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DEPARTMENT OF CHEMISTRY

COBB CHEMICAL LABORATORY

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CHARLOTTESVILLE, VA.

May 22, 1964 707778

Dr. Herman M. Roth
 Director, Research and Development Division
 U.S. Atomic Energy Commission
 P. O. Box E
 Oak Ridge, Tennessee 37831

Subject: Technological Spinoff Activities
 Contract AT-(40-1)-2683

Dear Doctor Roth:

I received your letter of March 11, 1964 (ORS:JER) emphasizing the importance of dissemination of information on subsidiary technological advances grown from Federally supported research in apparently unrelated areas.

Although my contract is in basic inorganic research, the spinoff has been of considerable importance. A new approach to the millenia old problem of kidney and bladder stones has been found, using an interpretation of "irregularities" encountered in "Exchange in Heterogeneous Systems". Clinical evaluation of the new principle is being carried out in the Bowman Gray Medical School, Winston-Salem, North Carolina.

The principles of the new method have been published in "Investigative Urology", and a couple of reprints are attached. Without use of a small amount of money from my AEC contract the crucial preliminary testing of the principle would have been impossible or delayed considerably.

I wish to thank you and your staff for the cooperation through all the years that I obtained support from your Division, even when progress was so slow. The results are finally coming off the presses now, but it is impossible to evaluate indirect consequences adequately.

Thanks to my experience in heterogeneous exchange it was possible to assist a group of obstetricians in the University of Virginia hospital in determination of the new flow of water from an unborn infant via the amniotic membrane to the blood of the mother. The average value of 2 1/2 quarts per day was determined by a combination of isotope exchange experiments. This work received the first prize in a contest sponsored by the South Atlantic Association of Obstetricians and Gynecologists in November, 1963, certainly an unexpected Association to be connected with as an analytical chemist!

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MAY 27 1964

UNIVERSITY OF VIRGINIA
DEPARTMENT OF CHEMISTRY

COBB CHEMICAL LABORATORY

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CHARLOTTESVILLE, VA.

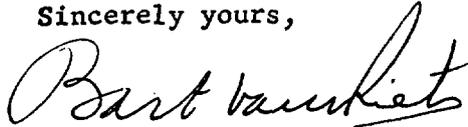
Dr. Herman M. Roth

May 22, 1964

Your contract has provided numerous students with an opportunity to apply radioisotopes in fundamental research. The effect of this "exposure" will last beyond the time that the files of this contract will be kept.

I'll keep you informed of any further spin-off activities from this contract, and I hope that the present information will be of value for reports to the Congress.

Sincerely yours,



Bart van't Riet
Senior Investigator
AT-(40-1)-2683

Bv'tR:meo
Encls. *OK*

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UNIVERSITY OF VIRGINIA
DEPARTMENT OF CHEMISTRY

COBB CHEMICAL LABORATORY

April 22, 1964
CHARLOTTESVILLE, VA.

Dear Dr. Roth:

The attached copy of a manuscript, entitled
"Isotope Labeling in the Determination of Net Flow
across Membranes" is a report submitted for
publication in "Science"

Your letter of March 11, 1964, stressing
Technological Spinoff Activities, seems to be
appropriate for this subject. I never guessed that
I would get involved in the determination of the net
flow of water from an unborn baby to the mother!

Sincerely yours

Bart Van't Riet
Senior Investigator
AT-(40-1)-2683

COBB CHEMICAL LABORATORY

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INDUSTRIAL DEV. AND REG. - 3

APR 24 1964

APR 24 1964

Isotope Labeling in the Determination
of Net Flow across Membranes.

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Abstract: The flow rate of an isotopic label across a membrane is not related exclusively to the net flow of the labeled chemical species. The direction and value of the net flow are found from two flow rates of the label, using the formulas derived in this report.

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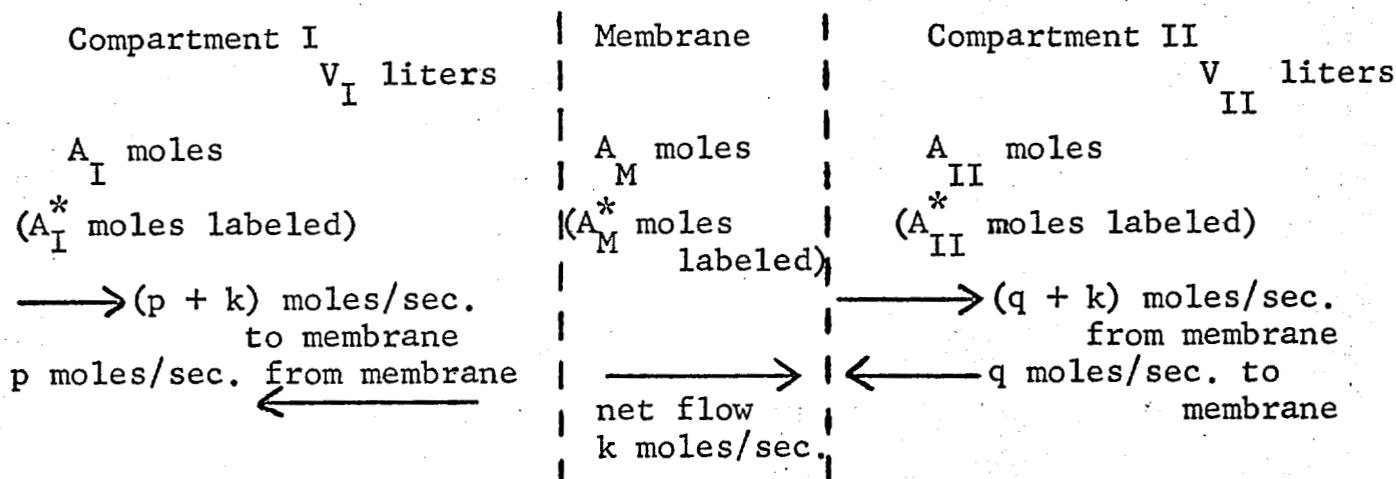
The net flow across a membrane can be determined by a variety of chemical and physical methods. However, analysis of the liquids may involve inaccuracies which vitiate small changes in the concentrations to be evaluated. Isotope labeling of one of the liquids is not adequate to determine net flow, because transport of the label through the membrane is often dominated by isotope exchange, rather than by net flow.

A combination of two experiments in which initially the label is in solution on opposite sides of the membrane can be used to determine the net flow. The present derivation is for a set of conditions which can be made to apply to a great variety of systems. Any specific action of the membrane is allowed if the labeled compound is not metabolized to a different substance.

Let a compartment I be separated from compartment II by a membrane which has a finite, but very small volume compared to the volumes V_I and V_{II} of the compartments. In compartment I there are A_I moles of transferring compound; A_I^* moles of these are labeled. Similarly A_{II} moles with A_{II}^* moles labeled are in compartment II. The membrane contains A_M moles with A_M^* moles labeled. A net flow of k moles/second is directed from compartment I to compartment II. The solutions in the compartments are kept homogeneous, and rapid isotopic equilibrium is maintained inside the membrane. Isotope effect is not considered in the derivation.

The flow system is given in the following diagram:

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The change of activity in each compartment is:

$$\frac{dA_I^*}{dt} = p \frac{A_M^*}{A_M} - (p + k) \frac{A_I^*}{A_I} \quad (1).$$

$$\frac{dA_{II}^*}{dt} = (q + k) \frac{A_M^*}{A_M} - q \frac{A_{II}^*}{A_{II}} \quad (2).$$

$$\frac{dA_I^*}{dt} + \frac{dA_{II}^*}{dt} + \frac{dA_M^*}{dt} = 0 \quad (\text{if allowance is made for decay}).$$

Because A_M is much smaller than either A_I or A_{II} , dA_M^* can be ignored in respect to dA_I^* and dA_{II}^* , and

$$-\frac{dA_I^*}{dt} \cong \frac{dA_{II}^*}{dt} \quad . \quad \text{Combine (1) and (2):}$$

$$\frac{A_M^*}{A_M} = \frac{(p + k) \frac{A_I^*}{A_I} + q \frac{A_{II}^*}{A_{II}}}{p + k + q} \quad ; \quad \text{substitute in (2):}$$

$$\frac{dA_{II}^*}{dt} = \frac{(p + k)(q + k)}{p + q + k} \cdot \frac{A_I^*}{A_I} - \frac{pq}{p + q + k} \frac{A_{II}^*}{A_{II}} = R_1 \frac{A_I^*}{A_I} - R_2 \frac{A_{II}^*}{A_{II}} .$$

$$R_1 - R_2 = k \text{ moles/second.}$$

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If the label is only present in compartment I at $t = 0$ and if during the early stages of exchange $\frac{A_{II}^*}{A_{II}}$ remains much smaller than $\frac{A_I^*}{A_I}$, the following relationship is obtained:

$$\frac{dA_{II}^*}{dt} \approx R_1 \frac{A_I^*}{A_I} \quad (3)$$

Similarly, if $A_I^* = 0$ initially, the early data give

$$\frac{dA_I^*}{dt} = - \frac{dA_{II}^*}{dt} \approx R_2 \frac{A_{II}^*}{A_{II}} \quad (4)$$

From two experiments R_1 and R_2 are found. The difference between R_1 and R_2 gives k and the direction of flow. The relative values of R_2 and k give an indication of the importance of isotope exchange compared to net flow.

Usually identical volumes of aliquots are used for activity measurements. Let the count rates of aliquots of f liters from compartments I and II be S_I and S_{II} , respectively. These count rates are a factor E times the number of moles of radioactive compound in the aliquot. Then

$$A_I^* = \frac{S_I V_I}{E \cdot f}, \text{ and } A_{II}^* = \frac{S_{II} V_{II}}{E \cdot f}$$

In the experiment in which $A_{II}^* = 0$ initially, during the period that $A_{II}^* \ll A_I^*$, equation (3) gives:

$$R_1 = \frac{A_I}{A_I^*} \frac{dA_{II}^*}{dt} = \frac{A_I V_{II}}{V_I \cdot S_I} \cdot \frac{dS_{II}}{dt} \quad (5)$$

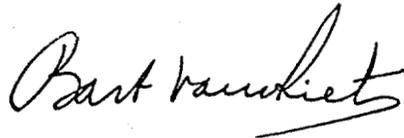
Similarly, for $A_I^* = 0$ initially, equation (4) gives:

$$R_2 = \frac{A_{II} V_I}{V_{II} S_{II}} \cdot \frac{dS_I}{dt} \quad (6)$$

Experiments for extended periods of time require the exact form of the differential equation. However, flow across the membrane would modify the solutions seriously in prolonged experiments. The various rate "constants" would change, and the exact equation loses its usefulness.

A paper is in preparation on results obtained in applying equations (5) and (6) to determinations of the flow of water across the amniotic membrane.

This report was prepared with support from the U. S. Atomic Energy Commission under Contract AT-(40-1)-2683.



Bart van't Riet

Department of Chemistry

University of Virginia

Charlottesville, Virginia 22903

1033683

Duke University
DURHAM
NORTH CAROLINA

DEPARTMENT OF BOTANY

POSTAL CODE 27706
TELEPHONE 919-681-0111

March 25, 1964

Mr. Herman M. Roth, Director
Research and Development Division
U.S. Atomic Energy Commission
Oak Ridge, Tennessee

Dear Mr. Roth:

Thank you for your recent letter concerning technological spin-off activities that are related to basic research under contracts with the Atomic Energy Commission. I am in complete sympathy with the Commission's desire that advances in methodology and basic information obtained under these contracts be transmitted as widely as possible to those who might make use of it. Although most of the results obtained from our research are published in relatively technical journals quite a bit of information is transmitted to people in Agronomy and Forestry who might make some use of it. This is done chiefly by attending their meetings and by correspondence and conversation with researchers in the more applied fields. For example we are obtaining information concerning absorption through the older roots of trees which is a great deal of interest to foresters and we are communicating that information to them by conversations and attendance at forestry meetings.

Yours truly,



Paul J. Kramer
James B. Duke Professor of Botany

PJK:sd

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INDUSTRIAL DEV. AND REG. -3

MAR 27 1964

TEXAS A&M UNIVERSITY

COLLEGE OF ENGINEERING

COLLEGE STATION, TEXAS

TEXAS ENGINEERING
EXPERIMENT STATION
Radiation Biology Laboratory

March 26, 1964

Mr. Herman M. Roth
Director
Research and Development Division
U.S. Atomic Energy Commission
Oak Ridge, Tennessee 37831

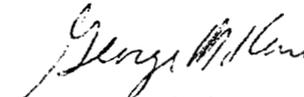
Dear Mr. Roth:

From Ltr.

Your letter of March 11 concerning Technological Spinoff Activities was read with interest. Contracts such as this one have as their usual outlet publication of results and information in the standard scientific channels thus reaching the audience most likely to convert this information into useful knowledge that can be applied for the general health and welfare.

However, rest assured that I will remain vigilant to the opportunity to make available to interested parties outside the immediate scientific circles any spinoff that might be of value arising from this research.

Sincerely yours,



George M. Krise
Research Zoologist

GMK:ls

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INDUSTRIAL DEV. AND REG. -3

MAR 27 1964

MAR 30 1964

HEADQUARTERS
U. S. ARMY MEDICAL RESEARCH LABORATORY
FORT KNOX, KENTUCKY

IN REPLY REFER TO

24 March 1964.

Dr. Herman M. Roth,
Director, Research & Development Div.,
U. S. Atomic Energy Commission,
Washington 25, D. C.

Your Ref: ORS:JER

Technological Spinoff Activities
Contract No. AT-(40-1)-2784

Through
Dr. W. W. Burr, Jr.,
Chief, Medical Research Branch,
Div. Biology & Medicine.

Dear Sir:

Your letter of March 11, 1964, regarding the dissemination of collateral information more or less incidentally acquired in the pursuit of research projects such as this one, has received and will continue to receive careful attention.

The study under the above contract deals primarily with the relationship of radio-activity to leukemia and related diseases. But it is interesting to note that already an incidental finding is to the effect that among the bovine animals used for food in this country the number of hearts affected with sarcosporidiosis (Sarcocystis blanchardi) amounts to 32 per cent. While this fact will not change the course of human events, it is of interest that man is also susceptible to this parasite. The determination was based upon examination of nearly 300 hearts and if someone had deliberately set up a separate project to accomplish it, considerable expense would have been inevitable. Ultimately we shall get this item into print, to be added to general scientific knowledge.

Very sincerely yours,

Hilton A. Smith.

Hilton A. Smith,
Principal Investigator.

INDUSTRIAL DEV. AND REC. -3

APR 1 1964

APR 2 1964

1033686

RICE UNIVERSITY

HOUSTON 1, TEXAS

DEPARTMENT OF PHYSICS

March 19, 1964

Dr. Herman M. Roth
Director
Research and Development Division
U. S. Atomic Energy Commission
Oak Ridge, Tennessee 37831

Subject: Technological Spinoff Activities
Contract No. AT-(40-1)-1316

Dear Dr. Roth:

Thank you for your letter of March 11, 1964 regarding technological spinoff activities. Your letter has struck a responsive chord with me and with a number of my colleagues at this university. I sincerely believe that the Atomic Energy Commission should engage itself more seriously in calling attention to the general public, and especially to technological industries, the importance of applying nuclear and the tools used in nuclear research to problems of their interest.

Any specific items that come to mind, I will be very pleased to report to you in the future.

Yours sincerely,



G. C. Phillips
Chairman

GCP:w

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MAR 23 1964