۷

† New York State Department of Health.

¹ Fleischman, J. B., R. R. Porter, and E. M. Press, Biochem. J., 88, 220 (1963).

² Edelman, G. M., and M. D. Poulik, J. Exptl. Med., 113, 861 (1961).

³ Grossberg, A. L., P. Stelos, and D. Pressman, these PROCEEDINGS, 48, 1203 (1962).

⁴ Fleischman, J. B., R. H. Pain, and R. R. Porter, Arch. Biochem. Biophys., Supplement 1, 174 (1962).

⁵ In a personal communication, S. Utsumi and F. Karush report activity by the H chain of rabbit anti-p-azo-phenyl- β -lactoside antibody.

⁶ Roholt, O. A., G. Radzimski, and D. Pressman, Science, 141, 726 (1963).

⁷ Metzger, H., and S. J. Singer, Science, 142, 674 (1963).

⁸ Franek, F., and R. S. Nezlin, Biokhimiya, 28, 193 (1963).

⁹ Edelman, G. M., D. E. Almis, J. A. Gally, and N. D. Zinder, these Proceedings, 50, 753 (1963).

¹⁰ Pressman, D., and O. Roholt, these PROCEEDINGS, 47, 1606 (1961).

¹¹ Kekwick, R. A., Biochem. J., 34, 1248 (1940).

¹² Gitlin, D., J. Immunol., 62, 437 (1949).

¹³ Yagi, Y., P. Maier, and D. Pressman, J. Immunol., 89, 736 (1962).

¹⁴ Yagi, Y., P. Maier, D. Pressman, C. E. Arbesman, R. E. Reisman, and A. R. Lenzner, J. Immunol., 90, 760 (1963).

¹⁵ Yagi, Y., P. Maier, D. Pressman, C. E. Arbesman, and R. E. Reisman, J. Immunol., 91, 38 (1963).

¹⁶ Onoue, K., Y. Yagi, and D. Pressman, J. Immunol., in press.

¹⁷ H and L chain preparations in 1 M propionic acid were mixed in the ratio of 3:1 based on O.D. and then dialyzed against cold water followed by borate buffer.

¹⁸ This arc was not apparent in the plate of the original γ -globulin nor in any of the other plates. It did not appear when the horse anti-rabbit globulin was absorbed with normal rabbit γ_2 -globulin prior to diffusion. Since it appears to fuse with the more prominent arc, the protein responsible for it presumably contains only some of the antigenic determinants on the rest of the reconstituted molecules.

¹⁹ Palmer, J. L., and A. Nisonoff, J. Biol. Chem., 238, 2393 (1963).

²⁰ The details of these experiments will be published elsewhere.

²¹ Pauling, L., D. Campbell, and D. Pressman, Physiol. Rev., 23, 203 (1943).

A SOLVABLE CASE OF THE TRAVELING SALESMAN PROBLEM*

BY P. C. GILMORE AND R. E. GOMORY

THOMAS J. WATSON RESEARCH CENTER, YORKTOWN HEIGHTS, NEW YORK

Communicated by William Feller, December 16, 1963

Given an nxn matrix D of nonnegative numbers d_{ij} , the traveling salesman problem for D is the problem of finding a cyclic permutation τ of $1, \ldots, n$, called a tour, for which $C(\tau)$, defined to be $\sum_{i=1}^{n} d_{i\tau_i}$ is a minimum. The bottleneck traveling salesman problem for D is the problem of finding a tour τ for which $MC(\tau)$, defined to be $\max_{1 \le i \le n} \{d_{i\tau_i}\}$, is a minimum.¹

The purpose of this note is to announce a solution to the traveling salesman problem and the bottleneck traveling salesman problem for a special class of matrices. The solution of the bottleneck traveling salesman problem provides also a solution to the problem of characterizing those directed graphs, of a certain welldefined class, which possess Hamiltonian circuits. Proofs will be given in outline Vol. 51, 1964

only, the details and the motivation being left for a later paper.

The class of matrices D for which a solution has been provided is characterized as follows: each nxn matrix D of the class is obtained from n pairs of nonnegative numbers R_i and S_i by defining d_{ij} to be max $\{0, S_j - R_i\}$. Given any such D, let α and β be permutations of $1, \ldots, n$ such that $R_{\alpha_1} \leq R_{\alpha_2} \leq \ldots \leq R_{\alpha_n}$ and $S_{\beta_1} \leq S_{\beta_2} \leq \ldots \leq S_{\beta_n}$. For any i and $j, 1 \leq i < j \leq n$, define $c(i,j) = \max\{0, c'(i, j)\}$, where $c'(i, j) = \min\{R_{\alpha_j} - R_{\alpha_i}, R_{\alpha_j} - S_{\beta_i}, S_{\beta_j} - S_{\beta_i}, S_{\beta_j} - R_{\alpha_i}\}$.

Essential to the solution of the traveling salesman problem for any given D of the given class is a nondirected graph G, with costs attached to its edges, defined as follows: G has 2n nodes, n of which are called R-nodes and n of which are called S-nodes. The edges of G are of one of the following kinds with their costs as stated:

(1) For each $i, 1 \leq i \leq n$, an edge [i,i] of zero cost, called an identity edge, joins the *R*-node *i* and the *S*-node *i*.

(II) For each $i, 1 \leq i \leq n$, an edge $[\alpha_i, \beta_i]$ of zero cost, called a level edge, joins the *R*-node α_i and the *S*-node β_i .

(III) For each $i, 1 \leq i \leq n-1$, an edge $[\alpha_i, \alpha_{i+1}]$ of $\cot c(i, i+1)$, called an α -edge, joins the R-nodes α_i and α_{i+1} if and only if $c'(i, i+1) = R_{\alpha_{i+1}} - R_{\alpha_i}$ or $c'(i, i+1) = R_{\alpha_{i+1}} - S_{\beta_i}$. (IV) For each $i, 1 \leq i \leq n-1$, an edge $[\beta_i, \beta_{i+1}]$ of $\cot c(i, i+1)$, called a

(IV) For each $i, 1 \leq i \leq n-1$, an edge $[\beta_i, \beta_{i+1}]$ of cost c(i, i+1), called a β -edge, joins the S-notes β_i and β_{i+1} if and only if $c'(i, i+1) = S_{\beta_{i+1}} - S_{\beta_i}$ or $c'(i, i+1) = S_{\beta_{i+1}} - R_{\alpha_i}$.

By a spanning tree of G we will mean a spanning tree in the usual sense² except that a spanning tree, of the subgraph of G with only identity and level edges, is assumed to be a subgraph of every spanning tree of G. The cost C(T) of a spanning tree of G is the sum of the costs of the edges of T.

For any permutation μ and ν of 1, ..., n, $C(\mu,\nu)$ is defined to be $\sum_{i=1}^{n} d_{\mu_i\nu_i}$ so that C(1, -) = C(-) where 1 is the identity permutation

 $C(1,\tau) = C(\tau)$, where 1 is the identity permutation.

THEOREM 1. For any spanning tree T of G there exists a tour τ such that $C(\tau) \leq C(\alpha,\beta) + C(T)$.

The tour τ is obtained as follows: let I_{α} be the set of interchanges (i, i + 1) for which $[\alpha_i, \alpha_{i+1}]$ is an α -edge of T, ordered in increasing size of i, and let I_{β} be the set of interchanges (i, i + 1) for which $[\beta_i, \beta_{i+1}]$ is a β -edge of T, similarly ordered. Let α° be α , and for each $r, a > r \ge 0$, where $a = |I_{\alpha}|$, define α^{r+1} to be $\alpha^r \cdot (i, i + 1)$, where (i, i + 1) is the r + 1 st interchange of I_{α} . Let β^s be similarly defined for each $s, b > s \ge 0$, where $b = |I_{\beta}|$. Then τ is the permutation $[(\alpha^a)^{-1} \cdot \beta^b]$.

Thus, if T_0 is a spanning tree of G for which $C(T_0)$ is minimum, it is possible to find a tour τ_0 such that $C(\tau_0) \leq C(\alpha,\beta) + C(T_0)$. Two theorems are proved to show that for every tour $\tau, C(\tau) \geq C(\tau_0)$.

Given any permutation ρ of 1, ..., *n* and any *i*, $1 \le i \le n$, define j(i) to be $(\beta^{-1} \cdot \alpha \cdot \rho)$, and define $\Delta(\rho) = \sum_{\substack{i \le j(i) \\ r = i}} \sum_{\substack{r = i \\ r = i}} c(r, r + 1).$

THEOREM 2. For any permutation ρ , $C(\rho) \geq C(\alpha,\beta) + \Delta(\rho)$.

There remains then only to prove:

THEOREM 3. For any tour τ , there exists a spanning tree T of G such that $\Delta(\tau) \geq C(T)$.

Since if τ is any tour, by Theorems 2 and 3 there exists a spanning tree T such that $C(\tau) \geq C(\alpha,\beta) + C(T)$, and since $C(T) \geq C(T_0)$, it follows by Theorem 1 that $C(\tau) \geq C(\tau_0)$.

For the solution of the bottleneck traveling salesman problem, it is possible to assume without loss that $R_{\alpha_i} \geq S_{\beta_i}$. For it can be shown that $(\alpha^{-1} \cdot \beta)$ is a permutation ρ minimizing $MC(\mathfrak{l})$, and therefore that for any τ , $\max \{d_{i\tau_i}\} = \max \{\max\{0, S_{\tau_i} - [R_i + MC(\alpha^{-1} \cdot \beta)]\}\} + MC(\alpha^{-1} \cdot \beta)$.

A graph H, very similar to G, has an essential role in the solution of the bottleneck traveling salesman problem. H differs only in the following details: there are no α -edges and for every $i, 1 \leq i < n$, there is a β -edge $[\beta_i \beta_{i+1}]$ joining the S-nodes β_i and β_{i+1} with cost mc(i,i+1) defined to be max $\{0, S_{\beta_{i+1}} - R_{\alpha_i}\}$. A spanning tree T of H now has a cost MC(T), which is the largest cost assigned to edges of T.

For permutations μ and ν of 1, ..., n, define $MC(\mu,\nu) = \underset{\substack{1 \leq i \leq n \\ 1 \leq i \leq n}}{\operatorname{Max}} \{d_{\mu_i\nu_i}\}$. Under the assumption that $R_{\alpha_i} \geq S_{\beta_i}$, i = 1, ..., n, note that $MC(\alpha,\beta) = 0$. Corresponding then to Theorem 1 is the following theorem for the bottleneck traveling salesman problem:

THEOREM 4. For any spanning tree T of H there exists a tour τ such that $MC(\tau) \leq MC(T)$.

For the graph H only a set I_{β} of interchanges is defined, so that τ is the tour $(\alpha^{-1} \cdot \beta^b)$. Again if τ_0 is a tour such that $MC(\tau_0) \leq MC(T_0)$ for the spanning tree T_0 of least cost $MC(T_0)$, there remain two theorems to be proved to show that τ_0 is a tour for which $MC(\tau_0)$ is minimum.

In place of $\Delta(\rho)$ in Theorems 2 and 3, $M\Delta(\rho)$ appears in Theorems 5 and 6, where it is defined to be $\max_{i < j(i)} \{\max_{1 \le r \le j(i) - 1} [mc(r, r + 1)]\}$.

THEOREM 5. For any permutation ρ , $MC(\rho) \geq M\Delta(\rho)$.

THEOREM 6. For any tour τ , there exists a spanning tree T of H such that $M\Delta(\tau) \geq MC(T)$.

The problem of characterizing those directed graphs which have a Hamiltonian circuit (and finding the circuit when it exists) has been solved for the following class of graphs: K is a directed graph of n nodes which is a member of the class if and only if $\Gamma_1 \subset \Gamma_2 \subset \ldots \subset \Gamma_n$, where Γ_i is the set of nodes j for which K has an edge directed from i to j. A Hamiltonian circuit for K is a tour τ such that for each $i, i = 1, \ldots, n$, there is an edge of K directed from i to τ_i . Clearly no K can have a Hamiltonian circuit if Γ_1 is empty so that without loss the class can be restricted to those graphs for which Γ_1 is nonempty.

Let K be any graph of the given class and let β be a permutation of $1, \ldots, n$ such that for each *i* there is a *j* for which $\Gamma_i = \{\beta_1, \ldots, \beta_j\}$. Let K^* be an undirected graph of *n* nodes with an edge (i,β_i) if and only if $\beta_i \in \Gamma_i$, for $i = 1, \ldots, n$, and an edge (i,β_{i+1}) if and only if $(i,\beta_{i+1}) \in \Gamma_{i+1}$, for $i = 1, \ldots, n - 1$.

THEOREM 7. A necessary and sufficient condition that K have a Hamiltonian circuit is that K^* be connected.

The proof can be completed by determining R_i and S_i , for i = 1, ..., n, such that the problem of finding a tour τ minimizing $MC(\tau)$ is equivalent to the problem of finding a Hamiltonian circuit for K.

* This research was supported in part by the Office of Naval Research under contract Nonr 3775(00), NR 047040.

¹ Although the bottleneck traveling salesman problem has not apparently been discussed before, the closely related bottleneck assignment problem has been discussed and solved by O. Gross, "The bottleneck assignment problem," the RAND Corporation P-1630, March 6, 1959.

² See Kruskal, J. B., "On the shortest spanning subtree of a graph and the travelling salesman problem," *Proc. Amer. Math. Soc.*, **7**, 48–50 (1956).

SENSITIZATION OF PURINE-STARVED BACTERIA TO X RAYS*

BY HENRY S. KAPLAN AND F. L. HOWSDEN

DEPARTMENT OF RADIOLOGY, STANFORD UNIVERSITY SCHOOL OF MEDICINE, PALO ALTO, CALIFORNIA

Communicated by Arthur Kornberg, December 4, 1963

The susceptibility of bacteria to the lethal effect of ionizing radiation is modified by a number of nutritional and physiologic factors.^{1, 2} We have observed an apparently new phenomenon: a striking increase in sensitivity to ionizing radiation in purine-deficient cultures of *E. coli*, which is reversible by subsequent purine supplementation.

Materials and Methods.—The bacterial strain employed in most of these experiments was E. coli K12, HfrH, substrain X-662 (pur⁻, thiamine⁻), which was kindly provided by Dr. Herbert Marcovich, Service de Radiobiologie et de Cancerologie, Institut Pasteur, Paris, France. This strain has an absolute requirement for a natural purine base; it grows equally well on a mixture of hypoxanthine and xanthine or on adenine.

The organisms were inoculated from agar slants or stationary phase cultures into minimal saltsglucose medium³ supplemented with thiamine hydrochloride, 10-20 μ g/ml, and adenine, except where otherwise indicated, at a concentration of 1 μ g/ml ("starved") or 100 μ g/ml ("supplemented"). They were incubated on a waterbath shaker at 37° overnight, or for shorter intervals as stated. In other experiments, the shift to purine starvation was made during exponential growth; after about 4 hr at 37°, cultures were rapidly filtered and washed on Millipore HA membrane filters, then resuspended and reincubated in prewarmed purine-free medium. Growth was often followed by serial turbidity determinations at 650 m μ on a Coleman spectrophotometer, but cell population data in all instances are based upon viable colony counts after plating on yeastextract agar.

For irradiation, aliquots of the cultures were appropriately diluted to yield $1-3 \times 10^7$ cells per ml. An aliquot of this dilution was saved as a zero-dose sample, and the remainder of the dilution distributed in 1.9 ml aliquots to the required number of 35-mm-diameter sterile plastic Petri dishes. The dishes were kept chilled on ice until the time of irradiation. Each dish was individually irradiated in a plastic holder suspended in an irradiation chamber midway between two opposed beryllium window X-ray tubes operating at 50 KVP and 48-50 ma, with 0.3 mm Al added filtration. Under these conditions, the average dose rate in the culture fluid within the dish was 9.9 Krads per minute.⁴ Ultraviolet (UV) irradiation was performed with similarly diluted cultures in plastic Petri dishes on a rotary platform under a low-pressure mercury lamp calibrated to deliver 2,537 Å irradiation at an output of 800 ergs/mm²/min at the level of the Petri dish. After irradiation, the samples were appropriately diluted in mineral medium, plated on yeastextract agar, and incubated overnight at 37°. Colony counts represent the average of 4 plates per dilution per radiation dose. Survival percentages are referred to the average colony count of the unirradiated (zero-dose) sample. In some experiments, the survival of various experimental groups was compared at a fixed radiation dose level of 20 Krads.

Results.—(1) Enhancement of X-ray sensitivity: Cultures which had been grown overnight on low purine levels $(1.25 \ \mu g/ml)$ were strikingly more sensitive to X rays than controls grown with a normal supplement of 100 $\mu g/ml$ (Fig. 1). The response to X ray was exponential over four decades of killing, reflecting homo-