Proc. Natl. Acad. Sci. USA
Vol. 85, pp. 3271–3275, May 1988
Applied Mathematical Sciences

Further properties of random walks on diagrams (graphs) with and without cycles

(first passage time/absorption/remainder theory/degradation)

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ABSTRACT **Three problems are considered. The first is the relation between ensemble-averaged state probabilities in a random walk with absorption and time-averaged state probabilities in the corresponding closed diagram. The second problem is concerned with random walks on diagrams with cycles in which the cycle completion rates and probabilities may depend on the "remainder" after the previously completed cycle. The final topic is a study of cycle completions prior to absorption for diagrams that involve both cycles and absorption (e.g., a cycling enzyme that binds a dead-end inhibitor or poison in one of its states).**

This is a continuation of an earlier paper (1) on the same general subject; the reader is assumed to be familiar with ref. 1. The first section contains further details on the relation between time-dependent state probabilities in a random walk with absorption and the constant time-averaged state probabilities found when the absorption transitions are replaced by appropriate one-way cycles (1). The second section presents the solution of a problem posed at the end of a 1975 paper (2) on cycle stochastics: how does one handle cycle probabilities and cycle completion times at the individual cycle level, where long-time averages do not apply? The solution depends on methods introduced in ref. 1. The third section is concerned with the stochastic properties of diagrams with cycles that also exhibit absorption from one or more states (e.g., a cycling enzyme or protein complex may be slowly inhibited or degraded).

Relations Between Two Kinds of State Probabilities

The same notation as in the first section of ref. 1 is used here. A kinetic diagram has absorption states κ and starting state s. The immediate precursor of a given κ state is denoted κ'. States i are the non-κ states, including the κ' states. In the random walk with absorption, $p_i(t)$ and $p_\kappa(t)$ are the ensemble-averaged state probabilities at t. The mean time to absorption is $\bar{t}$. The "closed diagram" (1) is formed by replacing each κ state in the original diagram by a one-way transition (transition probability $\alpha_{\kappa'\kappa}$) from state κ' back to state s. This diagram represents repeated walks in a single system. The time-averaged steady-state state probabilities in the closed diagram are denoted P_i.

If there are N walks in the ensemble, where N is large, the total time spent in a particular state i in these walks is $N \int_0^\infty p_i(t)dt$. The total time spent in *any* state i is $N\bar{t}$. The N walks on the original diagram are in parallel (all start at $t = 0$); on the closed diagram the same walks are in series. Hence

$$P_i = \frac{1}{\bar{t}} \int_0^\infty p_i(t)dt, \qquad \bar{t} = \sum_i \int_0^\infty p_i(t)dt. \qquad [1]$$

The second equation is a consequence of $\Sigma_i P_i = 1$. To confirm this, an integration by parts gives

$$\bar{t} = \int_0^\infty \sum_i p_i(t)dt = -\int_0^\infty t \sum_i \frac{dp_i}{dt}dt = \int_0^\infty t \sum_\kappa \frac{dp_\kappa}{dt}dt. \qquad [2]$$

Further confirmation of the expression for P_i comes from the differential equation for state i in the *original* diagram,

$$\frac{dp_i}{dt} = -p_i \sum_j \alpha_{ij} + \sum_j \alpha_{ji} p_j, \qquad [3]$$

where the sums are over those states j that can convert to state i, or vice versa. For any $i \neq s$, integration over all t results in

$$p_i(\infty) - p_i(0) = 0 = -\left(\sum_j \alpha_{ij}\right) \int_0^\infty p_i dt + \sum_j \alpha_{ji} \int_0^\infty p_j dt. \qquad [4]$$

Multiplication by $1/\bar{t}$ (normalization) then gives the complete set (except $i = s$) of steady-state equations for the P_i in the *closed* diagram. Integration of Eq. 3 for $i = s$ yields

$$-1 = -\left(\sum_j \alpha_{sj}\right) \int_0^\infty p_s dt + \sum_j \alpha_{js} \int_0^\infty p_j dt,$$

or

$$-\frac{1}{\bar{t}} = -\left(\sum_j \alpha_{sj}\right) P_s + \sum_j \alpha_{js} P_j. \qquad [5]$$

The right-hand side becomes the steady-state equation for state s in the *closed* diagram if we add to it $\Sigma_{\kappa'} \alpha_{\kappa'\kappa} P_{\kappa'}$ (these are the new one-way transitions to state s in the closed diagram, already mentioned). The right-hand side is then equal to zero. Hence, on the left-hand side,

$$-\frac{1}{\bar{t}} + \sum_{\kappa'} \alpha_{\kappa'\kappa} P_{\kappa'} = -\frac{1}{\bar{t}} + \sum_\kappa J_\kappa = 0,$$

or

$$\bar{t} = 1/J, \qquad J = \sum_\kappa J_\kappa. \qquad [6]$$

where J is the total absorption rate in the repeated (time-averaged) random walk on the closed diagram (1).

The number of visits to an arbitrary state i (or the number of transitions of a particular type) prior to absorption can also be handled by using appropriate closed diagrams and fluxes, but this topic will not be included here.

Detailed Cycle Fluxes and Probabilities

At the end of ref. 2, it was pointed out that mean steady-state one-way cycle fluxes, calculated from the diagram method

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(3), are correct as long-time averages but, in general, are not valid as cycle rate constants at the detailed cycle-by-cycle level. (The exceptions are cases in which every type of cycle completion brings the system back to the starting state in the random walk, as in Fig. 1*A* with starting state 1.) It is shown in this section that the cycle-by-cycle level can be handled by using methods introduced in ref. 1. First, a discussion will be given of the case in figures 2 and 3 of ref. 1; this is sufficiently complicated to make obvious the procedure for an arbitrary diagram. This will be followed by a simpler case for which explicit algebra can be carried out without difficulty.

We consider a long random walk on the diagram of Fig. 1*A*, starting at state 2. The diagram has three cycles (Fig. 1*B*) and six one-way cycles, denoted by the index η = a±, b±, c±. Fig. 1*C* is the closed-2 diagram (1) for a walk starting at state 2; it is equivalent to Fig. 1*A* but is more detailed. The diagram method (3) can be applied either to Fig. 1*A* or to Fig. 1*C* in order to find the six mean (long-time) one-way cycle fluxes J_η as explicit functions of the transition probabilities α_{ij}. Then the mean time between cycle completions (any cycle) in the long random walk is $\bar{t} = 1/J$, where $J = \Sigma_\eta J_\eta$.

Completed cycles, during the walk that starts at state 2, end and begin only at one of the three central states in Fig. 1*C*, with index ν = 1, 2, or 3. The respective "remainders" (2, 3) are 21, 2, and 23. Suppose that the walk comprises a total of N completed cycles (N is large). Of these, let NF_ν be the number of cycles that begin at the particular central state ν. Within this group of cycles, let $J_{\nu\eta}$ be the mean rate of cycle completions of type η. Then, within this group, the mean time per cycle completion is $\bar{t}_\nu = 1/J_\nu$, where $J_\nu = \Sigma_\eta J_{\nu\eta}$. The fact that $J_{\nu\eta}$ and $\bar{t}_\nu$ are different for different choices of ν (the beginning state for the next cycle in Fig. 1*C*) is the essence of the present problem.

The method introduced in the second section of ref. 1 can be used to find the $J_{\nu\eta}$. For example, the closed diagram in Fig. 2 will give the six $J_{3\eta}$ and figure 3*B* of ref. 1 will give the $J_{2\eta}$ (a figure similar to Fig. 2 will give the $J_{1\eta}$). Fig. 2 represents a long repeated walk that always begins a new cycle instantaneously at $\nu = 3$ after completion of a cycle at ν = 1, 2, or 3. (The repeated walk, always starting at $\nu = 3$, will produce the mean values $J_{3\eta}$ for cycle completion rates.) For example, the cycle labeled a− in Fig. 2 is actually completed by the transition $1 \rightarrow 2$ at state $\nu = 2$ with transition probability α_{12} but the bent arrow (a−) from 1 to 3 indicates that, in calculating the steady-state state probabilities in Fig. 2, this arrow is treated as a transition $1 \rightarrow 3$ with transition probability α_{12}—because the ending state $\nu = 2$ is instantaneously transferred to $\nu = 3$ to start a new cycle from $\nu = 3$.

The 11 steady-state state probabilities in Fig. 2 are found from the steady-state algebraic equations of the diagram by any convenient method (numerically, by matrix inversion, if necessary). Each of the 8 fluxes is then found as a product of a state probability and the appropriate α_{ij}. Note that each of J_{3b+} and J_{3b-} has two contributions, denoted, for example, J_{31b+} and J_{33b+} (the second index indicates the ending ν state of the cycle). The same comments apply to the diagrams for $\nu = 2$ (figure 3*B* of ref. 1) and $\nu = 1$ (not shown).

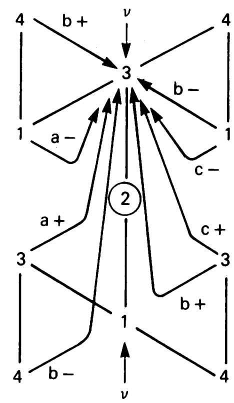

FIG. 2. Diagram used to obtain stationary properties for cycles that begin from state $\nu = 3$.

We return now to a consideration of F_ν, defined above. Let $p_{\nu\nu'}$ be the probability that a cycle that begins at ν ends at ν'. These probabilities are determined by the three sets of 8 fluxes mentioned above:

$$
\begin{aligned}
p_{\nu 1} &= (J_{\nu 1b+} + J_{\nu 1b-})/J_\nu \\
p_{\nu 2} &= (J_{\nu a+} + J_{\nu a-} + J_{\nu c+} + J_{\nu c-})/J_\nu \\
p_{\nu 3} &= (J_{\nu 3b+} + J_{\nu 3b-})/J_\nu.
\end{aligned} \qquad [7]
$$

The six $p_{\nu\nu'}$ ($\nu \neq \nu'$) then determine the three F_ν through Fig. 3. This discrete-time diagram shows cycle-by-cycle interconversion probabilities for ν; the unit of time is one cycle completion. The F_ν are the three steady-state state probabilities calculated from the steady-state algebraic equations, for example, by the diagram method (3). Note that the three $p_{\nu\nu}$ do not enter explicitly into the calculation of the F_ν.

We now have the main ingredients of this more detailed examination of one-way cycle fluxes, based on the beginning state ν for each cycle: $J_{\nu\eta}$, $\bar{t}_\nu$, and F_ν. The self-consistency relations with the more conventional long-time averages J_η and $\bar{t}$ are easily seen to be

$$\bar{t} = F_1\bar{t}_1 + F_2\bar{t}_2 + F_3\bar{t}_3 \qquad [8]$$

$$J_\eta = (F_1\bar{t}_1/\bar{t})J_{1\eta} + (F_2\bar{t}_2/\bar{t})J_{2\eta} + (F_3\bar{t}_3/\bar{t})J_{3\eta}. \qquad [9]$$

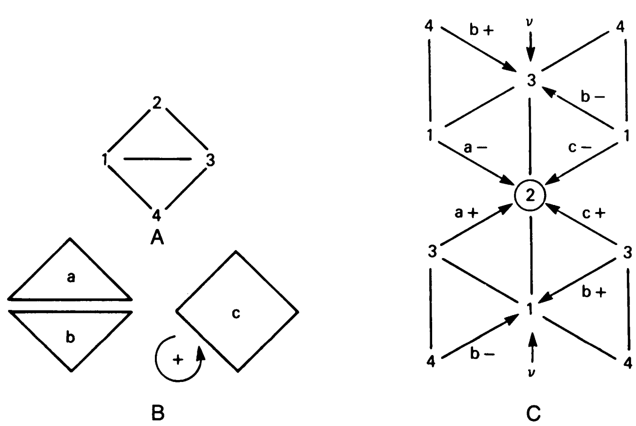

FIG. 1. (*A*) Diagram used as an example. (*B*) Cycles of the diagram. (*C*) The closed-2 diagram for a random walk starting at state 2. Cycles end only at the three central states with index ν.

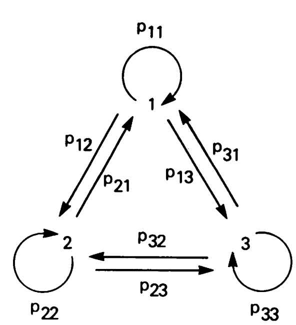

FIG. 3. Discrete-time diagram used to find the fraction of cycles F_ν that begin from each ν.

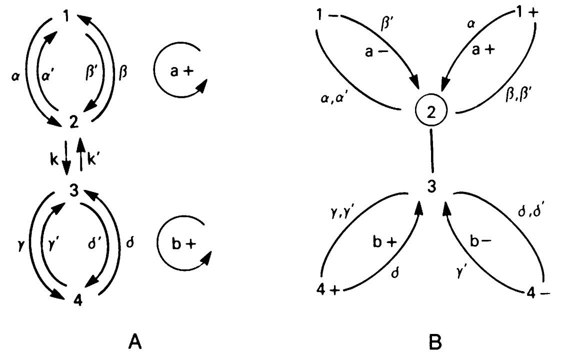

FIG. 4. (*A*) Diagram used as a simple example. (*B*) Closed-2 diagram for walk starting from state 2.

The cycle fluxes of Fig. 1*A* are subdivided into one-way cycle fluxes in Fig. 1*C*. These, in turn, are subdivided further, according to origin (value of ν), in Eq. **9**, based on Fig. 2 ($\nu = 3$) and its two analogues ($\nu = 1, 2$).

We consider now the much simpler diagram in Fig. 4*A*. There are two cycles, a (upper) and b (lower); i.e., $\eta = \mathrm{a}\pm$, $\mathrm{b}\pm$. If a walk starts in state 2, the closed-2 diagram is Fig. 4*B*. Cycles begin and end at either state 2 (remainder 2) or state 3 (remainder 23); i.e., $\nu = 2$ or 3. The closed diagrams for $\nu = 2$ and 3 (analogues of Fig. 2) are shown in Fig. 5 *A* and *B*, respectively.

For brevity below we define at this point

$$A = \alpha\beta + \alpha'\beta', \quad B = \gamma\delta + \gamma'\delta', \quad C = k(\alpha + \beta'),$$
$$D = k'(\delta + \gamma'), \quad E = \alpha + \beta' + \alpha' + \beta,$$
$$F = \gamma + \delta' + \gamma' + \delta. \qquad [10]$$

The state probabilities in Fig. 4*B* are easily found to be

$$P_{1-} = \alpha' D/\Sigma, \quad P_{1+} = \beta D/\Sigma, \quad P_{4+} = \gamma C/\Sigma,$$
$$P_{4-} = \delta' C/\Sigma, \quad P_2 = (\alpha + \beta')D/\Sigma, \quad P_3 = (\delta + \gamma')C/\Sigma,$$
$$\Sigma \equiv CF + DE. \qquad [11]$$

Then the four one-way cycle fluxes (J_η), and $\bar{t}$, are

$$J_{\mathrm{a}+} = \alpha P_{1+} = \alpha\beta D/\Sigma, \quad J_{\mathrm{a}-} = \beta' P_{1-} = \alpha'\beta' D/\Sigma,$$
$$J_{\mathrm{b}+} = \delta P_{4+} = \gamma\delta C/\Sigma, \quad J_{\mathrm{b}-} = \gamma' P_{4-} = \gamma'\delta' C/\Sigma \qquad [12]$$
$$\bar{t} = 1/\Sigma_\eta J_\eta = \Sigma/(AD + BC). \qquad [13]$$

The state probabilities for cycles that begin from $\nu = 2$ are, from Fig. 5*A*,

$$Q_{1-} = \alpha'(B + D)/S, \quad Q_{1+} = \beta(B + D)/S,$$
$$Q_{4+} = \gamma C/S, \quad Q_{4-} = \delta' C/S,$$
$$Q_2 = (\alpha + \beta')(B + D)/S, \quad Q_3 = (\delta + \gamma')C/S$$
$$S \equiv BE + CF + DE. \qquad [14]$$

The fluxes ($J_{2\eta}$), and $\bar{t}_2$, are then

$$J_{2\mathrm{a}+} = \alpha Q_{1+}, \quad J_{2\mathrm{a}-} = \beta' Q_{1-},$$
$$J_{2\mathrm{b}+} = \delta Q_{4+}, \quad J_{2\mathrm{b}-} = \gamma' Q_{4-} \qquad [15]$$
$$\bar{t}_2 = 1/\Sigma_\eta J_{2\eta} = S/U, \quad U \equiv AB + AD + BC. \qquad [16]$$

Also, for use in Fig. 5*C*,

$$p_{22} = (J_{2\mathrm{a}+} + J_{2\mathrm{a}-})/\Sigma_\eta J_{2\eta} = (AB + AD)/U$$
$$p_{23} = (J_{2\mathrm{b}+} + J_{2\mathrm{b}-})/\Sigma_\eta J_{2\eta} = BC/U. \qquad [17]$$

Similarly, the state probabilities for cycles that begin from $\nu = 3$ (Fig. 5*B*) are

$$R_{1-} = \alpha' D/T, \quad R_{1+} = \beta D/T, \quad R_{4+} = \gamma(A + C)/T,$$
$$R_{4-} = \delta'(A + C)/T, \quad R_2 = (\alpha + \beta')D/T,$$
$$R_3 = (\delta + \gamma')(A + C)/T$$
$$T \equiv AF + CF + DE. \qquad [18]$$

The fluxes ($J_{3\eta}$), and $\bar{t}_3$, are

$$J_{3\mathrm{a}+} = \alpha R_{1+}, \quad J_{3\mathrm{a}-} = \beta' R_{1-},$$
$$J_{3\mathrm{b}+} = \delta R_{4+}, \quad J_{3\mathrm{b}-} = \gamma' R_{4-} \qquad [19]$$
$$\bar{t}_3 = 1/\Sigma_\eta J_{3\eta} = T/U. \qquad [20]$$

Then

$$p_{33} = (J_{3\mathrm{b}+} + J_{3\mathrm{b}-})/\Sigma_\eta J_{3\eta} = (AB + BC)/U$$
$$p_{32} = (J_{3\mathrm{a}+} + J_{3\mathrm{a}-})/\Sigma_\eta J_{3\eta} = AD/U. \qquad [21]$$

Finally, from Fig. 5*C*, the fractions of cycles beginning from $\nu = 2, 3$ are

$$F_2 = p_{32}/(p_{32} + p_{23}) = AD/(AD + BC)$$
$$F_3 = 1 - F_2 = BC/(AD + BC). \qquad [22]$$

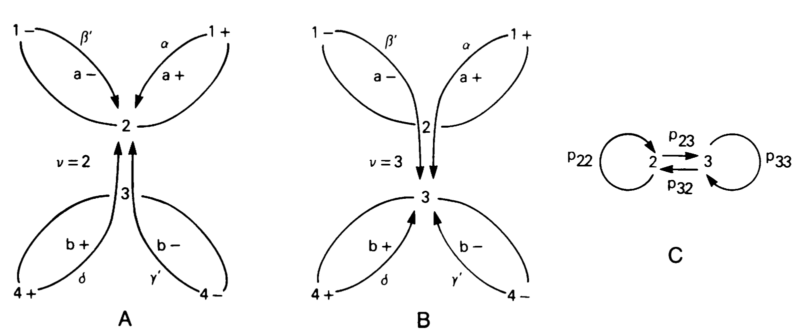

FIG. 5. (*A* and *B*) Diagrams used to obtain stationary properties for cycles that begin from state $\nu = 2$ or from $\nu = 3$. (*C*) Discrete-time diagram that determines F_2 and F_3.

One can check the self-consistency of the results by substituting the above ingredients into Eqs. **8** and **9** (omitting $\nu = 1$).

Random Walks with Absorption on Diagrams with Cycles

The first section of ref. 1 and also the first section here relate to diagrams with absorption at one or more states κ. In this section we consider the special case of such systems in which the diagram includes one or more cycles. In this case there are additional properties of interest—for example, what is the mean number of completed cycles of a given type before absorption occurs? This is actually a realistic problem in biophysics. Suppose that an enzyme (or protein complex) is engaged in some kind of cyclic activity. If the enzyme can be degraded at one or more or all of its states by binding a dead-end inhibitor, or by denaturation or proteolysis, any of these events would correspond to "absorption" (termination of the random walk). This subject is introduced in this section by a brief discussion of four examples.

In Fig. 6*A*, a random walk starts at state 1 and is terminated, eventually, by absorption at state 5. Except for γ, the transition probabilities are denoted by the usual α_{ij}. There are six one-way cycles, η = a±, b±, c±, as in Fig. 1*B*. Every cycle begins and ends at state 1. The ensemble-averaged transient state probabilities $p_i(t)$ can be studied in the usual way (1). (Incidentally, the time-dependent rate of completion of cycles of type η could be obtained by using the closed-2 diagram in figure 4 of ref. 1 with γ transitions to states 51, 52, and 53 out of 41, 42, and 43, respectively.) However, certain mean values are easier to deduce from the time-averaged properties of the closed diagram (1), Fig. 6*B*, with state probabilities P_i.

The properties of Fig. 6*B* follow from the diagram method (3). There are 13 partial diagrams: 8 are shown in figure 6 of ref. 1, and there are 5 more in which the γ transition replaces the line 1–4. Because the γ transition is one-way, states 1, 2, 3, and 4 have 13, 12, 11, and 8 directional diagrams, respectively. Hence, Σ (3) is a sum of 44 terms. The γ transition is not involved in the state 4 directional diagrams because it leads *away* from state 4. The six J_η are then (3)

$$J_{a\pm} = \Pi_{a\pm}(\alpha_{41} + \alpha_{43} + \gamma)/\Sigma$$
$$J_{b\pm} = \Pi_{b\pm}(\alpha_{21} + \alpha_{23})/\Sigma$$
$$J_{c\pm} = \Pi_{c\pm}/\Sigma, \qquad [23]$$

where $\Pi_{a+} = \alpha_{13}\alpha_{32}\alpha_{21}$, etc. The sum in $J_{a\pm}$ arises from the three flux diagrams in Fig. 6*C*. The total absorption flux J is

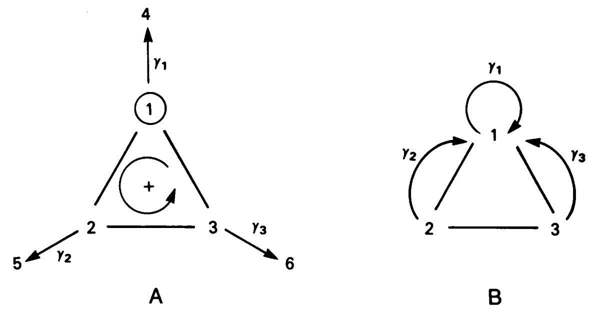

FIG. 7. (*A*) Three-state cycle with possible absorption from each state. The starting state is 1. (*B*) Corresponding closed diagram.

(see Fig. 6*D*)

$$J = (8 \text{ cyclic diagrams for } J)/\Sigma = \gamma P_4$$
$$= \gamma(8 \text{ state-4 directional diagrams})/\Sigma. \qquad [24]$$

It should be noted that the 8 cyclic diagrams for J in Fig. 6*D* include 3 different cycles and are constructed from the 8 state-4 directional diagrams plus the γ transition.

The mean (first passage) time to absorption is $\bar{t} = 1/J$. The mean number of completed (one-way) η cycles before absorption is

$$\frac{J_\eta}{J} = J_\eta \bar{t} = \frac{\Pi_\eta \Sigma_\eta}{\gamma(8 \text{ state-4 directional diagrams})}, \qquad [25]$$

where Σ_η is obvious in each case from Eqs. **23**. Note that Σ is not needed for this calculation (it *is* needed for $\bar{t}$). The probability that exactly n η-cycles will have been completed before absorption occurs is

$$\left(\frac{J}{J + J_\eta}\right)\left(\frac{J_\eta}{J + J_\eta}\right)^n. \qquad [26]$$

This simple result follows because all cycles η, in this example, begin and end at the same state, 1 (unlike Eq. **9**).

The second example is a three-state cycle with starting state 1 and with absorption possible from each state (Fig. 7*A*). The two one-way cycles are $\eta = \pm$. Time dependence can be studied in the usual way. The corresponding closed diagram is Fig. 7*B*. The state probabilities in Fig. 7*B* are (3)

$$P_1 = [\alpha_{32}(\alpha_{21} + \gamma_2) + \alpha_{23}(\alpha_{31} + \gamma_3)$$
$$+ (\alpha_{21} + \gamma_2)(\alpha_{31} + \gamma_3)]/\Sigma$$
$$P_2 = [\alpha_{12}\alpha_{32} + \alpha_{13}\alpha_{32} + (\alpha_{31} + \gamma_3)\alpha_{12}]/\Sigma$$
$$P_3 = [\alpha_{12}\alpha_{23} + \alpha_{23}\alpha_{13} + (\alpha_{21} + \gamma_2)\alpha_{13}]/\Sigma, \qquad [27]$$

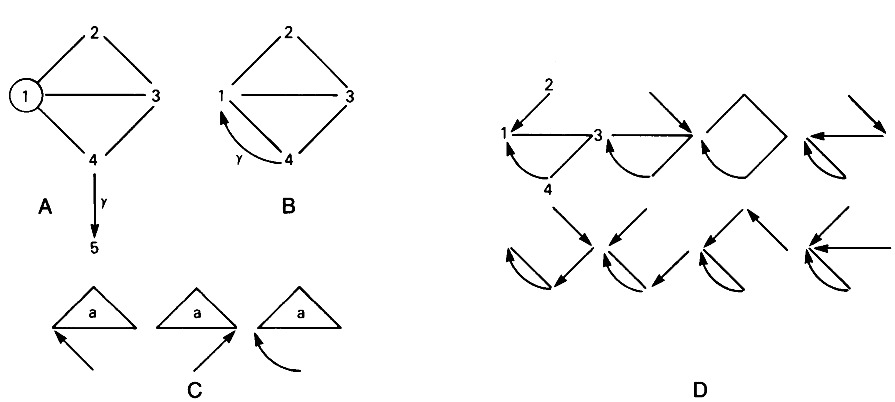

FIG. 6. (*A*) Example of a random walk on a diagram with cycles and with absorption (from state 4). The starting state is 1. (*B*) Corresponding closed diagram. (*C*) Flux diagrams for cycle a. (*D*) Eight cyclic diagrams for J (absorption).

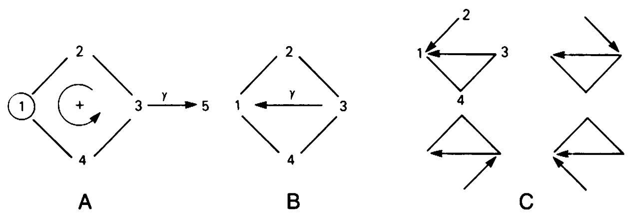

FIG. 8. (*A*) Four-state cycle with walk starting from state 1 and absorption from state 3. (*B*) Corresponding closed diagram. This can also be interpreted as an original diagram that includes a slip from state 3 to state 1. (*C*) Four cyclic diagrams for J (absorption or slip).

where Σ is the sum of the three numerators. Note that γ_1 does not appear in Eqs. **27**. The fluxes are

$$J_{\pm} = \Pi_{\pm}/\Sigma, \qquad J = \gamma_1 P_1 + \gamma_2 P_2 + \gamma_3 P_3. \qquad [28]$$

The probability of eventual absorption from state i is $\gamma_i P_i/J$; also, $\bar{t} = 1/J$. The mean number of $\eta = \pm$ cycles before absorption occurs is J_η/J (again Σ is not needed to evaluate this expression). Eq. **26** is applicable.

In the special case $\gamma_1 = \gamma_2 = 0$,

$$\frac{J_{\pm}}{J} = \frac{\Pi_{\pm}}{\gamma_3(\alpha_{12}\alpha_{23} + \alpha_{23}\alpha_{13} + \alpha_{21}\alpha_{13})}. \qquad [29]$$

This has the same form as Eq. **25**. It is easy to show that Eq. **29** is obtained, unchanged, if the starting state is 2 or 3 instead of 1. However, Σ and $\bar{t}$ depend on the starting state, as one would expect.

The third example is Fig. 8*A*: the walk starts in state 1 and absorption occurs from state 3. The two one-way cycles are $\eta = \pm$. This is a slight extension of the case in Eq. **29**. The closed diagram is Fig. 8*B*. The novel feature in this example is that Fig. 8*B* may also arise in a quite different context (suggested to me by Hans Westerhoff): this is the *original* diagram (not a closed diagram) for a system represented by the square cycle which has, in addition, an irreversible "slip" from state 3 to state 1 with transition probability γ. This slip short-circuits or decouples the business of the square cycle. After the γ transition (slip), the random walk continues from state 1. In the absorption problem (Fig. 8*A*), the walk on Fig. 8*B* is conceptual (we imagine the walk to be restarted, instantaneously, over and over); in the slip problem, the walk on Fig. 8*B* is real. The properties of Fig. 8*B* are the same in either case.

The numbers of directional diagrams in Fig. 8*B* are 8, 6, 4, and 6 for states 1, 2, 3, and 4, respectively (see figure 6 of ref. 1). Thus Σ has 24 terms. As in Eq. **29**,

$$\frac{J_{\pm}}{J} = \frac{\Pi_{\pm}}{\gamma(\text{4 state-3 directional diagrams})}. \qquad [30]$$

The denominator on the right is also the sum of 4 cyclic diagrams for J (absorption or slip), shown in Fig. 8*C*. Eq. **30** gives the mean number of completed $\pm$ cycles before absorption or per slip transition. Eq. **26** is again applicable.

The final example is Fig. 9*A*, which is closely related to Fig. 6*A*. Here, the starting state is 2. The closed diagram is Fig. 9*B*. Eqs. **23** and **24** are again obtained except that Σ is different (call it Σ') and in the 8 cyclic diagrams for J (Fig. 6*D*) the curved γ arrow $4 \rightarrow 1$ is replaced by a γ arrow $4 \rightarrow 2$ (these cyclic diagrams now include 4 different cycles). The numbers of directional diagrams for states 1, 2, 3, and 4 are 12, 16, 12, and 8, respectively. Hence Σ' has 48 terms. Eq. **25** is unchanged: the mean number of completed cycles of any type prior to absorption is the same whether the starting state is 1 or 2 (or 3). However, $\bar{t}$ is different because $\Sigma \neq \Sigma'$. Incidentally, if the starting state is 4, the two quotients $J_{a\pm}/J$ are altered because γ no longer appears in Σ_a (Eq. **23**).

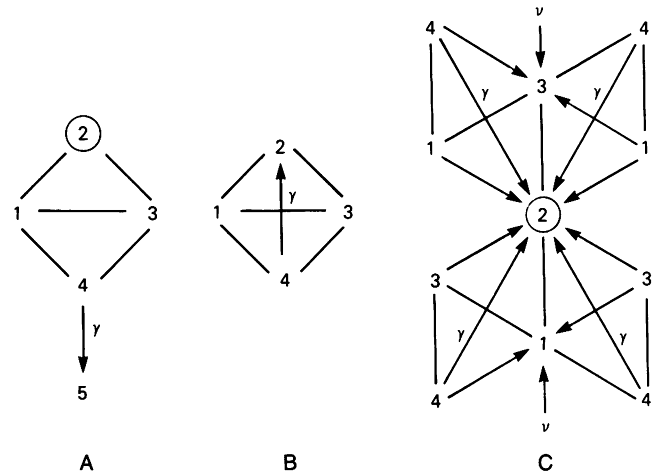

FIG. 9. (*A*) Example with starting state 2 and absorption from state 4. (*B*) Corresponding closed diagram. (*C*) Corresponding closed-3 diagram. Other cycle labels are as in Fig. 1*C*. A walk on this diagram shows more details than the same walk on the closed diagram.

Returning now to starting state 2, the new feature is that Eq. **26** no longer holds because the η cycles may end at $\nu = 1$, 2, or 3 (Fig. 1*C*) and cycle probabilities depend on the initial state ν of a new cycle (see the second section). If we apply the recipe for diagram $\rightarrow$ closed-2 diagram (1) to the closed diagram in Fig. 9*B*, we obtain Fig. 9*C* (a "closed-3" diagram). The properties of Fig. 9 *B* and *C* are the same except that Fig. 9*C* contains more details. Note, in Fig. 9*C*, the four γ cycles already mentioned. To obtain the ν dependence of all cycle fluxes and probabilities (including γ cycles), we would need to direct all arrows in Fig. 9*C* to $\nu = 1, 2$, or 3 (as in Fig. 2). These three diagrams would provide, in principle, the ingredients for a generalization of Eq. **26**.

I am indebted to Dr. Hans Westerhoff for his comments on applications of the third section and to Dr. Doron Zeilberger for his encouragement and for reading the manuscript.

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