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A Simplified "Ratchet" Model of Molecular Motors

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A limiting case of one of the ratchet models of Ajdari, Prost, *et al.* is analyzed. An explicit solution is obtained for the probability distribution as a function of the time for any initial distribution with all the transients included. In the long-time limit the drift velocity and diffusion coefficient are obtained in terms of the microscopic transition rates that are the parameters in the model. In spite of its extreme simplicity, with realistic values of its kinetic parameters the model yields values of the drift velocity and effective force that are of the right magnitude for a molecular motor. The model proves to be a simple special case of Derrida's periodic one-dimensional hopping model, for which he found a solution in the long-time limit.

KEY WORDS: Ratchet model; molecular motor; motor protein; hopping model.

1. INTRODUCTION

The directed motion of a motor protein such as kinesin (often with an attached vesicle) along a microtubule is a fundamental process in biology.[1-4] The motion is powered by the hydrolysis of ATP. A proposed chemical mechanism[3, 5] consists of steps in which ATP binds to the motor protein/microtubule complex, where it is hydrolyzed to ADP and inorganic phosphate, these (first the phosphate and then the ADP) being then released from the complex. During this process the protein's conformation and its grip on the microtubule are temporarily altered. The motor protein's interaction with the microtubule, while periodic along the microtubule's length, is asymmetric within a period, and when, at the end of the cycle described above, the protein has returned to its initial conformation it has not returned to its initial position on the microtubule but rather to

Dedicated to Leo P. Kadanoff as an expression of the authors' esteem.

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the equivalent position in the next period. From the point of view of the chemistry, all that has happened is that the motor protein and microtubule together have catalyzed the hydrolysis of one molecule of ATP to ADP and inorganic phosphate;[6] but from the point of view of the motor protein, what has happened is that it has advanced one unit of distance equal to the 8 nm spatial period of its interaction with the microtubule,[6] and almost always in the same direction—a direction dictated by the asymmetry within a period.

This mechanism has been abstracted and then incorporated in a variety of beautiful "ratchet" models by Ajdari, Prost, *et al.*[7-9,4] and others.[10-13] A common theme of these models is that the motor protein on the microtubule, in either of its two states (bound to ATP or its hydrolysis products, or free of them), is pictured as a particle that is confined to a line where it experiences either of two potential energies, each potential being a periodic function of position on the line but asymmetric within a period. The change in the protein's state is then modeled as a switching off of one of the potentials and a simultaneous switching on of the other. The particle is required to undergo Brownian motion within each potential while that potential is turned on.

In this article we analyze a simplified version—an extreme limiting case—of one of those models.[9] It is pictured schematically in Fig. 1, which shows the two alternative potentials at the same discrete sites, represented by small circles in the figure. The sites are arrayed horizontally. Each potential separately is plotted vertically, so that the points labeled A and A', for example, are two consecutive minima of the upper one of the two pictured potentials while B is one of the minima of the lower one. There is no quantitative significance to the vertical displacement of the two potentials from each other in the figure—they are displaced from each other vertically only

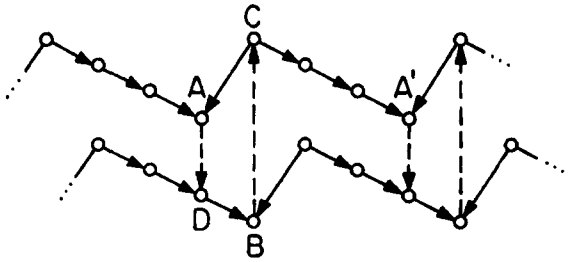

Fig. 1. The two alternative potential energies, at discrete positions marked by circles. Within each potential downward transitions (solid arrows) occur instantly and irreversibly, while transitions between the potentials (dotted arrows) occur at finite rates. States A and A' are at minima of the upper potential, B is at a minimum of the lower potential, and C and D are examples of states from which downward transitions occur instantly.

for ease of visualization—but their horizontal displacement from each other is a central feature of the model. Both potentials are periodic, and for simplicity are taken to extend infinitely far in both directions, so there are no end effects.

Within each potential downward transitions are taken to occur instantly and irreversibly, in this extreme version of the model, so that a particle representing the motor protein has vanishing residence time in states such as those marked C and D in the figure; it is always in one of the potential minima. Transitions between the potentials, corresponding to a change in the motor protein's interaction with the microtubule and represented by the vertical dotted arrows in the figure, are taken to occur at finite rates but only between states that are at the same location in the horizontal direction. Examples are the transitions $A \to D$ and $B \to C$ in the figure.

Suppose a representative particle is at A at some moment. The only transition it can undergo, and which it eventually will undergo, is to D, but it then goes immediately to B, where it will then reside for some time. Its next transition can only be to C, but from there it will immediately go either to A or to A'. If to A, then the particle has simply undergone a cycle of changes and returned to its starting point; but if to A', then it is now in a state that is indistinguishable from the state A in which we first observed it, but translated rightward by one spatial period. The analogous sequence of changes may then occur from A'. There is thus a steady drift to the right and none to the left, which models the motion of the motor protein along the microtubule.

Because in this model the residence time in any state other than at a minimum in one of the potentials vanishes, the observable transitions are effectively from a minimum in one potential to one in the other. These, as seen above, are then of three types: from A to B (via D), from B to A (via C), and from B to A' (via C). Let the respective finite transition rates (transition probabilities per unit time) be u, v, and w. These are the parameters in the model. The latter two imply that the instantaneous transition out of C is to A with probability $v/(v+w)$ and to A' with probability $w/(v+w)$.

Let the states corresponding to the minima in the potential pictured as the upper one in Fig. 1 be collectively called type A and those of the lower one type B. Then the kinetic scheme defined above may be alternatively depicted as in Fig. 2, where the successive minima in Fig. 1 are now indexed by the discrete variable $x = \ldots, -2, -1, 0, 1, 2, \ldots$. Minima of type A at odd x alternate with those of type B at even x. The array is periodic in x with period 2, and extends to infinity in both directions. Note that horizontal distances in Figs. 1 and 2 are proportional only on average: the

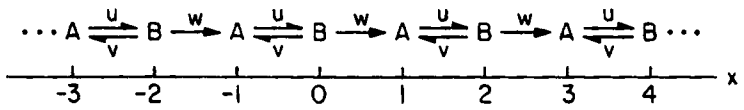

Fig. 2. A and B represent the minima in the upper and lower potentials of Fig. 1, respectively. Their locations are indexed by the discrete variable x. Allowed transitions are indicated by the arrows, each with its associated transition rate u, v, or w.

index x always changes by 1 between successive states in Fig. 2 while the horizontal distances between successive A and B minima in Fig. 1 are alternately shorter and longer. The one-way drift rightward of a representative point—modeling the unidirectional motion of the motor protein on the microtubule—is most evident in Fig. 2, since only rightward transitions occur from A states.

One now pictures a particle hopping from state to state in Fig. 2 with hopping rate (transition probability per unit time) u, v, or w, as indicated, and asks for the probability $P_x(t)$ that the particle will be at x at time t for any given initial $P_x(0)$. Alternatively, $P_x(t)$ may be taken to be that fraction of the total population of an ensemble of non-interacting particles that is at x at time t. In the next section this $P_x(t)$ is calculated for any given $P_x(0)$ for all t, thus including all the transients. The drift velocity and diffusion coefficient are obtained in the long-time limit, and the effective force driving the molecular motor is obtained from their ratio. With realistic values of the kinetic parameters the calculated drift velocity and force are found to have values that are of the magnitudes of those measured by experiment. The transient, short-time behavior of the model is discussed in Section 3, where the important relaxation times are identified. In Section 4 the model is shown to be a simple special case of the more general periodic one-dimensional hopping model introduced by Derrida[14] and solved by him in the long-time limit.

2. $P_x(t)$

The probability distribution $P_x(t)$ for the kinetic model in Fig. 2 is the solution of

$$\frac{\partial P_x(t)}{\partial t} = w_{x,x-1} P_{x-1}(t) + w_{x,x+1} P_{x+1}(t) - (w_{x-1,x} + w_{x+1,x}) P_x(t) \tag{2.1}$$

that reduces to a prescribed $P_x(0)$ at $t=0$, with

$$w_{x,x-1}=\begin{cases} w, & x \text{ odd} \\ u, & x \text{ even} \end{cases}$$
$$w_{x-1,x}=\begin{cases} 0, & x \text{ odd} \\ v, & x \text{ even} \end{cases} \tag{2.2}$$

The normalization

$$\sum_x P_x(t) \equiv 1 \qquad (\text{all } t) \tag{2.3}$$

is specified to hold at $t=0$ and then holds at all t, as noted.

The partial Fourier transforms $Q(q, t)$ and $R(q, t)$ defined by

$$Q(q, t)=\sum_{x \text{ odd}} P_x(t)\, e^{iqx}$$
$$R(q, t)=\sum_{x \text{ even}} P_x(t)\, e^{iqx} \tag{2.4}$$

then satisfy

$$\frac{\partial Q(q, t)}{\partial t}=(we^{iq}+ve^{-iq})\, R(q, t)-uQ(q, t)$$
$$\frac{\partial R(q, t)}{\partial t}=ue^{iq}Q(q, t)-(v+w)\, R(q, t) \tag{2.5}$$

Therefore $R(q, t)$ satisfies the second-order equation

$$\frac{\partial^2 R(q, t)}{\partial t^2}=uw(e^{2iq}-1)\, R(q, t)-(u+v+w)\frac{\partial R(q, t)}{\partial t} \tag{2.6}$$

The solution is of the form

$$R(q, t)=\Pi_1(q)\, e^{\lambda_1(q)\, t}+\Pi_2(q)\, e^{\lambda_2(q)\, t} \tag{2.7}$$

where $\Pi_1(q)$ and $\Pi_2(q)$ are to be determined from the prescribed $P_x(0)$ [or equivalently, by (2.4), from the prescribed $Q(q, 0)$ and $R(q, 0)$], while $\lambda_1(q)$ and $\lambda_2(q)$ are

$$\lambda_{1,2}(q)=\tfrac{1}{2}[-(u+v+w)\pm\sqrt{(u+v+w)^2+4uw(e^{2iq}-1)}] \tag{2.8}$$

with (let us henceforth agree) the top sign for λ_1 and the bottom sign for λ_2 when $-\pi < \arg[(u+v+w)^2 + 4uw(e^{2iq}-1)] \leqslant \pi$.

Once $R(q,t)$ is known, $Q(q,t)$ may be obtained from the second of Eqs. (2.5). One then finds that the coefficients $\Pi_1(q)$ and $\Pi_2(q)$ of the exponentials in (2.7), for prescribed $Q(q,0)$ and $R(q,0)$, are given by

$$\begin{aligned} \Pi_1(q) &= \frac{[\lambda_2(q)+v+w]\,R(q,0) - ue^{iq}Q(q,0)}{\lambda_2(q)-\lambda_1(q)} \\ \Pi_2(q) &= \frac{-[\lambda_1(q)+v+w]\,R(q,0) + ue^{iq}Q(q,0)}{\lambda_2(q)-\lambda_1(q)} \end{aligned} \tag{2.9}$$

and since from (2.4)

$$P_x(t) = \frac{1}{2\pi}\int_{-\pi}^{\pi} e^{-iqx}[R(q,t)+Q(q,t)]\,dq \tag{2.10}$$

one then has as the complete solution for $P_x(t)$,

$$\begin{aligned} P_x(t) = \frac{1}{2\pi}\int_{-\pi}^{\pi} e^{-iqx}\Bigg\{\left[1+\frac{\lambda_1(q)+v+w}{ue^{iq}}\right]\Pi_1(q)\,e^{\lambda_1(q)t} \\ +\left[1+\frac{\lambda_2(q)+v+w}{ue^{iq}}\right]\Pi_2(q)\,e^{\lambda_2(q)t}\Bigg\}\,dq \end{aligned} \tag{2.11}$$

With the abbreviations

$$W = u+v+w, \qquad U = 2\sqrt{uw} \tag{2.12}$$

one finds from (2.8) that the real parts $\mathscr{R}[\lambda_1(q)]$ and $\mathscr{R}[\lambda_2(q)]$ of $\lambda_1(q)$ and $\lambda_2(q)$, for q real, are

$$\begin{aligned} \mathscr{R}[\lambda_{1,2}(q)] = -\frac{1}{2}W \pm \frac{1}{2\sqrt{2}}\{[(W^2-U^2)^2 \\ +2(W^2-U^2)\,U^2\cos 2q + U^4]^{1/2} + W^2 - U^2 + U^2\cos 2q\}^{1/2} \end{aligned} \tag{2.13}$$

with, still, the $(+)$ sign for λ_1 and the $(-)$ sign for λ_2. Note that $W > U$ because $v > 0$ and the arithmetic mean of u and w is greater than their geometric mean. It is then seen that $\mathscr{R}[\lambda_2(q)]$ is negative for all real q while $\mathscr{R}[\lambda_1(q)]$ is negative for all real q other than integer multiples of π

(where $\cos 2q = 1$), where it is 0. Then the term containing $\exp[\lambda_2(q)\, t]$ in the integrand of (2.11) contributes only short-time transients to $P_x(t)$ while the leading long-time behavior, from the term containing $\exp[\lambda_1(q)\, t]$, comes from the neighborhoods of $q = 0, \pm\pi$.

One finds explicitly (as shown in the Appendix),

$$P_x(t) \sim \frac{2\begin{Bmatrix} u \\ v+w \end{Bmatrix}}{u+v+w} \cdot \frac{1}{2\sqrt{\pi D t}}\, e^{-(x-Vt)^2/4Dt} \qquad (t \to \infty) \tag{2.14}$$

where $\begin{Bmatrix} u \\ v+w \end{Bmatrix}$ means u for x even (B sites) and $v+w$ for x odd (A sites), and where

$$V = \frac{2uw}{u+v+w}, \qquad D = 2uw\,\frac{(u+v+w)^2 - 2uw}{(u+v+w)^3} \tag{2.15}$$

Thus, after long times, as expected, the probability distribution loses its dependence on the initial distribution. It becomes two Gaussians, one for the A sites and one for the B sites, the two differing in amplitude but drifting with the same velocity V and spreading with the same diffusion coefficient D.

If a is the average of the two distances between successive A and B sites in Fig. 1 then Va is the drift velocity and Da^2 the diffusion coefficient of this model molecular motor. [The V and D given by (2.15) both have the dimensions of time^{-1}.] The effective force f driving the motor is then, by the Einstein relation,

$$f = kT\,\frac{Va}{Da^2} = \frac{kT}{a}\,\frac{(u+v+w)^2}{(u+v+w)^2 - 2uw} \tag{2.16}$$

with k Boltzmann's constant and T the temperature. This lies between kT/a and $2kT/a$ for all positive u, v, and w.

The factors following the dot on the right-hand side of (2.14) are the standard expression for the normalized probability distribution of a biased random walk. The factors preceding the dot modulate the amplitude between A and B sites; their average is 1. Their ratio, $u/(v+w)$, is the ratio of the population of a B site to that of the preceding or following A site in the drifting distribution at any x that is within $o(t)$ of Vt after long times t. This could have been predicted from the steady-state approximation $0 \approx d[B]/dt = [A]\,u - [B](v+w)$, or equivalently $0 \approx d[A]/dt = [B](v+w) - [A]\,u$, where $[A]$ and $[B]$ are the populations or occupation probabilities in question.

While the model is too crude to be expected to give quantitatively accurate results in comparison with experiment, it does give the right orders of magnitude, and thus may be accepted as providing a credible and useful, albeit greatly oversimplified,[7,9-13] picture. The result $kT/a < f < 2kT/a$ found above leads, at room temperature, with $2a = 8$ nm, to a chemical driving force of 1 or 2 pN, which may be compared with a measured stall force of 6 pN for the kinesin motor.[6] Further, at an ATP concentration of 500 μM, which is typical in the laboratory studies, the measured rate constants for the kinesin motor[5] lead to the approximate values $u = 1000\ \text{sec}^{-1}$, $v = 200\ \text{sec}^{-1}$, and $w = 15\ \text{sec}^{-1}$ for the three kinetic parameters in the present model. From the first of (2.15), and again with $2a = 8$ nm, these imply a drift velocity $Va = 1 \times 10^{-5}$ cm/sec, to be compared with the measured drift velocity for the kinesin motor,[6] at that ATP concentration, of 6×10^{-5} cm sec^{-1}. If instead we use the kinetic data of Higuchi *et al.*,[15] then at that same concentration of ATP we estimate $u = 350\ \text{sec}^{-1}$, $v \approx 0$, $w = 45\ \text{sec}^{-1}$, hence a drift velocity $Va = 3 \times 10^{-5}\ \text{sec}^{-1}$, somewhat closer to the measured value. As anticipated, the orders of magnitude are right although the agreement is not fully quantitative.

3. TRANSIENTS

The two main sources of short-time transients in (2.11), where the influence of the initial distribution $P_x(0)$ is still felt, are the term in the integrand containing $\exp[\lambda_2(q)t]$, and values of q outside the immediate neighborhoods of $q = 0, \pm\pi$ in the integration of the term containing $\exp[\lambda_1(q)t]$. Each of these two transients is characterized by some relaxation time after which it is negligible.

It was remarked after (2.13) that $\mathscr{R}[\lambda_2(q)]$ is negative for all real q. It is seen from (2.13) that it is least negative when $\cos 2q = -1$ (i.e., when q is an odd multiple of $\pi/2$):

$$\mathscr{R}[\lambda_2(q)] \leqslant -\frac{1}{2}W - \frac{1}{2}\begin{cases}\sqrt{W^2 - 2U^2}, & W^2 > 2U^2 \\ 0, & W^2 < 2U^2\end{cases} \tag{3.1}$$

This bound lies between $-\frac{1}{2}W$ and $-W$. The contribution to $P_x(t)$ from the $\exp[\lambda_2(q)t]$ term in the integrand in (2.11) then becomes negligible only after times t that are long compared with a transient time τ_2 given by

$$\tau_2 = \frac{1}{W} = \frac{1}{u+v+w} \tag{3.2}$$

It was remarked earlier that the populations $[A]$ and $[B]$ of neighboring A and B sites approximately satisfy the conditions $d[A]/dt = -d[B]/dt = (v+w)[B] - u[A]$, with the time derivatives both effectively 0, i.e., much less than either $(v+w)[B]$ or $u[A]$ separately, in the steady state. Before setting the time derivatives to 0 one may observe the approach to the steady state. The quoted approximations for $d[A]/dt$ and $d[B]/dt$, together, may be rewritten $d(u[A] - (v+w)[B])/dt = -(u+v+w)(u[A] - (v+w)[B])$. This then identifies the τ_2 in (3.2) as the time for the ratio $[B]/[A]$ of the populations of neighboring B and A states to approach $u/(v+w)$.

One must wait a longer time for the contributions from values of q outside the immediate neighborhoods of $q = 0, \pm\pi$ in the integration of the term containing $\exp[\lambda_1(q)t]$ in (2.11) to become negligible. The behavior of $\lambda_1(q)$ near $q = 0$ is representative of its behavior near $q = \pm\pi$ as well because it is periodic in q with period π. Then expanding the real and imaginary parts $\mathscr{R}[\lambda_1(q)]$ and $\mathscr{I}[\lambda_1(q)]$ of $\lambda_1(q)$ in powers of q, from (2.8), one finds [with the abbreviations (2.12)],

$$\mathscr{R}[\lambda_1(q)] = -\frac{1}{2}\frac{U^2}{W}\left[\left(1-\frac{1}{2}\frac{U^2}{W^2}\right)q^2 - \left(\frac{1}{3}-\frac{7}{6}\frac{U^2}{W^2}+\frac{3}{2}\frac{U^4}{W^4}-\frac{5}{8}\frac{U^6}{W^6}\right)q^4 + \cdots\right]$$

$$\mathscr{I}[\lambda_1(q)] = \frac{1}{2}\frac{U^2}{W}q\left[1-\left(\frac{2}{3}-\frac{U^2}{W^2}+\frac{1}{2}\frac{U^4}{W^4}\right)q^2 + \cdots\right] \tag{3.3}$$

The leading terms in (3.3), from the definitions (2.15) and (2.12), are seen to be the expected $\mathscr{R}[\lambda_1(q)] = -Dq^2 + \cdots$ and $\mathscr{I}[\lambda_1(q)] = Vq + \cdots$ that led to (2.14) [Appendix]. For (2.14) to hold, the higher order terms in both expansions must contribute negligibly. From the first of them one sees that the main contribution to $P_x(t)$ from near $q = 0$ at long times t comes from values of q up to that at which $Dq^2t \simeq 1$. But $U < W$, as remarked earlier, so the q^4 term in $\mathscr{R}[\lambda_1(q)]$ and the q^3 term in $\mathscr{I}[\lambda_1(q)]$ are negligible when $q \ll 1$, but only then. Therefore these contributions become negligible only when the time t is greater than the transient time τ_1,

$$\tau_1 = 1/D \tag{3.4}$$

It follows from (2.15), (3.2), and (3.4) that $\tau_1/\tau_2 > \max(4, 2v/w, 2v/u)$ for all positive u, v, and w, where "max" means the largest of the three listed quantities. The τ_1 of (3.4) is thus the longest transient time in the problem: it is always greater than $4\tau_2$ and may be much greater. Then (2.14), which makes no reference to the initial distribution $P_x(0)$, holds for $t \gg 1/D$, and generally only then. We have $V > D$ [as was noted following

(2.16)], so $Dt \gg 1$ also implies $Vt \gg 1$. But Vt is the distance over which the distribution has drifted after long times t and $\sqrt{Dt}$ is the distance over which it has spread. Thus, the distribution becomes independent of the initial distribution after it has both drifted and spread over distances large compared with its initial span [assumed to be $O(1)$], which is the physically obvious condition.

4. CONNECTION TO DERRIDA'S HOPPING MODEL

Once the model has been formulated as in Fig. 2 it may be seen to be a simple special case of the periodic one-dimensional hopping model that Derrida introduced and for which he found the steady-state behavior.[14] His model is like that in Fig. 2 but with a period of any length N and any transition rates $w_{x,x-1}$ and $w_{x-1,x}$ within a period. The present model is the special case $N=2$ and $w_{x-1,x}=0$ for x odd [see (2.2)].

Derrida's general results for the drift velocity V and diffusion coefficient D are[14]

$$V=\frac{N}{\sum_{x=1}^{N} r_x}\left(1-\prod_{x=1}^{N}\frac{w_{x,x+1}}{w_{x+1,x}}\right) \tag{4.1}$$

and

$$D=\frac{1}{(\sum_{x=1}^{N} r_x)^2}\left(V\sum_{x=1}^{N} s_x \sum_{k=1}^{N} k r_{x+k} + N\sum_{x=1}^{N} w_{x+1,x} r_x s_x\right) - V\frac{N+2}{2} \tag{4.2}$$

where

$$r_x=\frac{1}{w_{x+1,x}}\left(1+\sum_{k=1}^{N-1}\prod_{j=1}^{k}\frac{w_{x+j-1,x+j}}{w_{x+j+1,x+j}}\right) \tag{4.3}$$

and

$$s_x=\frac{1}{w_{x+1,x}}\left(1+\sum_{k=1}^{N-1}\prod_{j=1}^{k}\frac{w_{x-j,x+1-j}}{w_{x+1-j,x-j}}\right) \tag{4.4}$$

For $N=2$ and for $w_{x-1,x}$ and $w_{x,x-1}$ as in (2.2) one finds

$$r_1=\frac{v+w}{uw}, \qquad r_2=\frac{1}{w}, \qquad s_1=\frac{1}{u}, \qquad s_2=\frac{u+v}{uw} \tag{4.5}$$

Then from (4.1) and (4.2) one obtains for V and D exactly the formulas (2.15).

The general periodic one-dimensional hopping model could then be adapted as a molecular-motor model embodying a general N-step mechanism for each elemental period. This could be a useful generalization of the 2-step models.

APPENDIX

This is an outline of the derivation of (2.14) as the long-time limit of the exact $P_x(t)$ in (2.11).

As remarked in the text, the leading contribution to $P_x(t)$ after long times comes only from the term in the integrand of (2.11) that is proportional to $\exp[\lambda_1(q)t]$ and then only from the immediate neighborhoods of $q=0, \pm\pi$. The respective contributions may then be called $P_x^{(0)}(t)$, $P_x^{(\pi)}(t)$, and $P_x^{(-\pi)}(t)$:

$$P_x(t) \sim P_x^{(0)}(t) + P_x^{(\pi)}(t) + P_x^{(-\pi)}(t) \qquad (t \to \infty) \tag{A.1}$$

Since $\lambda_1(q)$ is periodic in q with period π the leading terms in its expansion about any integer multiple n of π follow from (2.19) and the remarks immediately below it:

$$\lambda_1(q) = iV(q - n\pi) - D(q - n\pi)^2 + \cdots \tag{A.2}$$

with V and D as defined in (2.15).

From (2.8),

$$\lambda_1(n\pi) = 0, \qquad \lambda_2(n\pi) = -(u+v+w) \tag{A.3}$$

Then from (2.3), (2.4), and (2.9),

$$\Pi_1(n\pi) = \frac{u}{u+v+w} \tag{A.4}$$

so

$$\left[1 + \frac{\lambda_1(q)+v+w}{ue^{iq}}\right] \Pi_1(q) = \begin{cases} 1, & q=0 \\ \dfrac{u-v-w}{u+v+w}, & q=\pm\pi \end{cases} \tag{A.5}$$

For the asymptotic limit $t \to \infty$ the term containing $\exp[\lambda_2(q)t]$ in the integrand of (2.11) is ignored and the expansion (A.2) truncated after the $(q-n\pi)^2$ term. Since in this limit the contributions $P_x^{(0)}(t)$, $P_x^{(\pi)}(t)$, and

$P_x^{(-\pi)}(t)$ to $P_x(t)$ come only from the immediate neighborhoods of $q=0$, π, and $-\pi$, respectively, the ranges of integration for these three contributions may be taken to be $(-\infty, \infty)$, $(-\infty, \pi)$, and $(-\pi, \infty)$, respectively, while the factor $\{1+[\lambda_1(q)+v+w]/u \exp(iq)\}\, \Pi_1(q)$ in the integrand is set equal to its values at $q=0$, π, $-\pi$, respectively, as given by (A.5). One then calculates

$$P_x^{(0)}(t) = \frac{1}{2\sqrt{\pi Dt}} e^{-(x-Vt)^2/4Dt} \tag{A.6}$$

$$P_x^{(\pi)}(t) = \frac{1}{2\pi\sqrt{Dt}} \frac{u-v-w}{u+v+w} e^{-i\pi x} \times \left[\frac{1}{2}\sqrt{\pi}\, e^{-(x-Vt)^2/4Dt} + iH\left(\frac{x-Vt}{\sqrt{Dt}}\right)\right] \tag{A.7}$$

$$P_x^{(-\pi)}(t) = \frac{1}{2\pi\sqrt{Dt}} \frac{u-v-w}{u+v+w} e^{i\pi x} \times \left[\frac{1}{2}\sqrt{\pi}\, e^{-(x-Vt)^2/4Dt} - iH\left(\frac{x-Vt}{\sqrt{Dt}}\right)\right] \tag{A.8}$$

where the function $H(y)$ is defined as the integral

$$H(y) = \int_0^\infty e^{-z^2} \sin yz\, dz \tag{A.9}$$

From (A.1), the $P_x(t)$ we seek is asymptotically the sum of the quantities in (A.6)–(A.8). But x is integer valued, so $\exp(-i\pi x) = \exp(i\pi x) = (-1)^x$. Therefore the terms containing the functions H in (A.7) and (A.8) cancel in the sum, and one has $P_x(t)$ given asymptotically by (2.14), as quoted.

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