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Post-focus expansion of ion beams for low fluence and large area MeV ion irradiation: Application to human brain tissue and electronics devices

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ABSTRACT

Irradiation with ~3 MeV proton fluences of 10^6–10^9 protons cm^{-2} have been applied to study the effects on human brain tissue corresponding to single-cell irradiation doses and doses received by electronic components in low-Earth orbit. The low fluence irradiations were carried out using a proton microbeam with the post-focus expansion of the beam; a method developed by the group of Breese [1]. It was found from electrophysiological measurements that the mean neuronal frequency of human brain tissue decreased to zero as the dose increased to 0–1050 Gy. Enhancement-mode MOSFET transistors exhibited a 10% reduction in threshold voltage for 2.7 MeV proton doses of 10 Gy while a NPN bipolar transistor required ~800 Gy to reduce the h_{fe} by 10%, which is consistent the expected values.

1. Introduction

Complex systems such as vertebrates, automobiles, computers, satellites, mobile phones etc can be thought of as being made up of a large number of smaller communicating functional units. For example, different cell types (basic biological units [2]) are organized into different tissue types which in turn make up the organs of vertebrates [2]. MeV ion and nanobeams are very powerful tools for study of single events effects in individual units [3,4]. Table 1 presents the fluences for impingement of an average of one ion per unit for different size units. (Here "units" is taken to mean the basic building blocks of the system, e.g. biological cells or devices in a microcircuit.) The fluences in Table 1 should be considered as an approximate guideline because the average fluence to disrupt a system may be higher or lower depending on if the units are packed in 2D (one ion penetrates one unit) or 3D (where one ion can penetrate a number of units), the cross-section for disrupting a single unit and the system sensitivity due to disruption of a single unit. There is no a priori reason why scaling from a single disturbance in a single unit to disturbances in an entire system is linear. This is because processes such as DNA repair mechanisms and error-correcting algorithms may come into play. It should also be borne in mind that in a complex system, the ion induced damage may only be detrimental after a considerable period of time. (e.g. The evolution of a cancer tumour, or when corrupted data stored in disrupted memory cell is read-out and used.) Hence, it is not a reliable approach to determine the frequencies of different disruption modes of a complex system directly from single event studies, instead tests on either the whole, or a representative part of a complex system must be made.

MeV ion micro/nanobeams are serial scanning instruments. This means they are too slow to deliver fluences corresponding to single events in a unit over of an entire system consisting of 10^6–10^{12} units in a reasonable time (100–1000 s). The conventional approach for system-level studies in both electronic and radiobiological studies is to use scanned or broad high energy ion beams of 10–150 MeV which can penetrate overlying biological tissue or encapsulation and circuit boards. The cost of operating these facilities is very high and generally access for testing is low due to competing experiments. Lower energy scanned broad beam MeV ion irradiation systems such as used for ion implantation typically deliver current fluxes of 1 μA cm^2 s^{-1}. This would require just 1.6 ms to deliver a fluence of 10^8 ions cm^2. It is difficult to

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Table 1
Fluences for irradiation of the basic building units of typical complex biomedical and electronic systems with an average of one ion hit per unit.

Unit	Typical area	Fluence (ions cm^{-2})
Small transistor	1000 nm^2	1×10^{11}
Large transistor	3 μm^2	3.3×10^{7}
Cell nucleus	25 μm^2	4×10^{6}
Eukaryote cell	100 μm^2	1×10^{6}

reduce the ions source current and accelerator system transmission by the sufficiently large factors which are needed to perform the irradiation within a reasonable time (1–1000 s). Furthermore, slow (magnetic) scanning speeds may result in only part of the system being irradiated at such short exposure times. It should also be noted that for scanned beam systems only part of the system is irradiated at any one time. These cannot then be used to test disruption mechanisms due to correlated impacts. Such time-correlated disruptions may originate from particle showers.

The group of Breese [1] have developed a broad-beam MeV ion irradiation technique for line and area irradiations based on expanding the ion beam after the conjugate focus in a MeV micro/nanobeam. Focused beam spots of 1 pA to 1 nA beam current can easily be produced in a micro/nanobeam. The ion fluxes after allowing a 1 pA beam to diverge behind the conjugate focus to 1 cm^2 area are on average 6.3×10^6 ions cm^{-2} s^{-1} which are well suited to irradiation with fluences at the 10^8 ions cm^2 level. A special feature of the low MeV-energy ions, such as protons available with this technique is that they have closely similar energies to the energy with which the higher energy ions used in conventional radiation damage studies arrive at the Bragg peak. The excess energy in conventional experiments is dissipated in traversing overlying material such as overlying tissue or circuit boards and encapsulation.

Here we report work using the post-focus expansion method for study of proton irradiation of neurospheres (3D cohorts of neural cells) and developing qualification of highly integrated components-of-the-shelf (COTS) electronics for near-Earth orbit nanosatellite missions we have developed a system based on the beam expansion optics.

2. Experimental method

The Oxford Microbeam system attached to the 1.7 MV Tandetron accelerator at Haute Ecole Arc Ingénierie, La Chaux-de-Fonds, Switzerland was used for this study. 2.7 and 3 MeV proton beams were used. A drift section consisting of an extension tube with a KF-32 connection on one end, allowed an end-piece with a either a fluorescent screen or a 1 mm × 1 mm and 200 nm thick Si_3N_4 radiation window to be mounted after the drift length. A microfluidic cassette (Fig. 1) for neurosphere irradiation or a circuit board for testing electronic devices could be mounted behind the radiation window. (The energy loss in the radiation window and a mm or so of air between the exit window and sample was negligible compared to stopping in the sample.) The compact size of the set-up allowed the irradiation to be performed in a normal laboratory environment with the external beam enclosed by a PMMA box with door and i.r. motion interlocks that shut down the accelerator to prevent exposure to the external beam. In addition, precautions were taken to limit n- and γ-ray personnel exposure from the 2.7 and 3 MeV proton beam striking the apertures.

The fluence Θ was determined by measuring the beam current before and after each exposure from a metal sample moved into the beam focus and calculating the exposure time using a factor for the beam expansion determined from the WINTRAX code [5] and verified using an internal fluorescent screen. The use of this approach allowed the different objective and collimator sizes to

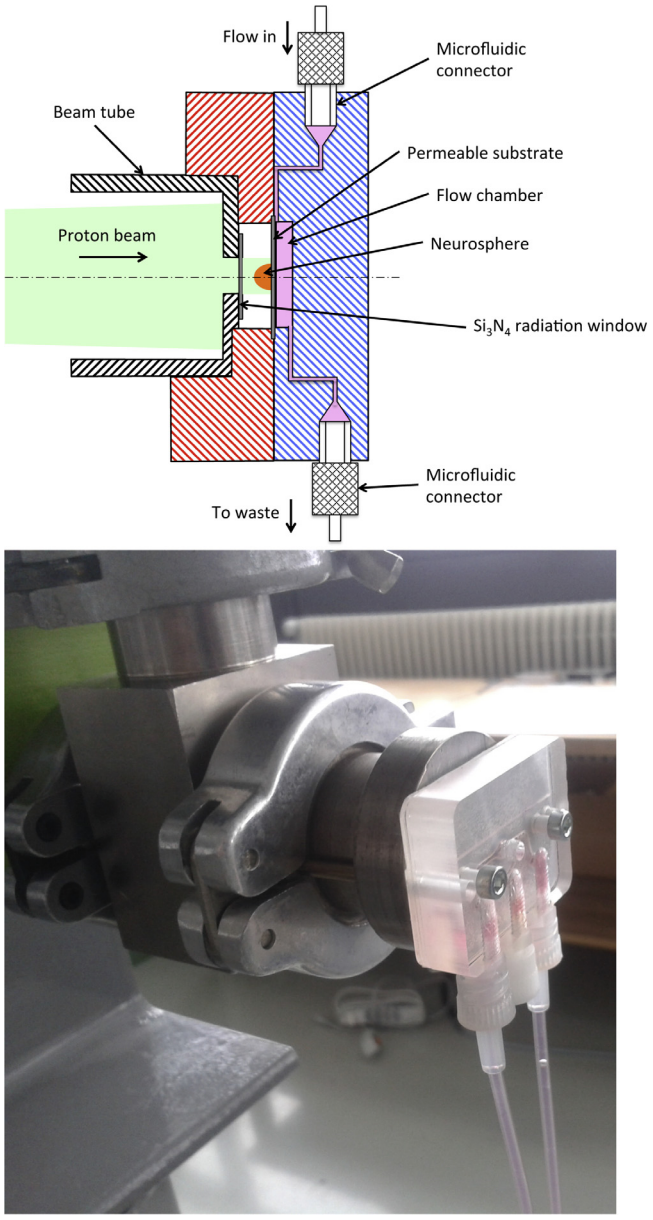

Fig. 1. Schematic illustration of the neuropshere microfluidic irradaition cassette. (a) Schematic section. (b) General view.

be taken into account. The average dose D in a sample of density ρ and thickness t is then:

$$D = \frac{\Theta}{\rho t} \int_0^t \frac{dE}{dx} dx \quad (1)$$

In the limit of small t, this reduces to:

$$D = \frac{\Theta}{\rho} \frac{dE}{dx} \quad (2)$$

The stopping forces in Eqs. (1) and (2) were obtained from the SRIM code [6,7].

2.1. Ion irradiation of neurospheres

The neurospheres were neural progenitors derived from induced pluripotent HIP stem cells, (from MTI-Globalstem Inc., USA). These were cultivated at an air–liquid interface on porous growth substrate (PTFE membrane) to generate a 3D brain tissue-like structure containing a few thousand cells. Human cells were used for the

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