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Nuclear Instruments and Methods in Physics Research B 231 (2005) 207–211

NIM B
Beam Interactions with Materials & Atoms

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A single-particle/single-cell microbeam based on an isotopic alpha source

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Abstract

A single-cell/single-particle microbeam has been designed in which the radiation source is a high specific-activity alpha-particle emitting radioisotope, rather than a particle accelerator. The source is imaged at the focal point of a compound magnetic lens array. A novel precision microscope stage with an extremely compact design is included with the endstation's locating, targeting and imaging system. This arrangement allows a 4 m long vertical beamline without any bending magnets. The permanent magnet lens design is derived from an electrostatic lens used in our laboratory in an accelerator-based microbeam. The stand-alone microbeam is expected to produce a 10 μm diameter beam, and will serve as a high-end instrument in a biology laboratory, to precisely deposit ionizing radiation damage within single cells.
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PACS: 41.90.+e; 41.85.Ew; 06.60.Sx

Keywords: Microbeam irradiation; Radiobiology; Isotopic; Stand-alone; Accelerator

1. Introduction and overall design

Columbia University's Radiological Research Accelerator Facility (RARAF) is home to a single-cell/single-particle microbeam based on a 4.2 MV Van de Graaff particle accelerator [1]. During the summer of 2005 this accelerator will be replaced with a 5 MV Singletron from High Voltage Engineering. Through the course of the replacement procedure, RARAF must provide its users who conduct biology-driven experiments an alternative single-particle/single-cell microbeam. This will be accomplished with a stand-alone microbeam (SAM) using a high specific-activity isotopic radiation source and a custom magnetostatic lens assembly as well as custom endstation components. RARAF will keep the SAM active after the new accelerator is installed to increase experimental microbeam capacity, and to reduce the competing demands of facility development

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doi:10.1016/j.nimb.2005.01.058

and biological experimentation. In addition, the design is simple and inexpensive enough that the SAM can become a routine tool in any biology laboratory.

The beam is to be focused by 24 magnetostatic elements constructed into a compound lens. The source for the ions will be a 6.5 mCi radioactive alpha-particle emitter, plated on the tip of a wire. Alpha particles emitted from the source will be focused using a compound magnetic lens (made from permanent magnets) into a 10 μm spot. The SAM will be fitted with a voice-coil stage (VCS) for placement of the cells to be irradiated. We will use our existing beam deflector, used to enable fast opening and closing of the beam, enabling single particle irradiations.

2. High specific-activity isotopic radiation source

The radioactive source at the base of the SAM must be a monochromatic alpha emitter; its half life should be short enough so that sufficient activity can be obtained, but long enough so that it has a reasonable working life. The most appropriate radioisotope for this purpose is ^{210}Po ($t_{1/2}$ = 138 d). It emits a monoenergetic 5.3 MeV alpha particle, practically no gamma radiation, and it decays to a stable daughter (^{206}Pb).

By plating a 200 nm thick layer of pure ^{210}Po onto the tip of a 1 mm diameter rod, our calculations indicate we will obtain a 6.5 mCi (2.4×10^8 dps) source with 40 keV energy spread [2]. Assuming the alpha particles are emitted to 4π and an acceptance of 10 mrad μm for the ion optics (see below) we expect this source to yield a beam flux of just over 1 alpha particle/s at the focal plane, which is sufficient for the single-particle microbeam.

3. Ion optics

We are constructing a compound lens system similar to the one used in the electrostatic version which relies on the accelerator as the source. However, the SAM lenses have been designed around permanent magnets [3], rather than an electrostatic source. It has been shown that the spherical aberrations in a magnetic triplet are about three times lower than in an equivalent electrostatic quadrupole triplet [4].

STI Optronics routinely manufacture tunable magnetic quadrupoles, based on movable permanent magnets (see Fig. 1) and will build 3000 of them for the planned Next Linear Collider. The lack of large coils in the design allows for a smaller pole-face gap for the magnet, resulting in better focusing properties. The use of permanent magnets eliminates the need for costly power supplies and bulky cooling equipment while also significantly simplifying SAM operation. The user will be able to optimize the magnet settings just once and then to "lock" them and not touch them again. As there is a single projectile particle with a fixed energy, the SAM will continue to operate without further adjustments (if the radioactive source is changed at appropriate intervals).

The compound lens has been designed by Dymnikov [5], (who also designed the electrostatic lenses used in RARAF's accelerator-based microbeam) to have a 100× demagnification resulting in a 10 μm spot size from the 1.0 mm diameter source.

The beam was then simulated in GIOS98 as well by using finite element analysis (FEA). FEA

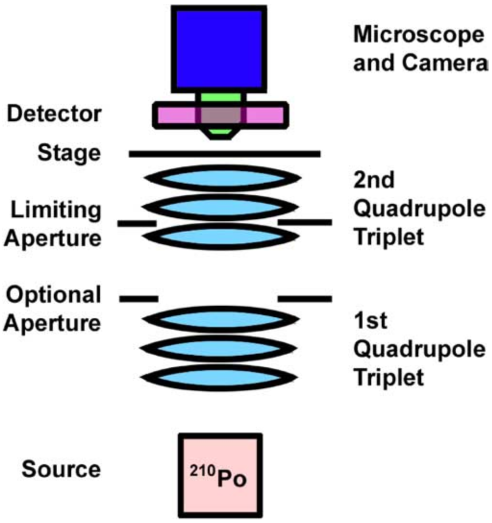


Fig. 1. The overall design of the stand-alone microbeam.

models enabled investigation into the cross-section of the beam to determine characteristics of the individual ions such as their final position in the beam spot at the biological sample in correlation with their position in a cross-sectional plane at intermediate axial locations along the beam path (see Fig. 3).

A simulation of the beam size in *X* and *Y*, incorporating a limiting aperture, as it passes through the ion optics system, is shown in Fig. 2. The optimized lens consists of two 4.25 cm long magnetic quadrupoles and a 8.5 cm long quadrupole with inter-magnet gaps of 1.67 cm and a bore of radius 6.35 mm. It should be noted that such a small bore radius is rather difficult to obtain with standard electromagnets. The design incorporates a strategically located rectangular aperture to reduce the spherical aberrations by catching particles on an unacceptable trajectory. The final design will likely also incorporate a pair of slit apertures (one each in *X* and *Y* at a location 5 cm from the last pole end of the final quadrupole element of the first triplet compound lens). While there may be some slit-scattering from the apertures (on the order of one per thousand, mostly from the rectangular aperture in the 2nd triplet), it should not be a problem for our specific biological applications.

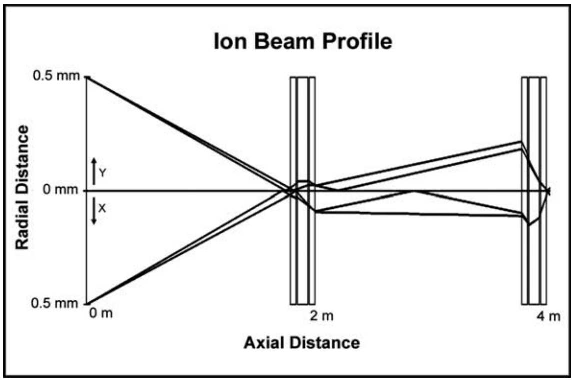
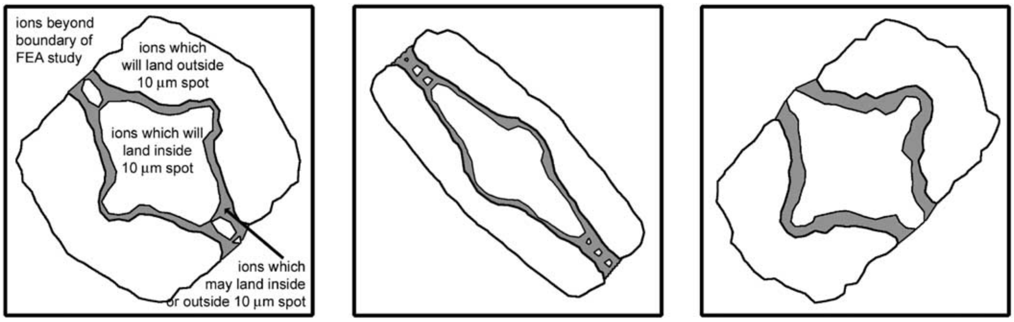


Fig. 2. Simulation of an alpha-particle beam passing through the compound magnetic lens system designed for the SAM. The two curves correspond to the two major axes of the beam.

4. Endstation

The non off-the-shelf components of the endstation include a custom gas detector developed at Columbia University [1] (mounted above the sample in such a way as to not interfere with the optics used to image the cells) as well as the voice-coil stage (VCS). And as is done with the present accelerator-based microbeam we will maintain the same minimal distance from the exit window to the sample to keep the particles from scattering too much in the open air.

The VCS is novel and designed at Columbia University [6] (see Fig. 4). It was built to meet or exceed: 4 mm range in *X* and *Y*, submicron precision, better than 5 μm accuracy over 5 mm deflections and better than 0.5 μm accuracy over 200 μm deflections, faster than 200 ms settling times, no



1.3 mm square view one centimeter before final triplet

5.6 mm square view one half meter before final triplet

0.7 mm square view between last two quadrupole elements of final triplet

Fig. 3. Sample beam cross-section FEA studies taken at various positions along the beam path as labeled. Does not incorporate limiting aperture.

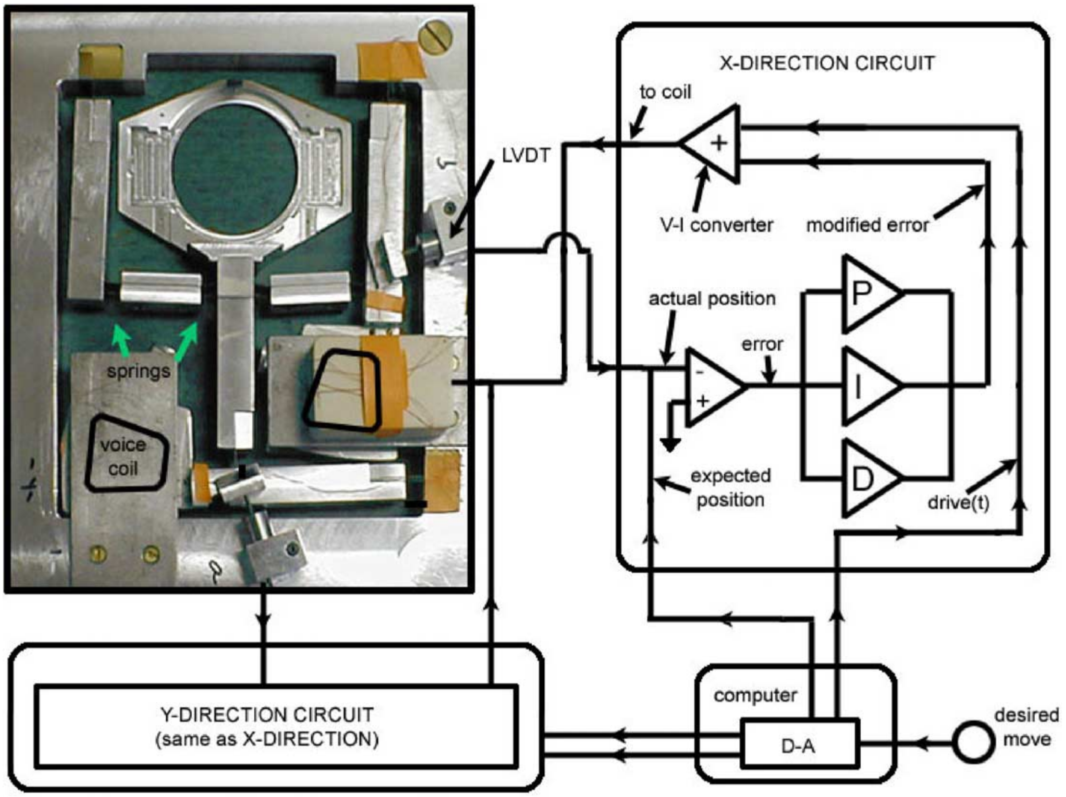


Fig. 4. Photograph of the microscope voice-coil stage as well as schematic of the control circuit.

taller than 2 cm, no wider than 20 cm, no longer than 25 cm, and portability from microscope station to station during experimentation. The VCS weighs about 1 kg and the majority of its construction material is aluminum.

The VCS utilizes principles similar to those found within sound wave transducers such as audio speakers. This use of current controlled actuators is attractive for the continuous positioning they provide. However, when operated in an open-loop configuration, they are not accurate because of hysteresis effects on the flexure mounts which were chosen as they are frictionless [7] and allow for very compliant motion in *x*–*y* directions and rigidity in the *z*-direction. Closed-loop feedback mode overcomes the hysteresis error. Such a mode of operation requires position monitors to send a signal into the feedback circuitry. For this, we have chosen a pair of linear variable differential transformers (LVDT) to measure the position of each pivot arm.

The closed-loop mode incorporates a proportional-integral (PI) circuit to provide improved positional precision. The PI utilizes the positional information from the LVDT and compares it with an expected position signal and feeds the resultant error signal (inverted) back into the voice-coil current drive. The errors that have been overcome include inaccuracies in mapping the *X* and *Y* position as a function of the two natural arcs of motion, non-linearities in the LVDT and other parts of the system, hysteresis effects, difference in microscope kinetic mount horizontal leveling, thermal expansion and other temperature effects, air currents and vibrations. For a 100 μm deflection (typical of a large deflection in a 40× view), the VCS with PI loop closed is able to deflect to within ±0.2 μm of the desired deflection.

A model predictive control (MPC) system [8] has been devised for driving the deflections. Rather than constantly polling the system, we use a non-standard MPC approach. While the forecast of the process is used (taken from the process model) it is only consulted once per deflection event. The handling of any errors is relegated to the PI closed-loop feedback system. Because the PI is not just referring to a step reference input to determine it's errors, the PI is able to provide the feedback that MPC models often require and the MPC is able to provide to the PI an expected system state.

5. Testing

The electrostatic compound lens is under vigorous testing and preliminary results confirm the modelling which was used for the design of both versions, the electrostatic and magnetostatic lenses. The electroplating process is under preliminary testing as well. The VCS has been fully tested and is ready for installation into the SAM.

Beam location will be determined by using a silicon wafer cleaved so that the crystalline structure creates an edge more than straight enough to resolve submicron beam profile details. Then we will use a 10 μm bead to obscure the beam and rotate in an outward spiral to confirm the exact center of the beam. Finally, a Secondary Electron Ion Microscope (SEIM) will be placed over the beam to visually confirm location and size [9].

6. Conclusions

The SAM has been designed and is under manufacture. FEA simulations indicate that the compound lens will provide a microbeam usable for single-particle single-cell irradiations. The isotopic ^{210}Po source will need to be replaced about once every few months. The system is designed using permanent magnets for focusing so that once settings are initially determined, we will not need further adjustment. The system uses off-the-shelf as well as custom endstation components for compact overall design.

Acknowledgments

The authors thank Alan Bigelow for discussions regarding the overall design and ion optics involved. This work was supported by the following grants: DE-FG02-01ER63226 and 8P41EB002033-08.

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