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CELL DIVISION SYNCHRONIZATION

Final Report

by

David W. Rooney

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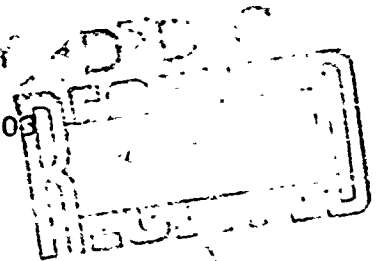
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Saint Louis University
Department of Biology
St. Louis, Missouri 63103



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13. ABSTRACT Reported is progress in the design and construction of automatic equipment for synchronizing cell division in culture by periodic hypoxia; problems and progress in testing appropriate carbohydrate sources for human cells in suspension cultures to be subjected to periodic hypoxia. Concurrent experiments in hypothermic synchronization of algal cell division are reported.			

To: U. S. Office of Naval Research

From: David W. Rooney, Ph.D.
Assistant Professor
Saint Louis University, Department of Biology
1504 South Grand Boulevard, St. Louis, Missouri 63104

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FINAL REPORT

The specific objective at the onset of research under N0014-69-A-0206-0001 was to determine if periodic hypoxia is a suitable method for synchronizing division in cell cultures. The basic underlying purpose was to establish an additional useful biophysical technique for the study of the division cycle of eukaryotic (nucleated) cells.

A portion of the research has consisted in the design, testing, and refinement of automatic equipment to impose upon cell cultures any desired cyclic program of oxygen concentration. A preliminary description of this equipment may be found in a technical report (2) submitted to ONR. Subsequent refinements, such as nylon inserts to speed O₂ concentration changes have been made.

Another portion of the research has consisted of testing various sugars (glucose, fructose, galactose) at various concentrations in human (HeLa) cell suspension cultures. This testing was done to determine if rapid division (growth) rates of mammalian cells in suspension culture can be achieved with low glycolytic rates. Only when glycolysis is slow would oxygen deprivation be effective in limiting ATP production (since ATP is generated by both glycolysis and oxidative phosphorylation). Only when growth is rapid can biophysical perturbations (such as temporary O₂ reductions) be expected to synchronize division. Extensive testing of growth rate and pH change (an index of glycolysis rate) with various sugars was carried out by Miss Judith O'Brien who reported the results in her master's Thesis (2). It was found that neither fructose nor galactose permitted rapid growth in suspension cultures.

Glucose permitted rapid growth -- but with rapid glycolysis.

In the course of these experiments, it became obvious that better facilities were needed to insure the absence of bacterial contamination in the human cell cultures. For this reason experiments with human cell suspensions have been temporarily halted. They will resume this summer (August, 1972) in a specially designed cell culture laboratory in the remodeled McDonnell Building at St. Louis University. Planned experiments will include steady-state culturing at low glucose concentration and imposition of periodic hypoxia.

Concurrent with the above described experimentation have been studies of periodic hypothermia as a method of synchronizing eukaryotic cell division. Because these studies are similar in objective, they are mentioned here. Briefly, I have found that periodic temperature reductions will effectively synchronize the division of an algal cell Chlamydomonas. The resulting publication (3) credits ONR support as do three additional publications (4, 5, 6) describing appropriate mathematical techniques for quantifying cell division synchrony in algal cultures.

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