885 (1974).
3. Pszona S. *A track ion counter*. In: Booz, J, Ebert HG, Smith BGR (eds) Proc 5<sup>th</sup> Symp on Microdosimetry. (Report EUR 3452) Commission of the European Communities, Luxembourg, pp 1107-1121 (1976).
4. Kellerer A. *Conditions for microdosimetry in region of diameter less than 0.1  $\mu$ m*. Annual report on research project COO 3243-3. USAEC, New York (1974).
5. Pszona S, Gajewski R. *An approach to experimental microdosimetry at the nanometre scale*. Radiat Prot Dosim 52: 427-430 (1994).

6. Shchemelinin S and all., *Ionization measurements in small gas samples by single ion counting* Nucl. Instr. and Meth. A 368 859-861 (1999).
7. Pszona S, Kula J, Marjanska S. *A new method for measuring ion clusters produced by charged particles in nanometre track sections of DNA size.* Nucl Instrum and Meth Phys Res A 447: 601-607 (2000).
8. P.Colautti et al., *Radiation quality Assessment Based on Physical radiation interaction at Nanometer level* LNL-INFN (REP) 161/2000: 57 (2000).
9. B.Grosswendt and S.Pszona. *The formation of ionisation clusters by alpha particles in „ nanometric” volumes of nitrogen: experiment and calculation,* 13 Symposium on microdosimetry to be published.
10. Kampf G. and Eichorn K. *DNA strand breakage by different radiation qualities and relations to cell killing: further results after the influence of alpha particles and carbon ions,* Stadia Biophysica **93**(1) 17-26 (1983)
11. Watt D.E. *A unified system of radiation bio-effectiveness and its consequences in practical application.* Radiation Protection Dosimetry 70(1-4) 529-536 (1997)

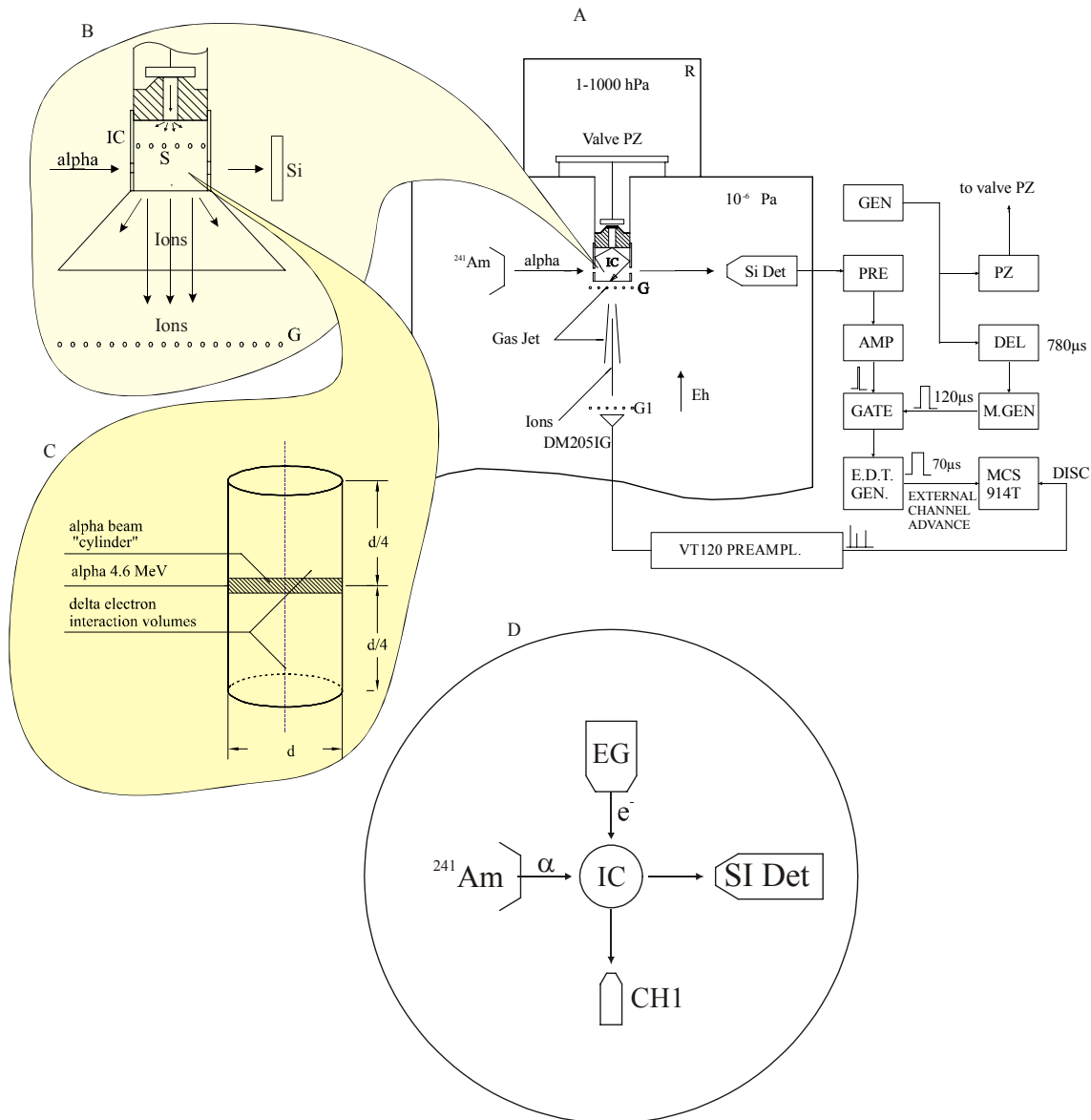


Figure 1. Schematic view of the Jet Counter: A- configuration for the experiments with alpha particles, B- sensitive volume inside the interaction chamber, IC; C- schematic presentation of sensitive volume in unit density scale with irradiation geometry. D- cross section of Jet Counter through sensitive volume at beam line pattern, showing the positions of detectors. EG- electron gun; PZ- piezoelectric valve; CH1- electron detector, DM205IG- ion detector, Si – alpha particle detector. IC interaction chamber.

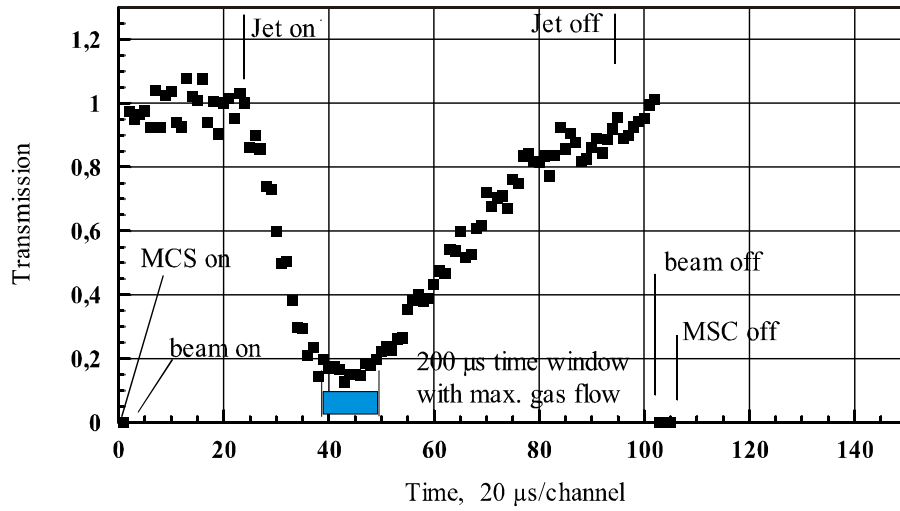


Figure 2. Transmission of 100 eV electrons through nitrogen jets, timing chart. The time window, 200  $\mu$ s, (as GATE ON) is shown.

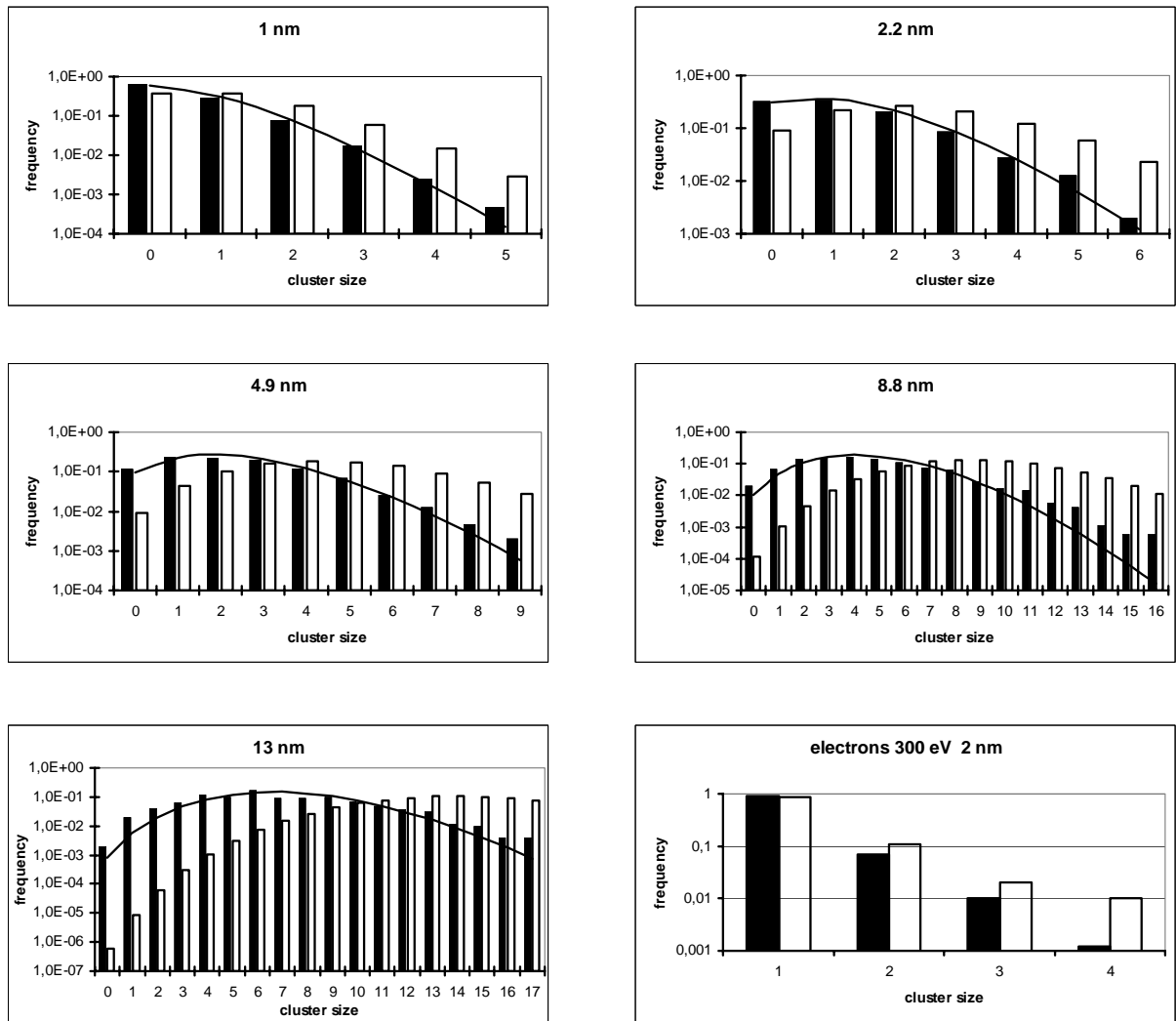


Figure 3. Frequency distribution spectra for different diameters of sensitive volume in nanometer irradiated by alpha particles. Separate spectrum for 300 eV electrons. Full bars – experimental spectra, open bars – deconvoluted spectra, solid line - Poisson distribution.