PHYSICAL REVIEW E **69**, 061904 (2004)

Replica model for an unusual directed polymer in 1+1 dimensions and prediction of the extremal parameter of gapped sequence alignment statistics

Yi-Kuo Yu

National Center for Biotechnology Information, National Library of Medicine, National Institutes of Health, Bethesda, Maryland 20894, USA

and Department of Physics, Florida Atlantic University, Boca Raton, Florida 33431, USA

(Received 13 September 2003; revised manuscript received 15 December 2003; published 1 June 2004)

Sequence alignment is one of the most important bioinformatics tools for modern molecular biology. The statistical characterization of gapped alignment scores has been a long-standing problem in sequence alignment research. In this paper, we provide a self-contained exposition of sequence alignment, a short review about how this problem is related to the directed polymer problem in statistical physics, and some analytical results that can be used for predicting alignment score statistics. Basically, we present two classes of solutions for the gapped alignment statistics by explicitly calculating the evolution of the few-replica partition function in 1 +1 dimensions. We have obtained the conditions under which the more important extremal parameter λ, characterizing the alignment score statistics, becomes predictable.

DOI: 10.1103/PhysRevE.69.061904 PACS number(s): 87.10.+e, 05.40.−a, 02.50.−r, 02.50.Fz

I. INTRODUCTION

The directed polymer (path) in random media (DPRM) problem [1–3] is one of the best studied systems with quenched disorder. In a $d+1$ dimensional DPRM system, there are d regular spatial dimensions and one timelike dimension that is singled out to specify the elongated direction of the path. The displacement made by the DP, when projected onto the timelike direction, is often identified as the *length* of the DP. Due to the presence of the quenched disorder, the system's free energy depends on the particular realization of the disorder involved, and it is the probability distribution function (pdf) of the free energy that characterizes the statistical properties of the system. The pdf of the free energy can be obtained in various ways. It can be obtained directly by numerical means, or it can be characterized by its moments which sometimes can be analytically calculated, or it can be mapped to other problems whose solutions are available.

The basic idea of the moment method is to use the replica trick [4] and the cumulant expansion [5]. One first writes down, under a given realization of the disorder potential, the partition function of n identical copies of the system; one then performs the anneal average of this n-replica partition function over the disorder; the replica number n is then treated as a continuous variable conjugate to the free energy to provide the cumulant expansion. Although there is some limitation to the validity of such inference [6–8], it nevertheless provides a valuable analytical route to tackle such problems. In $1+1$ dimensions, the replicated system can be mapped [2] into a one-dimensional n-particle system whose ground state energy can be found exactly, whence the physical properties of the original system in the infinite length limit can be inferred.

In terms of mapping to other problems, the DPRM can be mapped [9] into the noisy Burgers equation [10], whose critical exponents in $1+1$ dimensions have been worked out [11]. With a direct Hopf transformation, the DPRM can also be mapped into the Kardar-Parisi-Zhang (KPZ) equation [12] which describes surface growth (roughening) under spatiotemporal noise, and has been intensively studied for many years [13].

Recently, this system has found another manifestation[1] in sequence alignment [15,17], one of the most powerful tools in modern molecular biology. Computer-assisted sequence alignment has become increasingly important due to the rapid growth of DNA and protein databases. The use of sequence alignment ranges from identifying the possible functionality of newly sequenced DNA/protein to the construction of phylogenetic trees [18–20]. Under sequence alignment, the relatedness of two sequences compared is quantified by an alignment score and its associated p value. The latter is the probability of obtaining the same or even higher score by aligning two uncorrelated random sequences, and thus provides a more meaningful measure of homology detected.

Unfortunately, rigorous results relating the p values to alignment parameters (or scoring function) employed exist only for gapless alignment, which is less sensitive in detecting distant homology. When gaps are allowed, the score distribution is known empirically to follow a similar form but the full characterization is still incomplete. In a few previous publications [21–23], we have shown that the more important extremal parameter λ of the score distribution can be predicted if a simple procedure is followed. We call this case the first solvable class.

In this paper, we show that there exists a second solvable class, and provide the detailed procedure for obtaining this solution via computing the two-replica partition function exactly. We have also recently shown [24] that the combination

[1]When cast in the language of DPRM, there does exist a subtle difference between the sequence comparison and the regular DPRM problems in terms of the noise correlations [14]. Nevertheless, it has been argued [15] and shown numerically [16] that such a difference does not lead to much effect.

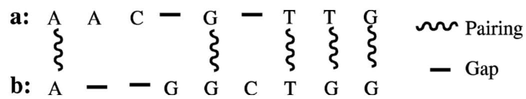

FIG. 1. An example of global alignment between sequence **a** and **b**.

of these two classes and the employment of a cooling map enables us to extend extremal parameter predictability to generic finite-temperature alignments, including the probabilistic alignments and the optimal alignments. The main results that are related to alignment score statistics are summarized by Eqs. (45), (90), (109)–(113), (119), (120), (126), and (127). Equation (59) and the remarks around it can also be of important use in the study of granular systems.

This paper is otherwise organized as follows. In the following section, we give a self-contained introduction to sequence alignment, establish notation, and explain the conditions for solvability. In the third section, we focus on the so-called linear gap case. Both the first solvable class and the second solvable class will be presented in detail to pave the way for the more elaborate affine gap case. Since this is the case that is closely related to the traditional DPRM problem, we also provide some details regarding the two-replica bound state which can potentially be used to construct the many-replica solutions. In the fourth section, the key results for the second solvable class under the affine gap costs will be described. The more detailed but important intermediate steps, however, are relegated to the appendixes for readers interested in the detailed procedure. A summary and some concluding remarks constitute the last section.

II. SEQUENCE ALIGNMENT AND THE DIRECTED PATH PROBLEM

Sequence alignment can be used to identify homology between protein or DNA sequences. An alignment between two sequences **a** and **b**, which themselves can be subsequences of some longer sequences, is given in Fig. 1. In this particular example, both sequences contain seven characters. $\mathbf{a}=[AACGTTG]$ while $\mathbf{b}=[AGGCTGG]$. We will use the notation a_i (b_j) to refer to the ith (jth) character of sequence $\mathbf{a}(\mathbf{b})$. Thus, a_3 is C, b_5 is T, etc.

The quality of an alignment is usually quantified by the associated alignment score, which is the sum of pairwise substitution scores $s(a_i,b_j)$ and gap penalties $\gamma(i_0,i_f|j_0,j_f)$. Here $s(a_i,b_j)$ denotes the pairwise substitution score when we pair up character a_i from sequence **a** with the character b_j from sequence **b**. Because of its dependence on two characters (indices), a set of substitution scores is often called a *substitution matrix* or *scoring matrix*. A gap is formed when a character from one sequence is not paired with any character from the other sequence, and the function $\gamma(i_0,i_f|j_0,j_f)$ returns the gap penalty when the substrings (of consecutive characters) $[a_{i_0+1},\ldots,a_{i_f}]$ and $[b_{j_0+1},\ldots,b_{j_f}]$ are not paired with characters from their respective countersequences. Apparently, the case $i_0=i_f$ (or $j_0=j_f$) indicates that the substring $[a_{i_0+1},\ldots,a_{i_f}]$ (or $[b_{j_0+1},\ldots,b_{j_f}]$) contains no characters.

It is a common practice to use the term *scoring function* to denote the combination of the substitution matrix and the gap penalty function used for sequence alignment. Under a given scoring function, the associated alignment score of the example in Fig. 1 will be $s(A,A)-\gamma(1,3|1,2)+s(G,G)-\gamma(4,4|3,4)+s(T,T)+s(T,G)+s(G,G)$, which consists of five pairwise substitution scores and two gap penalties. Although there are many possible alignments, corresponding to different arrangements of gaps and substitutions, between two sequences, one usually refers to the alignment with highest alignment score as the *optimal alignment* and its associated score as the *alignment score*. The alignment example above is often termed *global alignment* since the two sequences (**a** and **b**) are aligned from head to toe.

The more frequently used alignment method, however, is *local alignment*. Local alignment aims to find only the most homologous segments, one from each sequence compared, instead of finding the optimal global alignment between the two sequences. Under a scoring function, the most homologous pair of segments between two sequences **a** and **b** is identified with the subsequence $\hat{\mathbf{a}}$ of **a** and the subsequence $\hat{\mathbf{b}}$ of **b** such that the global alignment of these two subsequences $\hat{\mathbf{a}}$ and $\hat{\mathbf{b}}$ yields the highest alignment score. In this context, the *highest* global alignment score resulting from the global alignment of all possible subsequence pairs is also termed as the *optimal local alignment score* or simply the *alignment score*.

The scoring function used in sequence alignment is often designed by experienced biologists. Different substitution matrices are designed for capturing different types of similarity (or evolutionary distances). The most commonly used substitution matrices are the PAM series [25] and the BLOSUM series [26]. The careful curatorial work that has gone into the construction of the PAM and BLOSUM matrices has rendered them extremely valuable tools for studying and detecting similarities across a great spectrum of protein families, and these or related matrices are used by default in the most popular protein database search programs such as FASTA [27] and BLAST [28]. The gap penalty function can have many variants. The most commonly used gap function is the so-called affine gap function where the gap function $\gamma(i_0,i_f|j_0,j_f)$ depend only on the lengths of each unpaired substring, i.e.,

$$\gamma(i_0,i_f|j_0,j_f)=\gamma(\ell_1=i_f-i_0,\ell_2=j_f-j_0),$$

with

$$\gamma(\ell_1,\ell_2)=\begin{cases}0, & \ell_1=0,\ell_2=0\\ \delta+\varepsilon(\ell_1-1), & \ell_1\geqslant 1,\ell_2=0\\ \delta+\varepsilon(\ell_2-1), & \ell_1=0,\ell_2\geqslant 1\\ \bar{\delta}+2\delta+\varepsilon(\ell_1+\ell_2-2), & \ell_1\geqslant 1,\ell_2\geqslant 1.\end{cases} \tag{1}$$

The parameter ε is called the gap extension penalty, $\delta-\varepsilon$ is called the gap initialization cost, while $\bar{\delta}$ is an extra penalty when both ℓ_1 and ℓ_2 are not zero. As we will describe later,

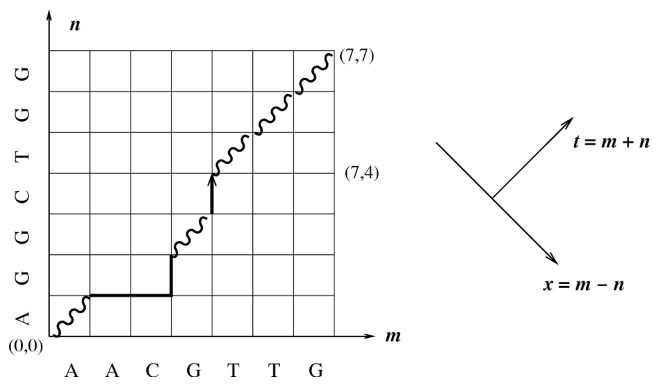

FIG. 2. The alignment lattice. Upon laying sequence **a** along the horizontal axes and sequence **b** along the vertical axes, we note that the directed path here uniquely represents the alignment shown in Fig. 1. The new coordinate system $(x=m-n, t=m+n)$ is also shown to illustrate the connection between the recursion relation (2) used in sequence alignment and the corresponding one (14) used in DPRM.

the case that is of strongest connection to DPRM is the linear gap limit, i.e., when $\varepsilon=\delta$ and $\overline{\delta}=0$.

The Needleman-Wunsch [29] algorithm for global alignment and Smith-Waterman algorithm [30] for local alignment are well established. In the following, we will sketch both algorithms together with their finite-temperature counterparts, including the Hidden-Markov-Model (HMM) based algorithms, and make connections to the DPRM problem. For a more detailed exposition relating the finite-temperature algorithm to the HMM based algorithm, see reference [21].

A. Alignment algorithms

We will first sketch the optimal alignment algorithms for both global alignment and local alignment, and continue with their finite temperature counterparts in order to elucidate their connection to the DPRM problem. Useful notation will also be established along the way.

Let $\mathbf{a}=[a_1,a_2,\ldots,a_M]$ and $\mathbf{b}=[b_1,b_2,\ldots,b_N]$ be two sequences of lengths M and N, respectively, with elements a_i and b_j taken from a finite character set χ. Under a given scoring function, i.e., a substitution matrix and a gap function, one can align these two sequences either locally or globally using the algorithms below.

1. Optimal algorithms

The optimal alignment algorithms aim to find the alignment resulting in the highest alignment score defined earlier. This is usually carried out by using the so-called dynamic programming method. Let us start with the global alignment algorithm by Needleman and Wunsch [29]. For clarity, we introduce the alignment lattice in Fig. 2 with sequence **a** laid along the x direction and sequence **b** laid along the y direction. Note that the alignment example given in Fig. 1 is shown as a (directed) path in the alignment lattice. In fact, each alignment is represented by a unique path and vice versa.

Define the auxiliary quantity $S_{m,n}$ that records the highest global alignment score for alignment paths starting at the origin $(0,0)$ and terminating at point (m,n). It is not hard to see that for the linear gap case the auxiliary quantity $S_{m,n}$ obeys the following recursion relation:

$$S_{m,n}=\max\left\{\begin{matrix} S_{m-1,n-1}+s(a_m,b_n) \\ S_{m-1,n}-\varepsilon, S_{m,n-1}-\varepsilon \end{matrix}\right\}, \tag{2}$$

with the boundary conditions

$$S_{0,n\geqslant 0}=-n\varepsilon \quad \text{and} \quad S_{m\geqslant 0,0}=-m\varepsilon. \tag{3}$$

The alignment score is then obtained as $S_{M,N}$ and the associated optimal alignment is obtained by the *trace-back* method [18].

For local alignment, one compares not only among the *global alignment paths*, which start at the origin and terminate at (M,N), but rather among the alignment paths whose starting point can be anywhere on the alignment lattice and whose terminating point can also be anywhere on the alignment lattice. In particular, the local alignment actually allows the *null* alignment, i.e., an alignment whose starting point and terminating point are the same on the alignment lattice. This seemingly difficult task was solved elegantly by the Smith-Waterman algorithm [30]. Here one again introduces the auxiliary quantity $H_{m,n}$ which now records the highest global alignment score for alignment paths terminating at point (m,n) regardless of where the path start. Interestingly, this new auxiliary quantity obeys a similar iterative equation

$$H_{m,n}=\max\left\{\begin{matrix} H_{m-1,n-1}+s(a_m,b_n) \\ H_{m-1,n}-\varepsilon, H_{m,n-1}-\varepsilon, 0 \end{matrix}\right\}, \tag{4}$$

with even simpler boundary conditions

$$H_{0,n\geqslant 0}=0 \quad \text{and} \quad H_{m\geqslant 0,0}=0. \tag{5}$$

Note that the introduction of 0 into the choice in Eq. (4) allows for a new starting point when the current best score is still below the threshold 0. The final alignment score is then obtained by

$$\mathsf{S}[\mathbf{a},\mathbf{b};s,\gamma]=\max_{\substack{1\leqslant m\leqslant M \\ 1\leqslant n\leqslant N}}\{H_{m,n}\}. \tag{6}$$

When the affine gap function is used, more auxiliary quantities are needed. Indeed, for global alignment with affine gaps, three auxiliary quantities $S^S_{m,n}$, $S^D_{m,n}$, and $S^I_{m,n}$ are defined through the recursion relations

$$S^S_{m,n}=S_{m-1,n-1}+s(a_m,b_n),$$

$$S^D_{m,n}=\max\{S^S_{m-1,n}-\delta, S^D_{m-1,n}-\varepsilon\}, \tag{7}$$

$$S^I_{m,n}=\max\left\{\begin{matrix} S^S_{m,n-1}-\delta, S^I_{m,n-1}-\varepsilon \\ S^D_{m,n-1}-\delta-\overline{\delta} \end{matrix}\right\},$$

with

$$S_{m,n} = \max\{S^S_{m,n}, S^D_{m,n}, S^I_{m,n}\}, \tag{8}$$

and boundary conditions

$$\begin{aligned} S^D_{0,n\geqslant 0} &= S^I_{n\geqslant 0,0} = -\infty, \\ S^D_{n>0,0} &= S^I_{0,n>0} = \delta + (n-1)\varepsilon, \\ S^S_{0,n>0} &= S^S_{n>0,0} = -\infty, \\ S^S_{0,0} &= 0. \end{aligned} \tag{9}$$

Similarly, for local alignment with affine gaps, three other auxiliary quantities $H^S_{m,n}$, $H^D_{m,n}$, and $H^I_{m,n}$ are defined through the recursion relations

$$\begin{aligned} H^S_{m,n} &= \max\begin{Bmatrix} H^S_{m-1,n-1} + s(a_m,b_n) \\ H^D_{m-1,n-1} + s(a_m,b_n) \\ H^I_{m-1,n-1} + s(a_m,b_n), 0 \end{Bmatrix}, \\ H^D_{m,n} &= \max\{H^S_{m-1,n} - \delta, H^D_{m-1,n} - \varepsilon\}, \\ H^I_{m,n} &= \max\begin{Bmatrix} H^S_{m,n-1} - \delta, H^I_{m,n-1} - \varepsilon \\ H^D_{m,n-1} - \delta - \overline{\delta} \end{Bmatrix}, \end{aligned} \tag{10}$$

with

$$H_{m,n} = \max\{H^S_{m,n}, H^D_{m,n}, H^I_{m,n}\}, \tag{11}$$

and the boundary conditions

$$\begin{aligned} H_{0,n\geqslant 0} &= H_{n\geqslant 0,0} = 0, \\ H^D_{0,m\geqslant 0} &= H^I_{0,m\geqslant 0} = H^D_{m\geqslant 0,0} = H^I_{m\geqslant 0,0} = -\infty. \end{aligned} \tag{12}$$

The optimal score S is still given in terms of the H's according to Eq. (6).

2. Finite temperature variants and DPRM

The recursion (2) in fact is a commonly used approach, i.e., the transfer matrix, in statistical physics. In particular, it is very similar to the transfer matrix used to tackle the zero temperature DPRM problem in 1+1 dimension. For a detailed review of the DPRM problems, readers are referred to Ref. [13] and references therein. In a 1+1 dimensional DPRM system, each lattice point is labeled by two discrete indices x and t for space and time, respectively.

To illustrate the connection between DPRM and the sequence alignment problem, we focus on the following variant of DPRM. A directed path $\mathcal{A}$ starting from the origin $(x=0,t=0)$ can be regarded as the "world line" of a particle in one dimension. For a given realization of randomness, a random potential $u(x,t)$ is assigned to the bond connecting lattice points $(x,t+1)$ and (x,t). There is also a *constant* elastic penalty associated with each bending of the path, e.g., going from (x,t) to $(x-1,t+1)$ instead of to $(x,t+1)$. The quantities of interest include the free energy $F(t)$ and the restricted free energy $F(x,t)$, which are related through $F(t)=\Sigma_x F(x,t)$. The restricted free energy is defined by

$$F(x,t) = -\tau \ln\left\{\sum_{\mathcal{A}|(x,t)} \exp[-E(\mathcal{A})/\tau]\right\} \tag{13}$$

where the sum is over the paths terminating at point (x,t), τ is the temperature of the system, and $E(\mathcal{A})$, sum of the random potentials and the elastic energies contributed by all the bonds traversed by the path $\mathcal{A}$, is the energy associated with the path $\mathcal{A}$.

At zero temperature, the free energy is the energy of the lowest energy path. Writing the elastic energy as $\overline{\varepsilon}$, one can write down easily the transfer matrix for finding the lowest energy path and its associated energy via the following recursion:

$$E(x,t) = \min\begin{Bmatrix} E(x,t-1) + u(x,t-1) \\ E(x-1,t-1) + \overline{\varepsilon} \\ E(x+1,t-1) + \overline{\varepsilon} \end{Bmatrix}. \tag{14}$$

The lowest energy at time T is then given by

$$\min_x E(x,T). \tag{15}$$

By introducing $x=m-n$ and $t=m+n$, we can rewrite the recursion (2) in terms of x and t

$$S(x,t) = \max\begin{Bmatrix} S(x,t-2) + s(x,t-1) \\ S(x-1,t-1) - \varepsilon \\ S(x+1,t-1) - \varepsilon \end{Bmatrix}, \tag{16}$$

with $s(a_m,b_n)$ rewritten as $s(x,t-1)$. The reason we did not write $s(a_m,b_n)$ as $s(x,t)$ comes from the observation that the letter pair (a_m,b_n) is located at $(m-1/2,n-1/2)$, not (m,n), on the alignment lattice (see Fig. 2). Note that if one defines $S(x,t)\equiv -E(x,t)$, then the above recursion is turned into

$$E(x,t) = \min\begin{Bmatrix} E(x,t-2) - s(x,t-1) \\ E(x-1,t-1) + \varepsilon \\ E(x+1,t-1) + \varepsilon \end{Bmatrix}. \tag{17}$$

Therefore, the negative of the substitution score plays the role of the potential and the gap cost plays the role of elastic energy. However, we also note that the recursion in Eq. (17) uses energies at time $t-2$ and $t-1$ to update energies at time t, while the energies at time t only depends on energies at time $t-1$ for the recursion (14). This slight difference actually makes the solution of the sequence alignment case considerably more involved than the DP case.

The similarity between the two recursions (14) and (16), however, immediately leads to the finite-temperature generalization of Eq. (16). Introducing the temperature τ, the "Boltzmann weight" $W(x,t)$, the gap weight $\nu\equiv\exp(-\varepsilon/\tau)$, and the substitution weight $\upsilon(x,t)=\exp[s(x,t)/\tau]$, we write down the recursion for the Boltzmann weight

$$\begin{aligned} W(x,t) = {}& \nu\,[W(x-1,t-1) + W(x+1,t-1)] \\ & + \upsilon(x,t-1)W(x,t-2), \end{aligned} \tag{18}$$

or using the original (m,n) indices

$$W_{m,n} = +\nu[W_{m-1,n} + W_{m,n-1}] + v_{m,n}W_{m-1,n-1}, \tag{19}$$

with $v_{m,n}=\exp[s(a_m,b_n)/\tau]=v(x,t-1)$. Using the appropriate boundary conditions,

$$W_{n\geqslant 0,0} = W_{0,n\geqslant 0} = \nu^n \quad \text{for } W_{m,n},$$
$$\left.\begin{aligned} W(x,t=0) &= \delta_{x,0}, \\ W(x,t<0) &= 0, \end{aligned}\right\} \quad \text{for } W(x,t)$$

it is easily shown that

$$W(x,t) = W_{m,n} = \sum_{\mathcal{A}|\{(m,n)\ \text{or}\ (x,t)\}} \exp[-E(\mathcal{A})/\tau] \tag{20}$$

sums the Boltzmann weight of every path starting from the origin and terminating at lattice point (m,n) or equivalently (x,t). Note that $W(x,t)=\exp[-F(x,t)/\tau]$ and $W_{m,n}=\exp[-F_{m,n}/\tau]$. Both recursions (18) and (19) can be regarded as finite-temperature generalization of Eq. (2). In fact, the zero temperature limit is recovered by taking

$$S_{m,n} = -\lim_{\tau\to 0} F_{m,n} = \lim_{\tau\to 0} \tau \ln W_{m,n} \tag{21}$$

for every (m,n). Furthermore, the total partition function is then obtained by summing $e^{-F_{m,n}/\tau}$ over the boundary points of consideration.

Along a similar line, the finite-temperature generalization of Eq. (4) can be written as

$$\begin{aligned} Z(x,t) = {} & \nu[Z(x-1,t-1) + Z(x+1,t-1)] \\ & + v(x,t-1)Z(x,t-2) + 1 \end{aligned} \tag{22}$$

or

$$Z_{m,n} = \nu[Z_{m-1,n} + Z_{m,n-1}] + v_{m,n}Z_{m-1,n-1} + 1. \tag{23}$$

Note that the boundary conditions are now given by

$$Z_{n\geqslant 0,0} = Z_{0,n\geqslant 0} = 1, \quad \text{for } Z_{m,n}$$
$$\left.\begin{aligned} Z(x,t=|x|) &= 1, \\ Z(x,t<|x|) &= 0, \end{aligned}\right\} \quad \text{for } Z(x,t),$$

and the total Boltzmann weights from paths with all allowed starting points and terminating points can be easily written as

$$\mathcal{Z} = \sum_{m,n} Z_{m,n}. \tag{24}$$

The +1 term in Eqs. (23) and (22) can be regarded as adding $\exp(0/\tau)$ or can be derived formally using the Green's function. Basically, any starting point is allowed for local alignments. For a path terminating at point (x,t), it can accommodate any starting point (x',t') with ranges $(-\tau+x\leqslant x'\leqslant\tau+x, t'=t-\tau)$ $\forall\tau\geqslant 0$, or in the backward "light cone" of the point (x,t). Let $\hat{g}(x,t)$ denote the retarded Green's function satisfying

$$\begin{aligned} \hat{L}\hat{g}(x,t;x',t') \equiv {} & \hat{g}(x,t;x,t') - \nu[\hat{g}(x-1,t-1;x',t') \\ & + \hat{g}(x+1,t-1;x',t')] \\ & - v(x,t-1)\hat{g}(x,t-2;x',t') = \delta_{t,t'}\delta_{x,x'}, \end{aligned} \tag{25}$$

where $\hat{L}$ is the discrete analog of $-\nu\nabla^2 - v$, and retardedness requires that

$$\hat{g}(x,t<t';x',t') = 0. \tag{26}$$

It is not hard to see that the $W(x,t)$ for global alignment is in fact the Green's function with source point $(x'=0,t'=0)$, i.e., $W(x,t)=\hat{g}(x,t;0,0)$. For local alignment, we can write the corresponding $Z(x,t)$ as

$$Z(x,t) = \sum_{x't'} \hat{g}(x,t;x',t'), \tag{27}$$

because Eq. (26) automatically takes care of the condition that the source point (x',t') must be within the backward light cone. Upon applying the linear operator $\hat{L}$ to $Z(x,t)$, we have

$$\hat{L}Z(x,t) = \sum_{x't'} \delta_{x,x'}\delta_{t,t'} = 1. \tag{28}$$

This formally explains why the +1 term appears in Eqs. (23) and (22).

For the finite-temperature version with affine gaps, we follow Eq. (1) to obtain the affine gap weights $g(\ell_1,\ell_2)$

$$g(\ell_1,\ell_2) = \begin{cases} 1, & \ell_1 = 0, \ell_2 = 0 \\ \mu\cdot\nu^{\ell_1-1}, & \ell_1 \geqslant 1, \ell_2 = 0 \\ \mu\cdot\nu^{\ell_2-1}, & \ell_1 = 0, \ell_2 \geqslant 1 \\ \mu'\cdot\mu^2\cdot\nu^{\ell_1+\ell_2-2}, & \ell_1 \geqslant 1, \ell_2 \geqslant 1, \end{cases} \tag{29}$$

with $\mu=\exp(-\delta/\tau)$ being the first gap weight and $\mu'=\exp(-\bar{\delta}/\tau)$ being the extra gap weight. We introduce $W^S_{m,n}$, $W^D_{m,n}$, and $W^I_{m,n}$ that are counterparts of $S^S_{m,n}$, $S^D_{m,n}$, and $S^I_{m,n}$ respectively in Eq. (7). The recursions of these auxiliary quantities are then given as

$$W^S_{m,n} = v_{m,n}[W^S_{m-1,n-1} + \mu^D_1\cdot W^D_{m-1,n-1} + \mu^I_1\cdot W^I_{m-1,n-1}],$$

$$W^D_{m,n} = \mu^D_2 W^S_{m-1,n} + \nu W^D_{m-1,n},$$

$$W^I_{m,n} = \mu^I_2 W^S_{m,n-1} + \nu W^I_{m,n-1} + \mu'\mu^I_2\mu^D_1 W^D_{m,n-1}, \tag{30}$$

where parameters $\mu^{D(I)}_{1(2)}$ satisfy and $\mu^D_1\cdot\mu^D_2=\mu^I_1\cdot\mu^I_2=\mu=\exp(-\delta/\tau)$. Note that the affine gap weight is not implemented in the simplest manner here, since the Boltzmann weight of each path satisfying the affine gap weight properties (29) can be achieved without introducing $\mu^{D(I)}_{1(2)}$s. The introduction of these extra parameters, however, is useful when we identify the relationship between the finite-temperature alignment and the *probabilistic alignment* that we will mention briefly later. The boundary conditions for $W^{S,D,I}$s are

$$W^D_{0,n\geqslant 0} = W^I_{n\geqslant 0,0} = 0,$$

$$W^D_{n>0,0} = \mu_2^D \nu^{n-1},$$

$$W^I_{0,n>0} = \mu_2^I \nu^{n-1}, \quad (31)$$

$$W^S_{0,n>0} = W^S_{n>0,0} = 0,$$

$$W^S_{0,0} = 1. \quad (32)$$

The total Boltzmann weight of paths starting from the origin and terminating at (m,n) is then given by

$$W_{m,n} = W^S_{m,n} + W^D_{m,n} + W^I_{m,n} = \exp[-F_{m,n}/\tau]. \quad (33)$$

For local alignment with affine gaps, we again introduce $Z^S_{m,n}$, $Z^D_{m,n}$, and $Z^I_{m,n}$ that are counterparts of $H^S_{m,n}$, $H^D_{m,n}$, and $H^I_{m,n}$, respectively. The recursions of these auxiliary quantities are then given as

$$Z^S_{m,n} = v_{m,n}[Z^S_{m-1,n-1} + \mu_1^D \cdot Z^D_{m-1,n-1} + \mu_1^I \cdot Z^I_{m-1,n-1}] + 1,$$

$$Z^D_{m,n} = \mu_2^D Z^S_{m-1,n} + \nu Z^D_{m-1,n},$$

$$Z^I_{m,n} = \mu_2^I Z^S_{m,n-1} + \nu Z^I_{m,n-1} + \mu' \mu_2^I \mu_1^D Z^D_{m,n-1}. \quad (34)$$

The total Boltzmann weight from paths that can start anywhere but terminate at (m,n) is then given by

$$Z_{m,n} = \exp[-F_{m,n}/\tau] = [Z^S_{m,n} + Z^D_{m,n} + Z^I_{m,n}]. \quad (35)$$

The total Boltzmann weight from all allowed paths on the alignment lattice is again given by Eq. (24).

B. Alignment score statistics

It is important to realize that the value of the optimal score S does not in itself convey any meaning regarding the degree of homology between the sequences being aligned. One way to assess sequence homology is to compare the score S with the optimal score of aligning sequences from a null model. A frequently used null model is that of the mutually uncorrelated Markov random chains of rank zero,[2] under which the joint probability of observing sequences **a** and **b** is given by

$$P_0[\mathbf{a},\mathbf{b}] = \prod_{\substack{1\leqslant m\leqslant M\\ 1\leqslant n\leqslant N}} p(a_m)\cdot p(b_n), \quad (36)$$

where $p(a)$ is the background frequency for the element a, with $\Sigma_{a\in\chi} p(a)=1$. The pdf of optimal scores for the alignment of random sequences is

$$\mathrm{pdf}(\mathsf{S}) = \langle \delta(\mathsf{S} - \mathsf{S}[\mathbf{a},\mathbf{b};s,\gamma])\rangle_0, \quad (37)$$

where $\langle\ldots\rangle_0$ denotes average over the null sequence distribution (36). The pdf (37) provides the p value that an alignment of two uncorrelated random sequences receives an optimal score S.

1. Gapless alignment

Clearly, the pdf (37) would depend generally on the sequence lengths M,N, and the scoring functions s and γ. For gapless alignment, the form of the distribution function is known exactly [31–34] in the asymptotic limit $M,N \gg 1$. For all scoring systems satisfying the condition

$$\sum_{a,b\in\chi} p(a)p(b)s(a,b) < 0, \quad (38)$$

which includes all the PAM [25] and BLOSUM [26] matrices, the pdf reaches the universal form

$$D(\mathsf{S}) = KMN\lambda\ \exp[-\lambda\mathsf{S} - KMNe^{-\lambda\mathsf{S}}], \quad (39)$$

known as the Gumbel distribution [35]. This distribution is specified completely by the two parameters λ and K, with a mean $\langle\mathsf{S}\rangle_0 \equiv \mathsf{S}_0 = \lambda^{-1}[\gamma_e + \ln KMN]$ where $\gamma_e = 0.577\,215\,6\ldots$ is the Euler constant, and an exponential tail

$$D(\mathsf{S} \gg \mathsf{S}_0) = \lambda KMNe^{-\lambda\mathsf{S}}, \quad (40)$$

characterized by the parameter λ.

The theory of Karlin and Altschul provides explicit formulas for these parameters in terms of the scoring function s. For example, λ can be found as the unique positive root of the equation

$$\sum_{a,b\in\chi} p(a)p(b)e^{\lambda s(a,b)} = 1. \quad (41)$$

A more complicated expression exists for the calculation of K, which we will not describe here but can be found in [32].

2. Gapped alignment

Compared to gapless alignment, the statistics of gapped alignment for the null model (36) are much more difficult to characterize. First of all, the average optimal score S_0 does not always have logarithmic dependence on sequence lengths. For sufficiently small gap cost, the mean score in fact acquires a *linear* dependence on sequence length even if condition (38) is satisfied, i.e., $\mathsf{S}_0 = cN$ (for sequences of lengths $M \approx N \gg 1$), with the proportionality factor $c \geqslant 0$ depending on the substitution scores and gap cost. The critical line $c=0$ defines the locus of *phase transition* points [36–38] separating the linear and logarithmic regimes of S_0. Various statistical properties in the vicinity of this log-linear phase transition have been characterized in several recent studies [39,40]. Also, ample empirical evidence [16,41–46] suggests that the optimal score S of gapped alignment again obeys the Gumbel distribution (39) in the logarithmic phase. However, the functional dependence of the Gumbel parameters λ and K on the scoring functions is not known.

Recently, an efficient numerical method was developed by Olsen *et al.* [16] to characterize the tail of the Gumbel distribution. The method utilizes intermediate computational results, e.g., the restricted local alignment score $H_{m,n}$, also known as the "score landscape." The landscape consist of a

[2]This type of Markov chain is also commonly referred to as independent identically distributed (iid) chain.

collection of positive scoring "islands," i.e. clusters of positive H's, separated by a "sea" at $H=0$. The peak scores of the islands are found to follow Poisson statistics. From this, the Gumbel distribution of the optimal score S can be derived.

The study of island statistics indicates that the key to understanding the Gumbel distribution is characterization of the probability tail of obtaining a *single* large island, the statistics of which can be more conveniently studied in the context of global alignment. Using the saddle point method, we gave [21] a heuristic derivation of the Poisson distribution of the large island scores. The results lead to the Gumbel distribution for the optimal scores, as well as the all-important Gumbel parameter λ, in terms of the solution of the equation

$$\Omega(\lambda) \equiv \lim_{N\to\infty} \langle e^{\lambda h(N)} \rangle_0 = 1. \tag{42}$$

Note that $h(N)=\max_{1\leq j\leq N}\{S_{j,N}, S_{N,j}\}$, with $S_{m,n}$ obeying Eqs. (2), (7), and (8), and $\langle S_{N,N}\rangle_0 < 0$ for large N is also required to ensure the system is in the logarithmic phase. The condition (42) for the Gumbel parameter λ was also derived [48] by first assuming the alignment score distribution follows the Gumbel distribution.

The function $\Omega(\lambda)$ contains a great deal of information and is difficult to compute in general. Only recently has it been computed [48] for a special choice of scoring functions,[3] with

$$s(a,b) = \begin{cases} 1, & \text{if} \quad a=b \\ -2\varepsilon, & \text{if} \quad a\neq b, \end{cases}$$

and linear gap cost ($\delta=\varepsilon, \bar{\delta}=0$), under the (weak) approximation that the scores $s(a_m, b_n)$ are uncorrelated for different m's or n's. The resulting $\lambda(\varepsilon)$ obtained in this case is in excellent agreement with extensive numerical simulation [48], and demonstrates the validity of the formula (42). However, the computation of $\Omega(\lambda)$ for *arbitrary* scoring functions remains unsolved. Along practical lines, Mott and Tribe [49] produced an empirical formula for λ which works reasonably well in the large gap-cost regime. Siegmund and Yakir [50] studied a similar limit where the maximum number of gaps is finite. Despite all of these studies, the current understanding of the statistics of gapped alignment remains very limited.

C. Hybrid alignment and solvability of λ

The Smith-Waterman algorithm (6) and (10)–(12) is an example of an algorithm which looks for the *optimal* solution to a combinatorial problem, the solution being in this case the optimal alignment and the optimal score S. An alternative approach to solving combinatorial problems such as sequence alignment is to look for a class of *probable* solutions. This approach has been taken in a number of previous studies of global alignment, e.g., the maximum-likelihood method [51,52], the finite-temperature method [17,53], and the hidden Markov model [54]. The probabilistic approach has also been used in Smith-Waterman–type local alignment: In the HMM approach as implemented in the "sequence alignment and modeling" software suite [55], local alignment is accomplished by embedding probabilistic global alignment in between "free insertion modules," which allows a part of a sequence to fit to the HMM. In a different approach [56] probabilistic Smith-Waterman is realized by normalizing the probabilistic version of global alignment against a reference with substitution weights all set to 1. In fact, probabilistic alignment can be regarded as a special case of finite-temperature alignment in which the alignment parameters are subjected to a *probability conservation condition*. The reason that the gap weight μ was split into $\mu=\mu_1^D\cdot\mu_2^D=\mu_1^I\cdot\mu_2^I$ is to make it possible to satisfy the probability conservation conditions.

The advantage of the probabilistic approach lies in the simple interpretation of the alignment parameters and results. For example, the abstract gap cost becomes a gap insertion probability, and the local alignment score ln $\mathcal{Z}$, with $\mathcal{Z}$ defined in Eq. (24), between two sequences becomes the overall log-likelihood of the evolutionary relation between the two sequences; see Ref. [21] for more details. However, the probabilistic approach also bears distinct disadvantages. Aside from a modest computational speed disadvantage, the probabilistic approach suffers from ill-characterized score statistics—unlike the Smith-Waterman local alignment, for which at least the form of the optimal score distribution is known for the null model, very little is known about the distribution of the log-likelihood score ln $\mathcal{Z}$ of the probabilistic local alignment of random sequences. Arbitrary use of the z score has been shown empirically not to produce very good results [57].

In a few previous publications [21,22], we proposed an alternative approach to sequence alignment. Our "semiprobabilistic" (or hybrid) alignment combines the advantages of both the optimizational and probabilistic approaches to local alignment. With the Boltzmann weight computed via Eq. (34), we construct the maximum log-likelihood (MLL) score

$$\Phi[\mathbf{a},\mathbf{b};v,g] = \max_{\substack{1\leq m\leq M\\ 1\leq n\leq N}} \{\ln Z_{m,n}\}. \tag{43}$$

The MLL score is manifestly a *hybrid* of both the probabilistic and optimizational approaches to local alignment. Following reference [21], we refer to alignment based on the MLL score as "Semiprobabilistic alignment," and refer to this algorithm as the "hybrid algorithm."

In fact, as indicated in Ref. [21], the MLL score statistics follow the Gumbel form even before the probability conservation conditions are imposed. The corresponding Gumbel parameter λ can again be obtained by solving an equation similar to Eq. (42) with $h(N)=\tau \ln \widetilde{W}_t$, i.e.,

$$\lim_{t\to\infty} \langle [\widetilde{W}_t(w,g)]^{\lambda\tau} \rangle_0 = 1 \tag{44}$$

with $\lambda > 0$. The quantity $\widetilde{W}_t$, which specifies the total Boltzmann weight flowing out of a fixed "time" slice t, is

[3] This choice of scoring functions corresponds to the problem of the longest common subsequences, see Chvtal and Sankoff [47].

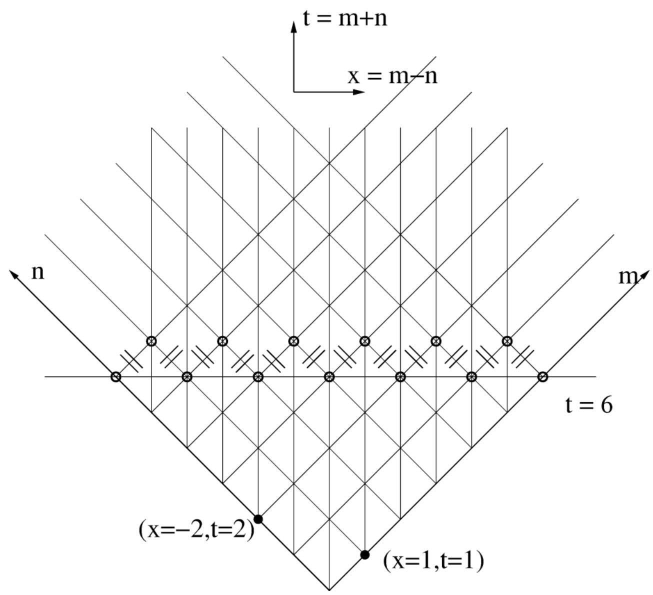

FIG. 3. The alignment lattice turned 45 ° counterclockwise compared to Fig. 2.

defined [4] by Eq. (50) for the linear gap case and defined by Eq. (103) for the affine gap case.

The solvability of Eq. (44) comes from the observation that when $\lambda\tau$ is an integer R, the condition (44) becomes

$$\lim_{t\to\infty}\langle[\widetilde{W}_t(w,g)]^R\rangle_0 = 1, \tag{45}$$

whose left-hand side is the disorder-averaged partition function of an R-replica system. Here the random substitution weight $v(a_m,b_n)$ resulting from random sequence pairs $[\mathbf{a},\mathbf{b}]$ will play the role of $\exp[-u(x,t-1)/\tau]$ of the DPRM problem.

When $R=1$, this corresponds to a one replica problem and was solved [21] by imposing the conservation of Boltzmann weight, i.e., the weight flowing in equals the weight flowing out *on average* at each lattice point. We call it the *first solvable class*. Within this solvable class, $\lambda=1/\tau$. Furthermore, at $\tau=1$ this class results in a direct mapping of the finite-temperature alignment to probabilistic alignment.

The *second solvable class*, having $\lambda=2/\tau$, comes from $R=2$ (two replicas). Here the disorder average, introducing the interactions between the two replicas, complicates the matter. For a generic DPRM problem, the disorders at different time are uncorrelated, therefore the interacting system can still be cast in the transfer matrix approach [8,58]. The random sequences $\mathbf{a}=[a_1,a_2,\ldots,a_N]$ and $\mathbf{b}=[b_1,b_2,\ldots,b_N]$, however, contain only $2N$ random characters which is much less than the $N(N-1)/2$ random potentials of the corresponding DPRM. The factor $N(N-1)/2$ is most easily seen from Fig. 3 in which there are $N(N-1)/2$ vertical bonds under the horizontal line $t=N$. Therefore, the random potential from $v(a_m,b_n)$ inevitably bears stronger correlations. The validity of ignoring such correlations in the context of match-mismatch–type of scoring was in fact raised [14] earlier and was also shown numerically [16,48] to be unimportant when large score statistics are considered. Furthermore, when the scoring function is more complicated, such as in the case of the 20×20 amino acid substitution matrix, the correlation effect will be further reduced. Therefore, although our second solvable class is based on the (weak) assumption that we can ignore the correlation of the disorder potential $v(x,t)$ at different times, it agrees with numerical studies quite well. Note that in the sequence alignment problem the disorder potential $v(x,t)$ resides at the mid point of the bond connecting the lattice points $(x,t-1)$ and $(x,t+1)$. This is what make the transfer matrix formalism of the system a little more involved than the conventional DPRM.

Since the λ parameter of the local alignment statistics happens to be expressed in terms of its global alignment counterparts, from this point on we shall focus on the *global alignment* unless otherwise stated. In the following two sections, we will provide the procedures for obtaining the second solvable class as well as review some of the relevant one replica results.

III. LINEAR GAP CASE

Recall that for the linear gap case the Boltzmann weight $W(x,t)$ follows the recursion (18)

$$W(x,t+1) = \nu\,[W(x+1,t) + W(x-1,t)] + v(x,t)W(x,t-1),$$

where $v(x,t)$ is the substitution weight and ν is the linear gap weight. In order to obtain the two solvable classes, we further introduce the equivalent of chemical potential σ in the following fashion [remembering that $v(x,t-1)=v(a_m,b_n)$]:

$$v(a_m,b_n) \to \exp[[s(a_m,b_n) + 2\sigma]/\tau], \tag{46}$$

$$\nu \to \exp[(-\varepsilon + \sigma)/\tau]. \tag{47}$$

Basically, σ can be regarded as the score gain per unit length or the quantity $-\sigma$ can be regarded as the chemical potential. For a fixed scoring matrix and fixed gap cost ε, the two solvable classes impose different conditions on σ at different temperature resulting into the two expressions, $\sigma_1(\tau;s,\gamma)$ and $\sigma_2(\tau;s,\gamma)$.

Although these expressions are important for the development of the "cooling map" [24], we will not delve into it here. For the purpose of providing the conditions for the two solvable classes, we simply focus on the relations among the substitution weights $v(x,t)$ and the gap weight ν.

A. One replica ($R=1$)

As explained earlier, the first solvable class happens at $\lim_{t\to\infty}\langle\widetilde{W}_t\rangle_0=1$. This condition was solved [21] by choosing

$$2\nu + \langle v(a_m,b_n)\rangle_0 = 1, \tag{48}$$

which then guarantees that $\langle\widetilde{W}_t\rangle_0=1$ for all t and consequently as $t\to\infty$. We will use v to denote the disorder averaged substitution weight, i.e.,

[4] The quantity $\widetilde{W}_t$ is analogous to the quantity $\widetilde{W}_{N,N}$ defined in [21] that sums the Boltzmann weights flowing out of the boundaries $(0\leqslant m\leqslant N, n=N)$ and $(m=N, 0\leqslant n\leqslant N)$.

$$v = \langle v(a,b)\rangle_0 \equiv \sum_{a,b\in\chi} p(a)p(b)v(a,b). \tag{49}$$

Before providing a rigorous derivation of the condition (48), let us first clearly define what $\widetilde{W}_t$ is in the context of the linear gap case:

$$\widetilde{W}_t = \sum_x W(x,t) + \sum_{x'} v(x',t)W(x',t-1). \tag{50}$$

Note that if x is summed over even integers then x' will be summed over odd integers and vice versa. The open circles in Fig. 3 indicate the vertices whose weights are summed over at time $t=6$. The double slash on the bonds indicate that no weight flow through those bonds should be included.

Let $\phi(x,t)$ denote $\langle W(x,t)\rangle_0$; we may then write down easily the corresponding iterative equation

$$\phi(x,t+1) = v\phi(x,t-1) + \nu[\phi(x+1,t) + \phi(x-1,t)], \tag{51}$$

whereas the quantity $\langle \widetilde{W}_t\rangle_0$ is obtained by

$$\langle \widetilde{W}_t\rangle_0 = \sum_x \phi(x,t) + v\sum_{x'} \phi(x',t-1). \tag{52}$$

Equation (51) can be easily solved by going through discrete Laplace transform and Fourier transforms. Defining

$$\phi_{\hat z}(x) \equiv \sum_{t=0}^{\infty} \hat z^t \phi(x,t), \tag{53}$$

$$\phi_{\hat z}(k) \equiv \sum_x e^{-ikx}\phi_{\hat z}(x), \tag{54}$$

we obtain

$$\phi_{\hat z}(x) - \delta_{x,0} = \hat z^2 v\phi_{\hat z}(x) + \hat z\nu[\phi_{\hat z}(x+1) + \phi_{\hat z}(x-1)],$$

$$\phi_{\hat z}(k) - 1 = [\hat z^2 v + 2\hat z\nu\cos(k)]\phi_{\hat z}(k).$$

Apparently, the quantity of interest $\langle \widetilde{W}_t\rangle_0$ corresponds to

$$\langle \widetilde{W}_t\rangle_0 = \oint \frac{d\hat z}{2\pi i}\left[\frac{\phi_{\hat z}(k=0)}{\hat z^{t+1}} + v\frac{\phi_{\hat z}(k=0)}{\hat z^{t}}\right] = \oint \frac{d\hat z}{2\pi i}\frac{1}{\hat z^{t+1}}\frac{1+v\hat z}{1-\hat z^2 v - 2\nu\hat z}.$$

When $\nu=(1-v)/2$, we may rewrite $v\hat z^2+2\nu\hat z-1$ as $v\hat z^2+\hat z-v\hat z-1=(v\hat z+1)(\hat z-1)$. Therefore the contour integral becomes

$$\oint \frac{d\hat z}{2\pi i}\frac{1}{\hat z^{t+1}}\frac{1}{1-\hat z} = 1 \quad \forall\, t.$$

When $\nu\neq(1-v)/2$, the quantity $\langle \widetilde{W}_t\rangle_0$ either diverges exponentially with time (when $2\nu+v>1$) or exponentially decreases with time (when $2\nu+v<1$). Because of the disorder potential, we know that $\widetilde{W}_t$ will assume different values for different realizations of the disorder potential. Therefore, $\langle(\widetilde{W}_t-\langle\widetilde{W}_t\rangle_0)^2\rangle_0>0$, and consequently $\langle \widetilde{W}_t^2\rangle_0>\langle\widetilde{W}\rangle_0{}^2$. For the two replica solution, we need to keep $\langle \widetilde{W}_t^2\rangle_0$ constant, which demands $2\nu+v<1$.

B. Two replicas ($R=2$)

To calculate $\langle \widetilde{W}_t^2\rangle_0$, we need to define a few notations first. Let us denote the variance of the disorder potential as Δ, i.e.,

$$\langle v(x,t)v(x',t')\rangle_0 - v^2 = \Delta\delta_{x,x'}\delta_{t,t'}. \tag{55}$$

We further define the following quantities:

$$\phi(x_1,x_2,t) \equiv \langle W(x_1,t)W(x_2,t)\rangle_0, \tag{56}$$

$$\phi^{>}(x_1,x_2,t) \equiv \langle W(x_1+1,t+1)W(x_2,t)\rangle_0, \tag{57}$$

$$\phi^{<}(x_1,x_2,t) \equiv \langle W(x_1,t)W(x_2+1,t+1)\rangle_0. \tag{58}$$

It is obvious that $\phi^{>}(x_1,x_2,t)=\phi^{<}(x_2,x_1,t)$ since the order inside the disorder average does not matter, i.e., the $W(x,t)$s are commuting entities. Nevertheless, it turns out to be more convenient to define both $\phi^{>}$ and $\phi^{<}$. The quantity $\langle \widetilde{W}_t^2\rangle_0$ can now be expressed in terms of the ϕs,

$$\begin{aligned}\langle \widetilde{W}_t^2\rangle_0 &= \sum_{x_1,x_2}\langle W(x_1,t)W(x_2,t)\rangle_0 \\ &\quad + \sum_{x_1,x_2'}\langle W(x_1,t)v(x_2',t)W(x_2',t-1)\rangle_0 \\ &\quad + \sum_{x_1',x_2}\langle v(x_1',t)W(x_1',t-1)W(x_2,t)\rangle_0 \\ &\quad + \sum_{x_1',x_2'}\langle v(x_1',t)v(x_2',t)W(x_1',t-1)W(x_2',t-1)\rangle_0 \\ &= \sum_{x_1,x_2}\phi(x_1,x_2,t) + \sum_{x_1,x_2}[\Delta\delta_{x_1,x_2}+v^2]\phi(x_1,x_2,t-1) \\ &\quad + v\sum_{x_1,x_2}[\phi^{>}(x_1,x_2,t-1)+\phi^{<}(x_1,x_2,t-1)].\end{aligned}$$

Note that because of our definition of $\phi^{>}$ and $\phi^{<}$, the sum over $x_1'(x_2')$ in $\langle WW\rangle_0$ is replaced by the sum over $x_1(x_2)$ in $\phi^{>}$ and $\phi^{<}$. If we Fourier transform ϕ and $\phi^{>(<)}$, we see that the most of the terms above contain only the zero momentum Fourier component, except the term multiplied by $\Delta\delta_{x_1,x_2}$, which gives rise to zero "center of mass" momentum, but collects the full spectrum of the "relative" momentum.

The reason that using Eqs. (56)–(58) is sufficient for solving this two-replica problem relies on the decomposition of unequal time correlations. Basically, if $|t-t'|\geqslant 2$, say $t-t'\geqslant 2$, we have[5]

[5]Although we will not exploit this decomposition here, we would like to point out that this feature can be used to compute the stress correlations [59] between two points at different depths in a granular system describable by the q model [60].

$$\langle W(x,t)W(y,t')\rangle_0 = \sum_{x'} \langle W(x',t')W(y,t')\rangle_0 \langle \hat{g}(x,t;x',t')\rangle_0$$
$$= \sum_{x'} \langle W(x',t')W(y,t')\rangle_0 \langle W(x-x',t-t')\rangle_0. \tag{59}$$

This decomposition happens because the disorder after time t' has no influence to $W(y,t')$ and it is in general true that $\hat{g}(x,t;0,0)=\Sigma_{x'}\hat{g}(x',t';0,0)\hat{g}(x,t;x',t')$ and that upon disorder average, $\langle W(x,t;x',t')\rangle_0$ becomes translationally invariant $\langle W(x-x';t-t')\rangle_0$, which is the $\phi(x-x',t-t')$ defined earlier in the one replica section.

We now study the iterative equations.

$$\begin{aligned}\phi(x_1,x_2,t+1) &= \langle W(x_1,t+1)W(x_2,t+1)\rangle_0 \\ &= \langle \{v(x_1,t)W(x_1,t-1) + \nu[W(x_1+1,t) \\ &\quad + W(x_1-1,t)]\}\{v(x_2,t)W(x_2,t-1) \\ &\quad + \nu[W(x_2+1,t) + W(x_2-1,t)]\}\rangle_0 \\ &= (\Delta\delta_{x_1,x_2} + v^2)\phi(x_1,x_2,t-1) \\ &\quad + \nu v[\phi^<(x_1,x_2,t-1) + \phi^<(x_1,x_2-2,t-1)] \\ &\quad + \nu v[\phi^>(x_1,x_2,t-1) + \phi^>(x_1-2,x_2,t-1)] \\ &\quad + \nu^2[\phi(x_1+1,x_2+1,t) + \phi(x_1+1,x_2-1,t) \\ &\quad + \phi(x_1-1,x_2+1,t) + \phi(x_1-1,x_2-1,t)],\end{aligned} \tag{60}$$

$$\begin{aligned}\phi^>(x_1,x_2,t+1) &= \langle W(x_1+1,t+2)W(x_2,t+1)\rangle_0 \\ &= \langle W(x_2,t+1)W(x_1+1,t+2)\rangle_0 \\ &= \langle W(x_2,t+1)\{v(x_1+1,t+1)W(x_1+1,t) \\ &\quad + \nu[W(x_1+2,t+1) + W(x_1,t+1)]\}\rangle_0 \\ &= v\phi^<(x_1+1,x_2-1,t) + \nu[\phi(x_1+2,x_2,t+1) \\ &\quad + \phi(x_1,x_2,t+1)],\end{aligned} \tag{61}$$

$$\begin{aligned}\phi^<(x_1,x_2,t+1) &= \langle W(x_1,t+1)W(x_2+1,t+2)\rangle_0 \\ &= \langle W(x_1,t+1)\{v(x_2+1,t+1)W(x_2+1,t) \\ &\quad + \nu[W(x_2+2,t+1) + W(x_2,t+1)]\}\rangle_0 \\ &= v\phi^>(x_1-1,x_2+1,t) + \nu[\phi(x_1,x_2+2,t+1) \\ &\quad + \phi(x_1,x_2,t+1)].\end{aligned} \tag{62}$$

Note that the recursive relations for Eqs. (61) and (62) hold true even if we set $t=-1$. This simply relates the initial conditions of $\phi^{>(<)}$ to that of ϕ.

Introducing the discrete Laplace and Fourier transforms similar to Eqs. (53) and (54), we have

$$\phi_{\hat{z}}(x_1,x_2) \equiv \sum_{t=0}^{\infty} \hat{z}^t \phi(x_1,x_2,t), \tag{63}$$

$$\phi_{\hat{z}}^k(y) \equiv \sum_{x_1,x_2} e^{-ik(x_1+x_2)}\delta_{x_1-x_2,2y}\phi_{\hat{z}}(x_1,x_2), \tag{64}$$

$$\phi_{\hat{z}}^{k,l} \equiv \sum_y e^{-2ily}\phi_{\hat{z}}^k(y). \tag{65}$$

Upon discrete Laplace transform, we have

$$\begin{aligned}\phi_{\hat{z}}(x_1,x_2) &= \delta_{x_1,0}\delta_{x_2,0} + \hat{z}^2(\Delta\delta_{x_1,x_2} + v^2)\phi_{\hat{z}}(x_1,x_2) \\ &\quad + \hat{z}^2\nu v[\phi_{\hat{z}}^<(x_1,x_2) + \phi_{\hat{z}}^<(x_1,x_2-2)] \\ &\quad + \hat{z}^2\nu v[\phi_{\hat{z}}^>(x_1,x_2) + \phi_{\hat{z}}^>(x_1-2,x_2)] \\ &\quad + \hat{z}\nu^2[\phi_{\hat{z}}(x_1+1,x_2+1) + \phi_{\hat{z}}(x_1+1,x_2-1) \\ &\quad + \phi_{\hat{z}}(x_1-1,x_2+1) + \phi_{\hat{z}}(x_1-1,x_2-1)],\end{aligned} \tag{66}$$

and

$$\phi_{\hat{z}}^>(x_1,x_2) = \hat{z}v\phi_{\hat{z}}^<(x_1+1,x_2-1) + \nu[\phi_{\hat{z}}(x_1+2,x_2) + \phi_{\hat{z}}(x_1,x_2)], \tag{67}$$

$$\phi_{\hat{z}}^<(x_1,x_2) = \hat{z}v\phi_{\hat{z}}^>(x_1-1,x_2+1) + \nu[\phi_{\hat{z}}(x_1,x_2+2) + \phi_{\hat{z}}(x_1,x_2)]. \tag{68}$$

We now do the first Fourier transform

$$\begin{aligned}\phi_{\hat{z}}^k(y) &= \delta_{y,0} + \hat{z}^2(\Delta\delta_{y,0} + v^2)\phi_{\hat{z}}^k(y) + \hat{z}^2\nu v[\phi_{\hat{z}}^{<k}(y) \\ &\quad + e^{-2ik}\phi_{\hat{z}}^{<k}(y+1)] + \hat{z}^2\nu v[\phi_{\hat{z}}^{>k}(y) + e^{-2ik}\phi_{\hat{z}}^{>k}(y-1)] \\ &\quad + \hat{z}\nu^2[e^{2ik}\phi_{\hat{z}}^k(y) + e^{-2ik}\phi_{\hat{z}}^k(y) + \phi_{\hat{z}}^k(y+1) + \phi_{\hat{z}}^k(y-1)],\end{aligned} \tag{69}$$

and

$$\phi_{\hat{z}}^{>k}(y) = \hat{z}v\phi_{\hat{z}}^{<k}(y+1) + \nu[e^{2ik}\phi_{\hat{z}}^k(y+1) + \phi_{\hat{z}}^k(y)], \tag{70}$$

$$\phi_{\hat{z}}^{<k}(y) = \hat{z}v\phi_{\hat{z}}^{>k}(y-1) + \nu[e^{2ik}\phi_{\hat{z}}^k(y+1) + \phi_{\hat{z}}^k(y)]. \tag{71}$$

We now proceed to do the second Fourier transform:

$$\begin{aligned}\phi_{\hat{z}}^{k,l} &= 1 + \hat{z}^2\Delta\phi_{\hat{z}}^k(y=0) + [\hat{z}^2v^2 + 2\hat{z}\nu^2(\cos 2k + \cos 2l)]\phi_{\hat{z}}^{k,l} \\ &\quad + \hat{z}^2\nu v(e^{-2ik+2il}+1)\phi_{\hat{z}}^{<k,l} + \hat{z}^2\nu v(e^{-2ik-2il}+1)\phi_{\hat{z}}^{>k,l},\end{aligned} \tag{72}$$

and

$$\phi_{\hat{z}}^{>k,l} = \hat{z}ve^{2il}\phi_{\hat{z}}^{<k,l} + \nu(e^{2ik+2il}+1)\phi_{\hat{z}}^{k,l}, \tag{73}$$

$$\phi_{\hat{z}}^{<k,l} = \hat{z}ve^{-2il}\phi_{\hat{z}}^{>k,l} + \nu(e^{2ik-2il}+1)\phi_{\hat{z}}^{k,l}, \tag{74}$$

which then leads to (upon solving for $\phi^{>(<)}$ in terms of ϕ)

$$\phi_{\hat{z}}^{>k,l} = \nu\phi_{\hat{z}}^{k,l}\frac{1 + e^{2ik+2il} + \hat{z}v(e^{2il} + e^{2ik})}{1 - \hat{z}^2v^2}, \tag{75}$$

$$\phi_{\hat{z}}^{<k,l} = \nu\phi_{\hat{z}}^{k,l}\frac{1+e^{2ik-2il}+\hat{z}\upsilon(e^{-2il}+e^{2ik})}{1-\hat{z}^2\upsilon^2}. \qquad (76)$$

It is then straightforward to calculate the following combination:

$$\begin{aligned}(1+e^{-2ik-2il})\phi_{\hat{z}}^{>k,l}&+(1+e^{-2ik+2il})\phi_{\hat{z}}^{>k,l}\\ &=(1-\hat{z}^2\upsilon^2)^{-1}\nu\phi_{\hat{z}}^{k,l}\{(1+e^{-2ik-2il})(1+e^{2ik+2il})\\ &\quad+\hat{z}\upsilon(1+e^{-2ik-2il})(e^{2il}+e^{2ik})\\ &\quad+(1+e^{-2ik+2il})(1+e^{2ik-2il})+\hat{z}\upsilon(1+e^{-2ik+2il})\\ &\quad\times(e^{-2il}+e^{2ik})\}\\ &=\frac{4\nu\phi_{\hat{z}}^{k,l}}{1-\hat{z}^2\upsilon^2}[1+\cos 2k\cos 2l+\hat{z}\upsilon(\cos 2k+\cos 2l)].\end{aligned} \qquad (77)$$

Substituting back into Eq. (72), we obtain

$$G_{\hat{z}}^{k.l-1}\phi_{\hat{z}}^{k,l} = 1+\Delta\hat{z}^2\phi_{\hat{z}}^{k}(y=0), \qquad (78)$$

where

$$\begin{aligned}G_{\hat{z}}^{k,l-1}\equiv{}&1-\hat{z}^2\upsilon^2-2\hat{z}\nu^2(\cos 2k+\cos 2l)\\ &-\frac{4\hat{z}^2\nu^2\upsilon}{1-\hat{z}^2\upsilon^2}[1+\cos 2k\cos 2l\\ &+\hat{z}\upsilon(\cos 2k+\cos 2l)].\end{aligned} \qquad (79)$$

The expression in Eq. (79) indicates that both $\hat{z}\upsilon$ and $\hat{z}\nu^2$ are dimensionless. For convenience, we introduce the following dimensionless parameters:

$$z\equiv\hat{z}\upsilon,$$

$$\tilde{\Delta}\equiv\Delta/\upsilon^2,$$

$$\omega\equiv\nu^2/\upsilon. \qquad (80)$$

Note that it is always the $k=0$ limit we need; we therefore can simplify the calculation by setting $k=0$ first. To lighten the notation, we only retain the variable l. Thus, $\phi_{\hat{z}}^{k=0,l}$ becomes ϕ^l and $\phi_{\hat{z}}^{k}(y=0)$ becomes $\phi(y=0)$. Upon setting $k=0$, Eq. (79) reads

$$\begin{aligned}G^{l-1}&=\left\{1-z^2-2z\omega\frac{1+z}{1-z}(1+\cos 2l)\right\}\\ &=\frac{1+z}{1-z}[(1-z)^2-2z\omega-2z\omega\cos 2l].\end{aligned} \qquad (81)$$

Therefore, we have

$$\phi^l=\frac{(1-z)[1+\tilde{\Delta}z^2\phi(y=0)]}{(1+z)[(1-z)^2-2z\omega-2z\omega\cos 2l]}. \qquad (82)$$

We now employ the following identities:

$$\phi_{\hat{z}}(y=0)=\frac{1}{\pi}\int_0^{\pi}\phi_{\hat{z}}^l\, e^{2il\times 0}dl, \qquad (83)$$

$$\frac{1}{\sqrt{a^2-b^2}}=\int_0^{2\pi}\frac{d\theta}{2\pi}\frac{1}{a-b\cos\theta}\quad \text{if } a^2>b^2. \qquad (84)$$

Note that if we assume $a=(1-z)^2-2z\omega$ and $b=2z\omega$, we immediately see $a^2-b^2=(1-z)^4-4z\omega(1-z)^2=(1-z)^2[(1-z)^2-4z\omega]>0$. The reason is that $(1-z)^2-4z\omega>0$. This can be seen by checking whether $1-z$ is greater than $2\sqrt{z\omega}$ or not. Equivalently, we are asking whether $\sqrt{\hat{z}}(\sqrt{\hat{z}}\upsilon+2\nu)<1$ is true. Since $\hat{z}\leqslant 1$ and $\upsilon+2\nu<1$, we see that is always true. Consequently, we have

$$\phi(y=0)=\frac{1+\tilde{\Delta}z^2\phi(y=0)}{(1+z)\sqrt{(1-z)^2-4z\omega}}, \qquad (85)$$

or equivalently

$$\phi(y=0)=\frac{1}{(1+z)\sqrt{(1-z)^2-4z\omega}-\tilde{\Delta}z^2}, \qquad (86)$$

Eq. (86) can then be substituted into Eq. (82) to obtain the complete expression for ϕ^l.

The expression for $\phi^{>(<)}$ also simplifies greatly when we set $k=0$. For example, we now have

$$\phi^{>l}=\frac{\nu\phi^l}{1-\hat{z}\upsilon}(1+e^{2il}), \qquad (87)$$

$$\phi^{<l}=\frac{\nu\phi^l}{1-\hat{z}\upsilon}(1+e^{-2il}). \qquad (88)$$

With the relations found above, it is now a good time to write down explicitly the quantity $\langle\tilde{W}_t^2\rangle_0$ we need to calculate,

$$\begin{aligned}\langle\tilde{W}_t^2\rangle_0=\oint\frac{d\hat{z}}{2\pi i}\Bigg\{&\frac{1+\hat{z}\upsilon^2}{\hat{z}^{t+1}}\phi^{l=0}+\upsilon\frac{\phi^{>l=0}+\phi^{<l=0}}{\hat{z}^t}\\ &+\Delta\frac{\phi(y=0)}{\hat{z}^t}\Bigg\}.\end{aligned} \qquad (89)$$

When $\Delta=0$, i.e., no randomness, we expect to see that $\tilde{W}_t=\langle\tilde{W}_t\rangle_0$ and $\langle\tilde{W}_t^2\rangle_0=\langle\tilde{W}_t\rangle_0{}^2$. Therefore, when $\Delta=0$ and $2\nu+\upsilon=1$, we expect the expression (89) to be simplified to

$$\oint\frac{d\hat{z}}{2\pi i}\frac{1}{\hat{z}^{t+1}}\frac{1}{1-\hat{z}}.$$

This disorder-free limit in fact can be verified in a straightforward manner.

When $\Delta\neq 0$, we need to make sure that $\phi(y=0)$ does not have any $\hat{z}$ pole such that $|\hat{z}|<1$ (or $|z|<\upsilon$) to guarantee that $\langle\tilde{W}_{t\to\infty}^2\rangle_0=$const. Furthermore, $\phi(y=0)$ should have a pole at $\hat{z}=1$ (or $|z|=\upsilon$) under the condition $2\nu+\upsilon<1$. To better visualize when this will happen, let us look at the expression $\phi(y=0)=1/[(1+z)\sqrt{(1-z)^2-4z\omega}-\tilde{\Delta}z^2]$. There are two parts

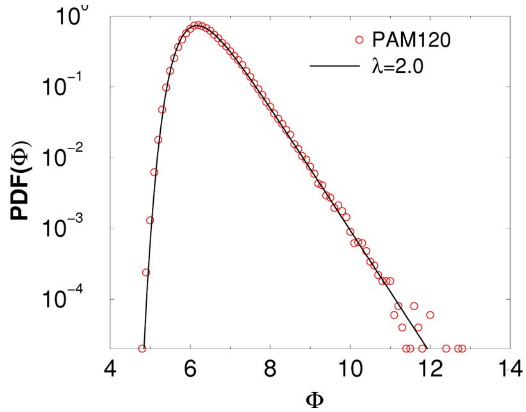

FIG. 4. The normalized histogram and the Gumbel fit under the condition (90) at $\tau=1$. The alignment scores were obtained by first generating sequence pairs according to probability distribution (36) and then aligning each sequence pair according to the algorithm described by Eqs. (23) and (43). The relations between the scoring function and the substitution weight and linear gap weight are summarized in Eqs. (46) and (47) with the chemical potential "$-\sigma$" chosen to satisfy the solvability condition (90). Each random sequence generated has length $N=600$. The circles represent the alignment score histogram of 500 000 random sequence pairs using the PAM120 scoring matrix and linear gap cost $\varepsilon=4.5$. The solid line corresponds to a fit to the Gumbel form (39) with $\lambda=2.0$ as expected, together with the other fitted parameter $\ln\kappa=\ln(KN^2)=12.4$. The error bar associated with λ is about 0.02, i.e., $\lambda=2\pm0.02$ from the fitting.

in the denominator. Let us call the expression $(1+z)\sqrt{(1-z)^2-4z\omega}$ the first part and $-\tilde{\Delta}z^2$ the second part. Note that both the first part and the second part have a negative derivative with respect to z for $\omega>0$ and $0<z<v<1$. Furthermore, when $z=0$, the first expression takes the value 1 while the second expression takes the value 0. Thus, the whole denominator of $\phi(y=0)$ is a decreasing function of z with value 1 when $z=0$. If we have the denominator set to zero at $z=v$, then the denominator will stay positive while $0\leqslant z<v$. This implies the following choice:

$$(1+v)\sqrt{(1-v)^2-4\nu^2}=\Delta. \tag{90}$$

This condition basically constrains the magnitude of Δ to be smaller than $(1+v)(1-v)=1-v^2$. It is obvious from Eq. (90) that the special case $2\nu+v=1$ will lead to $\Delta=0$.

Condition (90) is tested by an extensive numerical simulation at $\tau=1$ using the PAM120 scoring matrix of the PAM series substitution matrices [25] and a linear gap cost $\varepsilon=4.5$. Figure 4 shows the normalized score histogram obtained from aligning half a million pairs of random sequences of length $N=600$ along with a fit of the Gumbel form (39). The tail is given by the parameter $\lambda=2.0\pm0.02$ as expected from $2/\tau=2/1=2$.

C. Two-replica bound state

In the context of the regular R-replica DPRM problem, the partition function of a DP of length t is simply our previous definition of $\tilde{W}_t$. In a similar fashion, the disorder-averaged, normalized restricted partition function

$$\lim_{t\to\infty}\frac{\phi(x_1,x_2,\ldots,x_R,t)}{\sum_{x_1,x_2,\ldots,x_R}\phi(x_1,x_2,\ldots,x_R,t)} \tag{91}$$

gives the probability density of finding replica i at position x_i for all $i=1,2,\ldots,R$. The Laplace transformed quantity $\phi_{\hat{z}}(x_1,x_2,\ldots,x_R)$ is nothing but

$$\sum_{x_1,x_2,\ldots,x_R}\phi_{\hat{z}}(x_1,x_2,\ldots,x_R)=\sum_{t=0}^{\infty}\hat{z}^t\langle\tilde{W}_t^R\rangle_0.$$

By gradually increasing the value of $\hat{z}$ from 0, the above quantity increases; when $\hat{z}=\hat{z}_0$, the above quantity diverges. This suggests that we can write the expression in Eq. (91) as

$$\frac{\phi_{\hat{z}_0}(x_1,x_2,\ldots,x_R)}{\sum_{x_1,x_2,\ldots,x_R}\phi_{\hat{z}_0}(x_1,x_2,\ldots,x_R)}.$$

Actually, the quantity $\hat{z}_0$ is closely related to the ground state energy of the R-replica system. It has been used to calculate the ground state energy of a few-replica DPRM system [8].

In general, the disorder average results in an attractive potential among the replicas [2]. Therefore, one can write the disorder-averaged R-replica partition function as [8]

$$\langle\tilde{W}_t^R\rangle_0=e^{-\mathcal{F}_R(t)/\tau}\langle\tilde{W}_t\rangle_0{}^R,$$

with the ground state energy of the R replica given by [8]

$$E_R=\lim_{t\to\infty}[t^{-1}\mathcal{F}_R(t)].$$

This relation connects the Laplace variable $\hat{z}_0$ and the ground state energy of R-replica system

$$E_R=\tau\left[R\left(\lim_{t\to\infty}\frac{\ln\langle\tilde{W}_t\rangle_0}{t}\right)+\ln\hat{z}_0\right].$$

Another way to view E_R is to look at its continuous time counterpart. Basically, one may write down a time evolution equation for $\phi(x_1,x_2,\ldots,x_R,t)$, and the lowest eigenvalue of the time evolution operator is analogous to our E_R here.

For a two replica system, it is of interest to investigate how the probability density decays with the two replicas' relative distance y. That is, we consider the quantity

$$\lim_{t\to\infty}\frac{\phi^{k=0}(y,t)}{\phi^{k=0,l=0}(t)}=\frac{\phi^{k=0}_{\hat{z}_0}(y)}{\phi^{k=0,l=0}_{\hat{z}_0}}.$$

The quantity $\phi^{k=0}_{\hat{z}}(y)$ can be computed by the inverse Fourier transform of Eq. (65), i.e.,

$$\phi^{k=0}_{\hat{z}}(y)=\int_0^{\pi}\phi^{k=0,l}_{\hat{z}}e^{-2ily}\frac{dl}{\pi}. \tag{92}$$

Furthermore, since $\phi^{k=0,l=0}_{\hat{z}}$ is independent of y and l, we can simply divide both the left-hand side and right-hand side of Eq. (92) by $\phi^{k=0,l=0}_{\hat{z}_0}$ to achieve

$$\frac{\phi_{\hat{z}}^{k=0}(y)}{\phi_{\hat{z}}^{k=0,l=0}} = \int_0^\pi \frac{\phi_{\hat{z}}^{k=0,l}}{\phi_{\hat{z}}^{k=0,l=0}} e^{-2ily} \frac{dl}{\pi}. \quad (93)$$

Using the above expression, Eq. (86) and (82), we obtain

$$\frac{\phi_{\hat{z}}^{k=0}(y)}{\phi_{\hat{z}}^{k=0,l=0}} = \int_0^\pi \frac{[(1-z)^2 - 4z\omega]e^{-2ily}}{(1-z)^2 - 2z\omega - 2z\omega\cos(2l)} \frac{dl}{\pi}$$
$$= \int_0^{2\pi} \frac{d\theta}{2\pi} \frac{[(1-z)^2 - 4z\omega]e^{-iy\theta}}{(1-z)^2 - 2z\omega - 2z\omega\cos\theta}. \quad (94)$$

Because y takes integer value, it is easy to see that the final expression in Eq. (94) is an even function of y. Therefore one may assume $y>0$ and proceed without loss of generality. Let us introduce the complex variable $t=\rho e^{i\theta}$ together with the short notations $a=(1-z)^2-2z\omega$ and $b=2z\omega$, we rewrite the last expression of Eq. (94) as

$$\frac{1}{2\pi i}\oint_{|t|=1} \frac{dt}{t}\frac{1}{t^y}\frac{a-b}{a-\frac{b}{2}(t+1/t)} = \frac{1}{2\pi i}\oint_{|t|=1}\frac{dt}{t^y}\frac{a-b}{ta-\frac{b}{2}(t^2+1)}.$$

Note that for $\hat{z}$ in range of interest $0\leqslant\hat{z}\leqslant\hat{z}_0$, we have $a>b>0$. Aside from $b>0$ by definition, we see $a>b$ from Eq. (86) where we have $\sqrt{a-b}$ being real and positive in the range of interest $0\leqslant\hat{z}\leqslant\hat{z}_0$. The integrand, aside from the pole at the origin (when $y\geqslant 1$), has two poles at $t_1=(a+\sqrt{a^2-b^2})/b$ and $t_2=(a-\sqrt{a^2-b^2})/b$. Note that $0<t_2<1$ and $t_1>1$. Since we are mainly interested in the large y limit to find the decay length, it is most direct to deform the contour of integration to a large circle with $|t|\to\infty$. By doing this, we need to deform the contour around the t_1 pole and the integral becomes $t_1^{-y}(2/b)(b/2\sqrt{a^2-b^2})=e^{-2y[(\ln t_1)/2]}/\sqrt{a^2-b^2}$.

Therefore the decay length ℓ_d is given by $2/\ln[t_1(\hat{z}_0)]$ with $\hat{z}_0$ given by setting the denominator of Eq. (86) to zero. More explicitly, the decay length is given by

$$\left\{\ln\frac{1-\hat{z}_0 v+\sqrt{(1-\hat{z}_0 v)^2-4\hat{z}_0\nu^2}}{2\sqrt{\hat{z}_0}\nu}\right\}^{-1}, \quad (95)$$

with $\hat{z}_0$ satisfying

$$\frac{1+\hat{z}_0 v}{\hat{z}_0^2}\sqrt{(1-\hat{z}_0 v)^2-4\hat{z}_0\nu^2} = \Delta \quad (96)$$

for given $\nu=e^{-\overline{\varepsilon}/\tau}$, $v=\langle e^{-u(x,t)/\tau}\rangle_0$, and variance $\Delta=\langle e^{-2u(x,t)/\tau}\rangle_0-v^2$.

Our analysis here provides the two-replica bound state characteristics. These characteristics can form the bases of useful approximations when solving the general R-replica problem or even shed light on its exact solution. However, we will not delve into more details here since the main goal of this paper is to provide the details of the second solvable class. After our short exposition of the two replica bound state here, and the detailed description for the linear gap case in Sec. III A and III B, we now turn to the affine gap case whose solution can be more useful in terms of application in biosequence alignments.

IV. AFFINE GAP CASE

The algebra in this case becomes much more involved. However, we can exploit our experience from solving the linear gap case to make this tedious procedure more tractable. Similarly to the linear gap case (46) and (47), the "chemical potential," $-\sigma$, is introduced via

$$v(a_m,b_n)\to\exp[(s(a_m,b_n)+2\sigma))/\tau,$$
$$\nu\to\exp[(-\varepsilon+\sigma)/\tau],$$
$$\mu\to\exp[(-\delta+\sigma)/\tau]. \quad (97)$$

Let us now rewrite the recursion relation (30) in the (x,t) coordinate system. We have introduced here one new parameter μ'', which was set to zero in Eq. (30), to allow for a directed path running along the vertical direction to turn to the horizontal direction without moving along the diagonal direction first (see Fig. 2). We therefore have

$$W^S(x,t+1)=v(x,t)[W^S(x,t-1)+\mu_1^D W^D(x,t-1) + \mu_1^I W^I(x,t-1)],$$
$$W^D(x,t+1)=\mu_2^D W^S(x-1,t)+\nu W^D(x-1,t) + \mu_2^D\mu''\mu_1^I W^I(x-1,t),$$
$$W^I(x,t+1)=\mu_2^I W^S(x+1,t)+\nu W^I(x+1,t) + \mu_2^I\mu'\mu_1^D W^D(x+1,t), \quad (98)$$

with the initial condition given by $W^S(x,t=0)=\delta_{x,0}$, $W^{D(I)}(x,t=0)=0$, and $W^{S(D,I)}(x,t<0)=0$. Note that the condition $\mu_1^{D(I)}\mu_2^{D(I)}=\mu$, with μ being the gap opening weight, still holds true even when the extra parameter μ'' is introduced.

As we have shown earlier [21], probability conservation (good for the one replica solution) leads to the following equations which the weight parameters have to satisfy simultaneously:

$$\langle v(x,t)\rangle_0+\mu_2^D+\mu_2^I=1,$$
$$\mu_1^I\langle v(x,t)\rangle_0+\nu+\mu_2^D\mu''\mu_1^I=1, \quad (99)$$
$$\mu_1^D\langle v(x,t)\rangle_0+\nu+\mu_2^I\mu'\mu_1^D=1.$$

The interpretation of these conditions is exceedingly simple. Basically, each of these equations constrains the weight flow out of each $W^{S(D,I)}$ to be the same as what flows into each of those modes (substitutions, deletions, and insertions). For a more general purpose, however, we will set the right-hand sides of Eqs. (99) to be a constant κ with the understanding that for the one replica solution $\kappa=1$. Together with two other conditions, $\mu_2^{D(I)}\mu_1^{D(I)}=\mu$ that relate the $\mu^{D,I}$'s, we can uniquely determine the relationships among all of the alignment parameters using Eqs. (99). The results are

$$\mu_1^D = \frac{\mu}{\mu_2^D} = \frac{(\kappa + \mu - \nu)^2 - (1-\mu')(1-\mu'')\mu^2}{\kappa(\kappa + \mu'\mu - \nu)}, \quad (100)$$

$$\mu_1^I = \frac{\mu}{\mu_2^I} = \frac{(\kappa + \mu - \nu)^2 - (1-\mu')(1-\mu'')\mu^2}{\kappa(\kappa + \mu''\mu - \nu)}, \quad (101)$$

$$\langle v \rangle_0 = \frac{\kappa[(\kappa - \nu)^2 - \mu'\mu''\mu^2]}{(\kappa + \mu - \nu)^2 - (1-\mu')(1-\mu'')\mu^2}. \quad (102)$$

In the application to the one replica solution, where $\kappa = 1$, Eq. (102) can be used [21] to obtain the value $\langle v \rangle_0$ and thus the amount of shift in score needed. In the two replica solution, however, we would like to make sure that the probability in the three possible states are depleted by the same amount. As we will show later, the condition analogous to Eq. (90) for the two replica system can be obtained and will determine the value of $\langle v \rangle_0$. Therefore Eq. (102) determines the κ value, which then determines the $\mu_{1(2)}^{D(I)}$ values uniquely. Before embarking on the solution, let us first clearly write down what $\widetilde{W}_t$ is:

$$\widetilde{W}_t = \sum_x W(x,t) + \sum_{x'} W^S(x', t+1). \quad (103)$$

As before, $W(x,t) \equiv W^S(x,t) + W^D(x,t) + W^I(x,t)$, and if x is summed over even integers then x' will be summed over odd integers, and vice versa.

For our analytical computation, we found another definition of auxiliary field more useful, namely,

$$Y^S(x,t) \equiv W^S(x,t) + Y^D(x,t) + Y^I(x,t),$$

$$Y^D(x,t) \equiv \mu_1^D W^D(x,t),$$

$$Y^I(x,t) \equiv \mu_1^I W^I(x,t). \quad (104)$$

Interestingly, $W^S(x', t+1) = v(x,t) Y^S(x, t-1)$ and we can write $W(x,t) = Y^S(x,t) + C_d Y^D(x,t) + C_i Y^I(x,t)$ where the new constants $C_d \equiv (1/\mu_1^D) - 1$ and $C_i \equiv (1/\mu_1^I) - 1$ are introduced for convenience. Before discussing the details involved in solving the affine gap case, let us write down first the iterative Eq. (98) in terms of the new auxiliary quantities defined in Eq. (104),

$$Y^S(x,t+1) = v(x,t) Y^S(x,t-1) + Y^D(x,t+1) + Y^I(x,t+1),$$

$$Y^D(x,t+1) = \mu Y^S(x-1,t) + (\nu - \mu) Y^D(x-1,t) - \mu(1-\mu'') Y^I(x-1,t),$$

$$Y^I(x,t+1) = \mu Y^S(x+1,t) + (\nu - \mu) Y^I(x+1,t) - \mu(1-\mu') Y^D(x+1,t). \quad (105)$$

Using the above recursion relations and the methods in Sec. III A, we can establish the one replica result (first solvable class) more mathematically. We will, however, not delve into this known solution [21] here. Instead, we would like to focus more on the two replica solution to obtain the second solvable class.

We start by writing down the quantity $\widetilde{W}_t^2$ in terms of the newly defined Y variables.

$$\begin{aligned}\widetilde{W(t)}^2 = &\sum_{x_1,x_2} [Y^S(x_1,t) + C_d Y^D(x_1,t) + C_i Y^I(x_1,t)] \\ &\times [Y^S(x_2,t) + C_d Y^D(x_2,t) + C_i Y^I(x_2,t)] \\ &+ \sum_{x_1,x_2'} [Y^S(x_1,t) + C_d Y^D(x_1,t) + C_i Y^I(x_1,t)] \\ &\times v(x_2',t) Y^S(x_2',t-1) \\ &+ \sum_{x_1',x_2} v(x_1',t) Y^S(x_1',t-1) \\ &\times [Y^S(x_2,t) + C_d Y^D(x_2,t) + C_i Y^I(x_2,t)] \\ &+ \sum_{x_1',x_2'} v(x_1',t) v(x_2',t) Y^S(x_1',t-1) Y^S(x_2',t-1).\end{aligned} \quad (106)$$

Because $Y^{D(I)}(x,t)$ can be expressed as linear combinations of $Y^{S(D,I)}$ at time $t-1$, the only unequal time piece comes from $Y^S(x,t) Y^S(x', t-1)$. Before embarking on the study of the time evolution of quantities such as $\langle Y^S(x_1,t) Y^S(x_2', t-1)\rangle_0$ and $\langle Y^S(x_1', t-1) Y^D(x_2,t)\rangle_0$, let us define all the relevant quantities needed for future calculation.

$$\phi^{S^+S}(x_1,x_2,t) \equiv \langle Y^S(x_1+1,t+1) Y^S(x_2,t)\rangle_0,$$

$$\phi^{SS^+}(x_1,x_2,t) \equiv \langle Y^S(x_1,t) Y^S(x_2+1,t+1)\rangle_0,$$

$$\phi^{SS}(x_1,x_2,t) \equiv \langle Y^S(x_1,t) Y^S(x_2,t)\rangle_0,$$

$$\phi^{SD}(x_1,x_2,t) \equiv \langle Y^S(x_1,t) Y^D(x_2,t)\rangle_0,$$

$$\phi^{SI}(x_1,x_2,t) \equiv \langle Y^S(x_1,t) Y^I(x_2,t)\rangle_0,$$

$$\phi^{DS}(x_1,x_2,t) \equiv \langle Y^D(x_1,t) Y^S(x_2,t)\rangle_0,$$

$$\phi^{DD}(x_1,x_2,t) \equiv \langle Y^D(x_1,t) Y^D(x_2,t)\rangle_0,$$

$$\phi^{DI}(x_1,x_2,t) \equiv \langle Y^D(x_1,t) Y^I(x_2,t)\rangle_0,$$

$$\phi^{IS}(x_1,x_2,t) \equiv \langle Y^I(x_1,t) Y^S(x_2,t)\rangle_0,$$

$$\phi^{ID}(x_1,x_2,t) \equiv \langle Y^I(x_1,t) Y^D(x_2,t)\rangle_0,$$

$$\phi^{II}(x_1,x_2,t) \equiv \langle Y^I(x_1,t) Y^I(x_2,t)\rangle_0.$$

Apparently, there is symmetry that we should spell out. For example, $\phi^{DS}(x_1,x_2,t) = \phi^{SD}(x_2,x_1,t)$. The consequence of this is that $\phi^{DS}(k,l) = \phi^{SD}(k,-l)$. Pairs exhibiting such symmetry include $[\phi^{SI},\phi^{IS}]$, $[\phi^{ID},\phi^{DI}]$, etc. In a similar fashion to the definition of ϕ^{S^+S} and ϕ^{SS^+}, we find the following intermediate variables useful:

$$\phi^{D^+S}(x_1,x_2,t) \equiv \langle Y^D(x_1+1,t+1)Y^S(x_2,t)\rangle_0,$$

$$\phi^{SD^+}(x_1,x_2,t) \equiv \langle Y^S(x_1,t)Y^D(x_2+1,t+1)\rangle_0,$$

$$\phi^{I^+S}(x_1,x_2,t) \equiv \langle Y^I(x_1+1,t+1)Y^S(x_2,t)\rangle_0,$$

$$\phi^{SI^+}(x_1,x_2,t) \equiv \langle Y^S(x_1,t)Y^I(x_2+1,t+1)\rangle_0.$$

As before, we see easily that $\phi^{SD^+}(x_1,x_2,t)=\phi^{D^+S}(x_2,x_1,t)$. There are four such pairs above. Furthermore, such symmetry implies $\phi^{SD^+}(k,l)=\phi^{D^+S}(k,-l)$. Therefore, in the final Laplace-Fourier form, there are $(11-3)+(8-4)=12$ independent variables to take care of. This number of variables is considerably larger than the linear gap case where only two independent variables were needed. After introducing the relevant variables, the next step is to write down their corresponding evolution equations, and then perform the discrete Laplace and Fourier transforms analogous to those in Eq. (63)–(65). Although the framework so far is quite general, we will focus mainly on three scenarios in our analytical effort, i.e., $\mu'=\mu''=1$, $\mu'=\mu''=0$, and $\mu'=1,\mu''=0$. The first two cases are symmetric, while the last one is asymmetric.

Experience from solving the linear gap case tells us that the most important quantity to consider is $\phi^{SS}_{\hat{z}}(y=0)$, which is nothing but taking $y=0$ in the expression

$$\sum_{x_1,x_2}\delta_{x_1-x_2,2y}e^{-ik(x_1+x_2)/2}\left[\sum_{t=0}^{\infty}\hat{z}^t\phi^{SS}(x_1,x_2,t)\right].$$

Because of the extensive algebra involved in the derivation, we will only document the key results from the three cases (i.e., $\mu'=\mu''=1$, $\mu'=\mu''=0$, and $\mu'=1,\mu''=0$) where this important quantity $\phi^{SS}_{\hat{z}}(y=0)$ is calculated. The detailed procedure will be described in the appendixes where the evolution equations, their general developments, and the specialized cases of interest will be documented.

As before, the variance of the random potential is defined to be Δ, i.e.,

$$\langle v(x,t)v(x',t')\rangle_0 - v^2 = \Delta\,\delta_{x,x'}\delta_{t,t'}.$$

Before documenting the main results for the three cases, let us first define a few notations similar to these in Eq. (80)

$$z=\hat{z}v,$$

$$\alpha=(\nu-\mu)/\mu,$$

$$\beta=\mu^2/v,$$

$$\tilde{\Delta}=\Delta/v^2, \tag{107}$$

where $\hat{z}$ is the variable introduced for the discrete Laplace transform. As discussed in the linear gap case, the key ingredient for making $\langle\tilde{W}_t^2\rangle_0$ finite is to make sure that $\phi^{SS}_{\hat{z}}(y=0)$ has no pole with $0<|\hat{z}|<1$ and that it has a pole at exactly $\hat{z}=1$. Since in general the quantity $\phi^{SS}_{\hat{z}}(y=0)$ can be written as

$$\phi^{SS}_q(y=0)=\frac{1}{G^{-1}_{\exp}(\hat{z})-\Delta\hat{z}^2}, \tag{108}$$

the aforementioned condition can be achieved by setting

$$G_{\exp}{}^{-1}(\hat{z})-\Delta\hat{z}^2|_{\hat{z}=1}=0. \tag{109}$$

To investigate how condition (109) can be satisfied, we need the explicit expression for $G_{\exp}$, which unfortunately is quite complicated for each case. But in general, it always contains three components and the first component is always the same. That is, we can write

$$G_{\exp}=G^1_{\exp}+G^2_{\exp}+G^3_{\exp} \tag{110}$$

with

$$G^1_{\exp}=\frac{\alpha^2}{(1+\alpha)^2-\alpha^2z^2}. \tag{111}$$

We now document the three cases $(\mu'=1,\mu''=1)$, $(\mu'=0,\mu''=0)$, and $(\mu'=1,\mu''=0)$ separately.

A. $\mu'=1$ and $\mu''=1$

In this case, we have

$$G^2_{\exp}=\frac{(1-\alpha^2\beta z)^{3/2}}{(1+\alpha-\alpha z)D^a(z)\sqrt{F^a_2(z)}}, \tag{112}$$

$$G^3_{\exp}=\frac{2\alpha[1-\alpha(1+\alpha)\beta z]\sqrt{N^a_3(z)}}{(1+\alpha+\alpha z)D^a(z)\sqrt{F^a_{31}(z)F^a_{32}(z)}}, \tag{113}$$

with

$$D^a(z)=(1+\alpha)+[1-3\alpha^2\beta-\alpha^3\beta-2\alpha(1+\beta)]z + \alpha(1+\alpha\beta+2\alpha^2\beta)z^2-\alpha^3\beta z^3, \tag{114}$$

$$F^{\,a}_{\,2}(z)=1-[2+(2+\alpha)^2\beta]z+[1+2\alpha(2+\alpha)\beta]z^2-\alpha^2\beta z^3, \tag{115}$$

$$N^{\,a}_{\,3}(z)=1-\alpha(2+\alpha)\beta z-\alpha^2\beta z^2+\alpha^4\beta^2z^3, \tag{116}$$

$$F^{\,a}_{\,31}(z)=1+[1-\alpha(2+\alpha)\beta]z-\alpha^2\beta z^2, \tag{117}$$

$$F^{\,a}_{\,32}(z)=1+z-\alpha(2+\alpha)\beta z^2-\alpha^2\beta z^3. \tag{118}$$

Figure 5(a) demonstrates our numerical test of the above analytical result. The histogram presented is obtained from aligning uncorrelated random sequence pairs using the PAM120 matrix [25] with the so-called (11,1) affine gap cost at temperature $\tau=1$. As expected, the resulting λ is $\lambda=2/\tau=2$. See figure caption for more details.

Although the algebra needed to arrive at this result is complicated, this nevertheless is the case where we can take

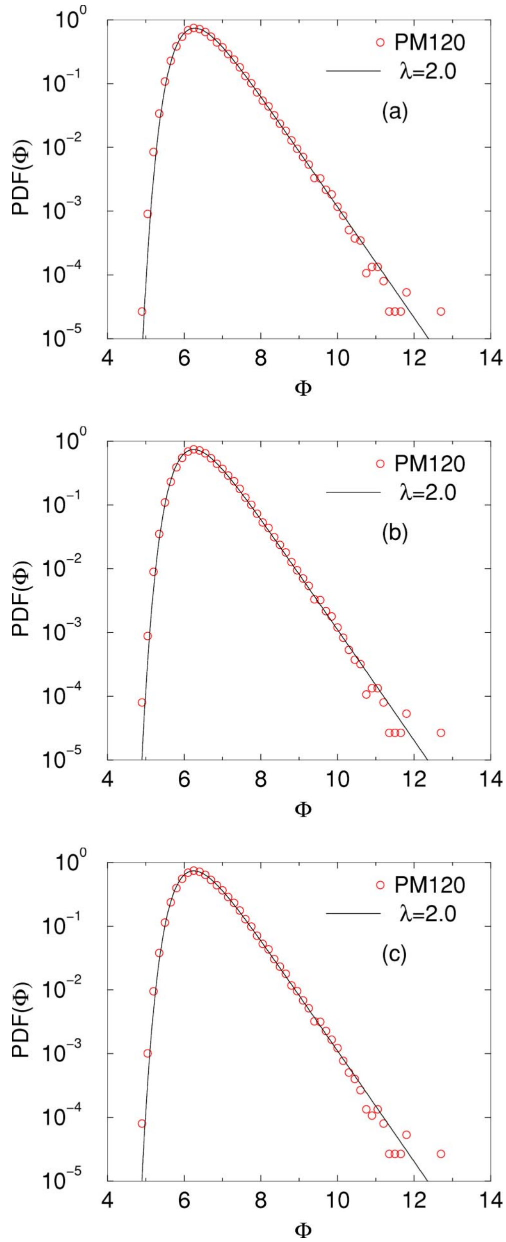

FIG. 5. The histograms and the Gumbel fits using the conditions (109) at $\tau=1$ for three cases studied analytically. The alignment scores were obtained by first generating sequence pairs according to probability distribution (36) and then aligning each sequence pair according to the algorithm described by Eqs. (34), (35), and (43). The relations between the scoring function and the substitution weight and gap weights are summarized in Eq. (97) with the chemical potential "$-\sigma$" chosen to satisfy the solvability condition (109). Each random sequence generated has length $N=600$. The circles represent the alignment score histogram of 500 000 random sequence pairs using the PAM120 scoring matrix and (11,1) affine gap costs, i.e., $\delta=12$ and $\varepsilon=1$. The numerical fitting of the normalized histogram (pdf) results in $\lambda=2.0\pm0.02$ as expected. The solid lines correspond to fits to the Gumbel form (39) with $\lambda=2.0$, together with the other fitted parameter $\ln\kappa=\ln(KN^2)$. For case (a), where $\mu'=\mu''=1$, $\ln(KN^2)$ is found to be 12.55 from fitting; for case (b), where $\mu'=\mu''=0$, $\ln(KN^2)$ is found to be 12.5 from fitting; for case (c), where $\mu'=1$ and $\mu''=0$, $\ln(KN^2)$ is found to be 12.52 from fitting.

the linear gap limit. In the linear gap limit, we have $\mu=\nu$, and thus $\alpha=0$. Upon setting $\alpha=0$ and $\beta=\omega$, we find that $G^1_{\rm exp}=G^3_{\rm exp}=0$ and

$$G_{\rm exp}=G^2_{\rm exp}=\frac{1}{(1+z)\sqrt{1-2z-4\omega z+z^2}}.$$

This is consistent with the former expression (86) for the linear gap case.

B. $\mu'=0$ and $\mu''=0$

In this case, we have

$$G^2_{\rm exp}=\frac{[1-(1+\alpha)^2\beta z]^{3/2}}{(1+\alpha-\alpha z)D^b(z)\sqrt{F^b_2(z)}}, \tag{119}$$

$$G^3_{\rm exp}=\frac{2[\alpha+(1-\alpha)(1+\alpha)^2\beta z]\sqrt{N^b_3(z)}}{(1+\alpha+\alpha z)D^b(z)\sqrt{F^b_{31}(z)F^b_{32}(z)}}, \tag{120}$$

with

$$D^b(z)=(1+\alpha)+[1-2\alpha-(1+\alpha)^3\beta]z + [\alpha-(1+\alpha)^2(3-2\alpha)\beta]z^2+(1-\alpha^2)\alpha\beta z^3, \tag{121}$$

$$F^b_2(z)=1-[2+(1+\alpha)^2\beta]z+[1-2(1-\alpha^2)\beta]z^2 -(1-\alpha)^2\beta z^3, \tag{122}$$

$$N^b_3(z)=1-(1+\alpha)^2\beta z-(1+\alpha)^2\beta z^2-(1-\alpha)(1+\alpha)^3\beta^2 z^3, \tag{123}$$

$$F^b_{31}(z)=1+[1-(1+\alpha)^2\beta]z+(1-\alpha^2)\beta z^2, \tag{124}$$

$$F^b_{32}(z)=1+z+(1-\alpha^2)\beta z^2-(1-\alpha)^2\beta z^3. \tag{125}$$

Figure 5(b) demonstrates our numerical test of the above analytical result. The histogram presented is obtained from aligning uncorrelated random sequence pairs using the PAM120 matrix [25] with the so-called (11,1) affine gap cost at temperature $\tau=1$. As expected, the resulting λ is $\lambda=2/\tau=2$. See figure caption for more details.

C. $\mu'=1$ and $\mu''=0$

This is the case that was adopted in the hybrid alignment method [21]. The purpose of having $\mu''=0$ is to avoid overcounting of equivalent gapping in alignment. In this case, we have

$$G_{\text{exp}}^2 = \frac{[1-\alpha(1+\alpha)\beta z]^2}{(1+\alpha-\alpha z)D^c(z)\sqrt{F_2^c(z)}}, \tag{126}$$

$$G_{\text{exp}}^3 = \frac{2\alpha[1-\alpha(1+\alpha)\beta z]N_3^c(z)}{(1+\alpha+\alpha z)D^c(z)\sqrt{F_{31}^c(z)F_{32}^c(z)F_{33}^c(z)}}, \tag{127}$$

with

$$D^c(z) = (1+\alpha) + [1-2\alpha-(1+\alpha)^3\beta]z + \alpha[1-(1+\alpha)(1-2\alpha)\beta]z^2 - \alpha^3\beta z^3, \tag{128}$$

$$F_2^c(z) = 1 - 2[1+(1+\alpha)^2\beta]z + [1+\beta(-2+4\alpha(1+\alpha) + (1+\alpha)^4\beta)]z^2 - 2\alpha^2\beta[1+(1+\alpha)^2\beta]z^3 + \alpha^4\beta^2 z^4, \tag{129}$$

$$N_3^c(z) = 1-(1+\alpha)^2\beta z - \alpha(1+\alpha)\beta z^2 + \alpha^3(1+\alpha)\beta^2 z^3, \tag{130}$$

$$F_{31}^c(z) = 1-\alpha^2\beta z^2, \tag{131}$$

$$F_{32}^c(z) = 1 + [1-(1+\alpha)^2\beta]z - \alpha^2\beta z^2, \tag{132}$$

$$F_{33}^c(z) = 1 + [1-(1+\alpha)^2\beta]z - 2\alpha(2+\alpha)\beta z^2 - \alpha^2\beta[1-(1+\alpha)^2\beta]z^3 + \alpha^4\beta^2 z^4. \tag{133}$$

Figure 5(c) demonstrates our numerical test of the above analytical result. The histogram presented is obtained from aligning uncorrelated random sequence pairs using the PAM120 matrix [25] with the so-called $(11,1)$ affine gap cost at temperature $\tau=1$. As expected, the resulting λ is $\lambda=2/\tau=2$. See figure caption for more details.

V. SUMMARY AND OUTLOOK

In this paper we give a self-contained introduction to the sequence alignment problem and its connection to the DPRM problem. This introduction by no means can be regarded as a review of the subject. For a more detailed exposition of this subject, readers are referred to Ref. [18] and references therein. We have also provided the connection between the linear gap cost case of sequence alignment and the DPRM problem. In particular, we provide the connection between the alignment score statistics and the evaluation of the few-replica partition function of the DPRM system via Eq. (45). The main results that are related to the alignment score statistics application include Eqs. (90), (109)–(113), (119), (120), (126), and (127). Equation (59) and the remarks around it can also be of important use in the study of granular systems.

We explained here two solvable classes. The result obtained in Ref. [21] is termed the first solvable class. We report here the detailed procedure for obtaining the second solvable class for both the linear gap case (Sec. III) and the *affine gap* case (Sec. IV). Similarly to the first solvable class case, the condition that allows for the existence of the second solvable class imposes an equation (solvability condition) relating different alignment parameters. By introducing the "chemical potential," $-\sigma_{1(2)}(\tau,\gamma)$, to satisfy the solvability condition, we find two different hypersurfaces in phase space for the two solvable classes. Within the first solvable class the extremal parameter $\lambda=1/\tau$, while in the second solvable class $\lambda=2/\tau$.

When using this prediction, however, some caution is necessary. Basically, the predicted statistics from the two solvable classes agree well with numerical studies for most frequently used scoring functions and for moderate temperatures. When the temperature used is very high, the hypersurfaces from solvable classes are very close to the phase transition hypersurface, because the local alignment characteristics $\lambda=1/\tau$ (or $2/\tau)\to 0$. In this case, the highest scoring configuration tends to have its Boltzmann weight contributed from lots of paths of length comparable to the system size. In other words, the system easily runs into the "critical region" and one therefore needs a much larger system size to recover the local alignment characteristics.

When temperature is very low, the quantity $2\sigma_{1(2)}(\tau,\gamma)$ needed to achieve the solvability condition tends to be close to the largest entry of the scoring matrix. This means that only *very few* character pairs out of all possible character pairs can have substitution weight $\exp[[s(a,b)-2\sigma]/\tau]$ greater than one. Note that this is similar to using $s(a,b)-2\sigma$ as the effective substitution score in the optimal sequence alignment. Therefore, when the system size is not large enough, the highest score path will contain only a very small number of character pairs but each with substantial substitution weight. Because this scenario precludes the application of the law of large numbers, our method of using global alignment to predict local alignment statistics is not applicable to moderate system size when the temperature is too low.

Although there are finite size problems at both high temperature and low temperature, these finite size problem can in principle be resolved if one is willing to perform the simulations on a much larger system, which of course can be very time consuming. The agreement, between numerically obtained and theoretically predicted λ values for generic cases (not belonging to the solvable classes), does lend support to our solvability conditions even at the extreme temperature cases in which direct numerical verifications becomes difficult (finite size effect). In the future, we plan to combine the two solvable classes to explore the potential use of the cooling map [24] in both uniform scoring schemes as well as position-specific scoring schemes.

ACKNOWLEDGMENTS

The author wishes to thank Stephen Altschul for useful discussion and the NSF for the partial support through Grant No. DMR-0110903.

APPENDIX A: GENERAL DEVELOPMENT OF THE EVOLUTION EQUATIONS

In this appendix, we provide the details of how to obtain the iterative equations of the auxiliary quantities before specializing to the three cases. Before calculating $\langle \widetilde{W}_t^2\rangle_0$, we first reiterate the definition (55) of the variance Δ of the disorder potential, i.e.,

$$\langle v(x,t)v(x',t')\rangle_0 - v^2 = \Delta \delta_{x,x'}\delta_{t,t'}. \tag{A1}$$

We now present the iterative equations of those fifteen quantities defined above. We will do them strictly in order.

$$\begin{aligned}\phi^{S^+S}(x_1,x_2,t+1) &= \langle Y^S(x_1+1,t+2)Y^S(x_2,t+1)\rangle_0\\ &= v\phi^{SS^+}(x_1+1,x_2-1,t) + \phi^{D^+S}(x_1,x_2,t+1) + \phi^{I^+S}(x_1,x_2,t+1),\end{aligned} \tag{A2}$$

$$\begin{aligned}\phi^{SS^+}(x_1,x_2,t+1) &= \langle Y^S(x_1,t+1)Y^S(x_2+1,t+2)\rangle_0\\ &= v\phi^{S^+S}(x_1-1,x_2+1,t) + \phi^{SD^+}(x_1,x_2,t+1) + \phi^{SI^+}(x_1,x_2,t+1),\end{aligned} \tag{A3}$$

$$\begin{aligned}\phi^{SS}(x_1,x_2,t+1) &= \langle Y^S(x_1,t+1)Y^S(x_2,t+1)\rangle_0 = \tfrac{1}{2}[\langle[v(x_1,t)Y^S(x_1,t-1) + Y^D(x_1,t+1) + Y^I(x_1,t+1)]Y^S(x_2,t+1)\rangle_0\\ &\quad + Y^S(x_1,t+1)[v(x_2,t)Y^S(x_2,t-1) + Y^D(x_2,t+1) + Y^I(x_2,t+1)]_0]\\ &= \tfrac{1}{2}\langle v(x_1,t)Y^S(x_1,t-1)Y^S(x_2,t+1) + Y^S(x_1,t+1)v(x_2,t)Y^S(x_2,t-1)\rangle_0\\ &\quad + \tfrac{1}{2}[\phi^{DS}(x_1,x_2,t+1) + \phi^{SD}(x_1,x_2,t+1) + \phi^{IS}(x_1,x_2,t+1) + \phi^{SI}(x_1,x_2,t+1)]\\ &= \frac{v}{2}\langle Y^S(x_1,t-1)[Y^D(x_2,t+1) + Y^I(x_2,t+1)] + [Y^D(x_1,t+1) + Y^I(x_1,t+1)]Y^S(x_2,t-1)\rangle_0\\ &\quad + (v^2 + \Delta\delta_{x_1,x_2})\phi^{SS}(x_1,x_2,t-1) + \tfrac{1}{2}[\phi^{DS}(x_1,x_2,t+1) + \phi^{SD}(x_1,x_2,t+1) + \phi^{IS}(x_1,x_2,t+1) + \phi^{SI}(x_1,x_2,t+1)]\\ &= \tfrac{1}{2}[\phi^{DS}(x_1,x_2,t+1) + \phi^{SD}(x_1,x_2,t+1) + \phi^{IS}(x_1,x_2,t+1) + \phi^{SI}(x_1,x_2,t+1)] + (v^2 + \Delta\delta_{x_1,x_2})\phi^{SS}(x_1,x_2,t-1)\\ &\quad + \frac{v}{2}\{\mu[\phi^{SS^+}(x_1,x_2-2,t-1) + \phi^{SS^+}(x_1,x_2,t-1) + \phi^{S^+S}(x_1-2,x_2,t-1) + \phi^{S^+S}(x_1,x_2,t-1)] + (\nu-\mu)\\ &\quad \times[\phi^{SD^+}(x_1,x_2-2,t-1) + \phi^{SI^+}(x_1,x_2,t-1) + \phi^{D^+S}(x_1-2,x_2,t-1) + \phi^{I^+S}(x_1,x_2,t-1)] - \mu(1-\mu'')\\ &\quad \times[\phi^{SI^+}(x_1,x_2-2,t-1) + \phi^{I^+S}(x_1-2,x_2,t-1)] - \mu(1-\mu')[\phi^{SD^+}(x_1,x_2,t-1) + \phi^{D^+S}(x_1,x_2,t-1)]\},\end{aligned} \tag{A4}$$

$$\begin{aligned}\phi^{SD}(x_1,x_2,t+1) &= \langle Y^S(x_1,t+1)Y^D(x_2,t+1)\rangle_0\\ &= \langle[v(x_1,t)Y^S(x_1,t-1) + Y^D(x_1,t+1) + Y^I(x_1,t+1)]Y^D(x_2,t+1)\rangle_0\\ &= v\langle Y^S(x_1,t-1)Y^D(x_2,t+1)\rangle_0 + \phi^{DD}(x_1,x_2,t+1) + \phi^{ID}(x_1,x_2,t+1)\\ &= v[\mu\phi^{SS^+}(x_1,x_2-2,t-1) + (\nu-\mu)\phi^{SD^+}(x_1,x_2-2,t-1) - \mu(1-\mu'')\phi^{SI^+}(x_1,x_2-2,t-1)] + \phi^{DD}(x_1,x_2,t+1)\\ &\quad + \phi^{ID}(x_1,x_2,t+1),\end{aligned} \tag{A5}$$

$$\begin{aligned}\phi^{DS}(x_1,x_2,t+1) &= \langle Y^D(x_1,t+1)Y^S(x_2,t+1)\rangle_0\\ &= \langle Y^D(x_1,t+1)[v(x_2,t)Y^S(x_2,t-1) + Y^D(x_2,t+1) + Y^I(x_2,t+1)]\rangle_0\\ &= v\langle Y^D(x_1,t+1)Y^S(x_2,t-1)\rangle_0 + \phi^{DD}(x_1,x_2,t+1) + \phi^{DI}(x_1,x_2,t+1)\\ &= v[\mu\phi^{S^+S}(x_1-2,x_2,t-1) + (\nu-\mu)\phi^{D^+S}(x_1-2,x_2,t-1) - \mu(1-\mu'')\phi^{I^+S}(x_1-2,x_2,t-1)] + \phi^{DD}(x_1,x_2,t+1)\\ &\quad + \phi^{DI}(x_1,x_2,t+1),\end{aligned} \tag{A6}$$

$$\begin{aligned}\phi^{SD^+}(x_1,x_2,t+1) &= \langle Y^S(x_1,t+1)Y^D(x_2+1,t+2)\rangle_0\\ &= \langle Y^S(x_1,t+1)[\mu Y^S(x_2,t+1) + (\nu-\mu)Y^D(x_2,t+1) - \mu(1-\mu'')Y^I(x_2,t+1)]\rangle_0\\ &= \mu\phi^{SS}(x_1,x_2,t+1) + (\nu-\mu)\phi^{SD}(x_1,x_2,t+1) - \mu(1-\mu'')\phi^{SI}(x_1,x_2,t+1),\end{aligned} \tag{A7}$$

$$\begin{aligned}\phi^{D^+S}(x_1,x_2,t+1) &= \langle Y^D(x_1+1,t+2)Y^S(x_2,t+1)\rangle_0 \\ &= \langle [\mu Y^S(x_1,t+1) + (\nu-\mu)Y^D(x_1,t+1) - \mu(1-\mu'')Y^I(x_1,t+1)]Y^S(x_2,t+1)\rangle_0 \\ &= \mu\phi^{SS}(x_1,x_2,t+1) + (\nu-\mu)\phi^{DS}(x_1,x_2,t+1) - \mu(1-\mu'')\phi^{IS}(x_1,x_2,t+1),\end{aligned} \tag{A8}$$

$$\begin{aligned}\phi^{SI}(x_1,x_2,t+1) &= \langle Y^S(x_1,t+1)Y^I(x_2,t+1)\rangle_0 \\ &= \langle [v(x_1,t)Y^S(x_1,t-1) + Y^D(x_1,t+1) + Y^I(x_1,t+1)]Y^I(x_2,t+1)\rangle_0 \\ &= v\langle Y^S(x_1,t-1)Y^I(x_2,t+1)\rangle_0 + \phi^{DI}(x_1,x_2,t+1) + \phi^{II}(x_1,x_2,t+1) \\ &= v[\mu\phi^{SS^+}(x_1,x_2,t-1) + (\nu-\mu)\phi^{SI^+}(x_1,x_2,t-1) - \mu(1-\mu')\phi^{SD^+}(x_1,x_2,t-1)] + \phi^{DI}(x_1,x_2,t+1) \\ &\quad + \phi^{II}(x_1,x_2,t+1),\end{aligned} \tag{A9}$$

$$\begin{aligned}\phi^{IS}(x_1,x_2,t+1) &= \langle Y^I(x_1,t+1)Y^S(x_2,t+1)\rangle_0 \\ &= \langle Y^I(x_1,t+1)[v(x_2,t)Y^S(x_2,t-1) + Y^D(x_2,t+1) + Y^I(x_2,t+1)]\rangle_0 \\ &= v\langle Y^I(x_1,t+1)Y^S(x_2,t-1)\rangle_0 + \phi^{ID}(x_1,x_2,t+1) + \phi^{II}(x_1,x_2,t+1) \\ &= v[\mu\phi^{S^+S}(x_1,x_2,t-1) + (\nu-\mu)\phi^{I^+S}(x_1,x_2,t-1) - \mu(1-\mu')\phi^{D^+S}(x_1,x_2,t-1)] + \phi^{ID}(x_1,x_2,t+1) \\ &\quad + \phi^{II}(x_1,x_2,t+1),\end{aligned} \tag{A10}$$

$$\begin{aligned}\phi^{SI^+}(x_1,x_2,t+1) &= \langle Y^S(x_1,t+1)Y^I(x_2+1,t+2)\rangle_0 \\ &= \mu\phi^{SS}(x_1,x_2+2,t+1) + (\nu-\mu)\phi^{SI}(x_1,x_2+2,t+1) - \mu(1-\mu')\phi^{SD}(x_1,x_2+2,t+1),\end{aligned} \tag{A11}$$

$$\begin{aligned}\phi^{I^+S}(x_1,x_2,t+1) &= \langle Y^I(x_1+1,t+2)Y^S(x_2,t+1)\rangle_0 \\ &= \mu\phi^{SS}(x_1+2,x_2,t+1) + (\nu-\mu)\phi^{IS}(x_1+2,x_2,t+1) - \mu(1-\mu')\phi^{DS}(x_1+2,x_2,t+1),\end{aligned} \tag{A12}$$

$$\begin{aligned}\phi^{DD}(x_1,x_2,t+1) &= \langle Y^D(x_1,t+1)Y^D(x_2,t+1)\rangle_0 \\ &= \langle [\mu Y^S(x_1-1,t) + (\nu-\mu)Y^D(x_1-1,t) - \mu(1-\mu'')Y^I(x_1-1,t)] \\ &\quad \times [\mu Y^S(x_2-1,t) + (\nu-\mu)Y^D(x_2-1,t) - \mu(1-\mu'')Y^I(x_2-1,t)]\rangle_0 \\ &= \mu^2[\phi^{SS}(x_1-1,x_2-1,t) + (1-\mu'')^2\phi^{II}(x_1-1,x_2-1,t)] + (\nu-\mu)^2\phi^{DD}(x_1-1,x_2-1,t) \\ &\quad + \mu(\nu-\mu)[\phi^{SD}(x_1-1,x_2-1,t) + \phi^{DS}(x_1-1,x_2-1,t)] \\ &\quad - \mu(\nu-\mu)(1-\mu'')[\phi^{ID}(x_1-1,x_2-1,t) + \phi^{DI}(x_1-1,x_2-1,t)] \\ &\quad - \mu^2(1-\mu'')[\phi^{SI}(x_1-1,x_2-1,t) + \phi^{IS}(x_1-1,x_2-1,t)],\end{aligned} \tag{A13}$$

$$\begin{aligned}\phi^{II}(x_1,x_2,t+1) &= \langle Y^I(x_1,t+1)Y^I(x_2,t+1)\rangle_0 \\ &= \langle [\mu Y^S(x_1+1,t) + (\nu-\mu)Y^I(x_1+1,t) - \mu(1-\mu')Y^D(x_1+1,t)] \\ &\quad \times [\mu Y^S(x_2+1,t) + (\nu-\mu)Y^I(x_2+1,t) - \mu(1-\mu')Y^D(x_2+1,t)]\rangle_0 \\ &= \mu^2[\phi^{SS}(x_1+1,x_2+1,t) + (1-\mu')^2\phi^{DD}(x_1+1,x_2+1,t)] + (\nu-\mu)^2\phi^{II}(x_1+1,x_2+1,t) \\ &\quad + \mu(\nu-\mu)[\phi^{SI}(x_1+1,x_2+1,t) + \phi^{IS}(x_1+1,x_2+1,t)] \\ &\quad - \mu(\nu-\mu)(1-\mu')[\phi^{ID}(x_1+1,x_2+1,t) + \phi^{DI}(x_1+1,x_2+1,t)] \\ &\quad - \mu^2(1-\mu')[\phi^{SD}(x_1+1,x_2+1,t) + \phi^{DS}(x_1+1,x_2+1,t)],\end{aligned} \tag{A14}$$

$$\begin{aligned}\phi^{ID}(x_1,x_2,t+1) &= \langle Y^I(x_1,t+1)Y^D(x_2,t+1)\rangle_0 \\ &= \langle [\mu Y^S(x_1+1,t) + (\nu-\mu)Y^I(x_1+1,t) - \mu(1-\mu')Y^D(x_1+1,t)] \\ &\quad \times [\mu Y^S(x_2-1,t) + (\nu-\mu)Y^D(x_2-1,t) - \mu(1-\mu'')Y^I(x_2-1,t)]\rangle_0\end{aligned}$$

$$=\mu^2\phi^{SS}(x_1+1,x_2-1,t)+(\nu-\mu)^2\phi^{ID}(x_1+1,x_2-1,t)+\mu^2(1-\mu')(1-\mu'')\phi^{DI}(x_1+1,x_2-1,t)$$
$$+\mu(\nu-\mu)[\phi^{SD}(x_1+1,x_2-1,t)+\phi^{IS}(x_1+1,x_2)-1,t]$$
$$-\mu^2(1-\mu'')\phi^{SI}(x_1+1,x_2-1,t)-\mu^2(1-\mu')\phi^{DS}(x_1+1,x_2-1,t)$$
$$-\mu(\nu-\mu)[(1-\mu')\phi^{DD}(x_1+1,x_2-1,t)+(1-\mu'')\phi^{II}(x_1+1,x_2-1,t)], \tag{A15}$$

$$\phi^{DI}(x_1,x_2,t+1)=\langle Y^D(x_1,t+1)Y^I(x_2,t+1)\rangle_0$$
$$=\langle[\mu Y^S(x_1-1,t)+(\nu-\mu)Y^D(x_1-1,t)-\mu(1-\mu'')Y^I(x_1-1,t)]$$
$$\times[\mu Y^S(x_2+1,t)+(\nu-\mu)Y^I(x_2+1,t)-\mu(1-\mu')Y^D(x_2+1,t)]\rangle_0$$
$$=\mu^2\phi^{SS}(x_1-1,x_2+1,t)+(\nu-\mu)^2\phi^{DI}(x_1-1,x_2+1,t)+\mu^2(1-\mu')(1-\mu'')\phi^{ID}(x_1-1,x_2+1,t)$$
$$+\mu(\nu-\mu)[\phi^{SI}(x_1-1,x_2+1,t)+\phi^{DS}(x_1-1,x_2+1,t)]$$
$$-\mu^2(1-\mu'')\phi^{IS}(x_1-1,x_2+1,t)-\mu^2(1-\mu')\phi^{SD}(x_1-1,x_2+1,t)$$
$$-\mu(\nu-\mu)[(1-\mu')\phi^{DD}(x_1-1,x_2+1,t)+(1-\mu'')\phi^{II}(x_1-1,x_2+1,t)]. \tag{A16}$$

The next step is to perform the Laplace-Fourier transform: Basically, we transform $\phi(x_1,x_2,t)$ into $\phi_{\hat z}(k,l)$ with

$$\phi_{\hat z}(k,l) = \sum_y e^{-ily}\left\{\sum_{x_1,x_2}\delta_{x_1-x_2,2y}e^{-ik(x_1+x_2)/2}\left[\sum_{t=0}^{\infty}\hat z^t\phi(x_1,x_2,t)\right]\right\}. \tag{A17}$$

The final goal is to express all $\phi_{\hat z}(k,l)$ in terms of the free case (i.e., $\Delta=0$) and something we can calculate analytically. To this end, we shall work on each individual equation separately first. We also would like to remind the readers of the symmetries that we mentioned earlier. For example, $\phi_{\hat z}^{IS}(k,l)=\phi_{\hat z}^{SI}(k,-l)$. In performing the Laplace transform step, $\phi_{\hat z}(x_1,x_2)=\sum_{t=0}^{\infty}\phi(x_1,x_2,t)\hat z^t$, we have to pay attention to the following initial conditions:

$$\phi^{S^+S}(x_1,x_2,t=0)=\langle Y^S(x_1+1,t=1)Y^S(x_2,t=0)\rangle_0$$
$$=\langle[Y^D(x_1+1,t=1)+Y^I(x_1+1,t=1)]\delta_{x_2,0}\rangle_0$$
$$=\mu[\delta_{x_1,0}+\delta_{x_1,-2}]\delta_{x_2,0}, \tag{A18}$$

$$\phi^{SS^+}(x_1,x_2,t=0)=\langle Y^S(x_1,t=0)Y^S(x_2+1,t=1)\rangle_0$$
$$=\langle\delta_{x_1,0}[Y^D(x_2+1,t=1)+Y^I(x_2+1,t=1)]\rangle_0$$
$$=\mu\delta_{x_1,0}[\delta_{x_2,0}+\delta_{x_2,-2}], \tag{A19}$$

$$\phi^{SI^+}(x_1,x_2,t=0)=\langle Y^S(x_1,t=0)Y^I(x_2+1,t=1)\rangle_0$$
$$=\mu\delta_{x_1,0}\delta_{x_2+2,0}, \tag{A20}$$

$$\phi^{I^+S}(x_1,x_2,t=0)=\langle Y^I(x_1+1,t=1)Y^S(x_2,t=0)\rangle_0$$
$$=\mu\delta_{x_1+2,0}\delta_{x_2,0}, \tag{A21}$$

$$\phi^{SD^+}(x_1,x_2,t=0)=\langle Y^S(x_1,t=0)Y^D(x_2+1,t=1)\rangle_0$$
$$=\mu\delta_{x_1,0}\delta_{x_2,0}, \tag{A22}$$

$$\phi^{D^+S}(x_1,x_2,t=0)=\langle Y^D(x_1+1,t=1)Y^S(x_2,t=0)\rangle_0$$
$$=\mu\delta_{x_1,0}\delta_{x_2,0}, \tag{A23}$$

$$\phi^{SS}(x_1,x_2,t=0)=\langle Y^S(x_1,t=0)Y^S(x_2,t=0)\rangle_0=\delta_{x_1,0}\delta_{x_2,0}. \tag{A24}$$

The rest of the quantities have their initial values equal to zero. With these initial conditions given, one can now start the Laplace-Fourier transform. Even though there are seven quantities having nonzero initial values, it turns out that the majority of them do not play much role after the Laplace transform. To see explicitly, we will go through a couple of those transforms. Using the first recursion relation, we have

$$\phi_{\hat z}^{S^+S}(x_1,x_2)-\mu[\delta_{x_1,0}+\delta_{x_1+2,0}]\delta_{x_2,0}$$
$$=\hat z\upsilon\phi_{\hat z}^{SS^+}(x_1+1,x_2-1)+[\phi_{\hat z}^{D^+S}(x_1,x_2)-\mu\delta_{x_1,0}\delta_{x_2,0}]$$
$$+[\phi_{\hat z}^{I^+S}(x_1,x_2)-\mu\delta_{x_1+2,0}\delta_{x_2,0}]. \tag{A25}$$

With all the initial values canceling each other, we then have

$$\phi_{\hat z}^{S^+S}(x_1,x_2)=\hat z\upsilon\phi_{\hat z}^{SS^+}(x_1+1,x_2-1)+\phi_{\hat z}^{D^+S}(x_1,x_2)$$
$$+\phi_{\hat z}^{I^+S}(x_1,x_2),$$

$$\phi_{\hat z}^{S^+S}(k,y)=\hat z\upsilon\phi_{\hat z}^{SS^+}(k,y+1)+\phi_{\hat z}^{D^+S}(k,y)+\phi_{\hat z}^{I^+S}(k,y),$$

$$\phi_{\hat z}^{S^+S}(k,l)=\hat z\upsilon e^{il}\phi_{\hat z}^{SS^+}(k,l)+\phi_{\hat z}^{D^+S}(k,l)+\phi_{\hat z}^{I^+S}(k,l). \tag{A26}$$

A similar calculation on ϕ^{SS^+} then leads to

$$\phi_{\hat{z}}^{SS^+}(x_1,x_2) = \hat{z}v\phi_{\hat{z}}^{S^+S}(x_1-1,x_2+1) + \phi_{\hat{z}}^{SD^+}(x_1,x_2) + \phi_{\hat{z}}^{SI^+}(x_1,x_2),$$

$$\phi_{\hat{z}}^{SS^+}(k,l) = \hat{z}ve^{-il}\phi_{\hat{z}}^{S^+S}(k,l) + \phi_{\hat{z}}^{SD^+}(k,l) + \phi_{\hat{z}}^{SI^+}(k,l). \tag{A27}$$

Combining these two equations, we can express $\phi_{\hat{z}}^{SS^+}(k,l)$ and $\phi_{\hat{z}}^{S^+S}(k,l)$ in terms of other correlators. That is to say,

$$\phi_{\hat{z}}^{S^+S}(k,l) = \frac{\phi_{\hat{z}}^{D^+S}(k,l) + \phi_{\hat{z}}^{I^+S}(k,l) + \hat{z}ve^{il}[\phi_{\hat{z}}^{SD^+}(k,l) + \phi_{\hat{z}}^{SI^+}(k,l)]}{1-\hat{z}^2v^2}$$

$$\phi_{\hat{z}}^{SS^+}(k,l) = \frac{\phi_{\hat{z}}^{SD^+}(k,l) + \phi_{\hat{z}}^{SI^+}(k,l) + \hat{z}ve^{-il}[\phi_{\hat{z}}^{D^+S}(k,l) + \phi_{\hat{z}}^{I^+S}(k,l)]}{1-\hat{z}^2v^2}. \tag{A28}$$

The major equation comes from the ϕ^{SS} part which we now turn to:

$$\begin{aligned}\phi_{\hat{z}}^{SS}(x_1,x_2) &= \delta_{x_1,0}\delta_{x_2,0} + (v^2 + \Delta\delta_{x_1,x_2})\hat{z}^2\phi_{\hat{z}}^{SS}(x_1,x_2)\\ &+ \tfrac{1}{2}[\phi_{\hat{z}}^{DS}(x_1,x_2) + \phi_{\hat{z}}^{SD}(x_1,x_2) + \phi_{\hat{z}}^{IS}(x_1,x_2)\\ &+ \phi_{\hat{z}}^{SI}(x_1,x_2)] + \frac{v}{2}\{\mu\hat{z}^2[\phi_{\hat{z}}^{SS^+}(x_1,x_2-2)\\ &+ \phi_{\hat{z}}^{SS^+}(x_1,x_2) + \phi_{\hat{z}}^{S^+S}(x_1-2,x_2) + \phi_{\hat{z}}^{S^+S}(x_1,x_2)]\\ &+ (\nu-\mu)\hat{z}^2[\phi_{\hat{z}}^{SD^+}(x_1,x_2-2) + \phi_{\hat{z}}^{SI^+}(x_1,x_2)\\ &+ \phi_{\hat{z}}^{D^+S}(x_1-2,x_2) + \phi_{\hat{z}}^{I^+S}(x_1,x_2)] - \mu\hat{z}^2(1-\mu'')\\ &\times \phi_{\hat{z}}^{SI^+}[(x_1,x_2-2) + \phi_{\hat{z}}^{I^+S}(x_1-2,x_2)]\\ &- \mu\hat{z}^2(1-\mu')[\phi_{\hat{z}}^{SD^+}(x_1,x_2) + \phi_{\hat{z}}^{D^+S}(x_1,x_2)]\}.\end{aligned} \tag{A29}$$

After the Fourier transform, we then have

$$\begin{aligned}\phi_{\hat{z}}^{SS}(k,l) &= 1 + v^2\hat{z}^2\phi_{\hat{z}}^{SS}(k,l) + \Delta\hat{z}^2\phi_{\hat{z}}^{SS}(k,y=0)\\ &+ \tfrac{1}{2}[\phi_{\hat{z}}^{DS}(k,l) + \phi_{\hat{z}}^{SD}(k,l) + \phi_{\hat{z}}^{IS}(k,l) + \phi_{\hat{z}}^{SI}(k,l)]\\ &+ \frac{v}{2}\{\mu\hat{z}^2[e^{-ik+il}\phi_{\hat{z}}^{SS^+}(k,l) + \phi_{\hat{z}}^{SS^+}(k,l)\\ &+ e^{-ik-il}\phi_{\hat{z}}^{S^+S}(k,l) + \phi_{\hat{z}}^{S^+S}(k,l)]\\ &+ (\nu-\mu)\hat{z}^2[e^{-ik+il}\phi_{\hat{z}}^{SD^+}(k,l) + \phi_{\hat{z}}^{SI^+}(k,l)\\ &+ e^{-ik-il}\phi_{\hat{z}}^{D^+S}(k,l) + \phi_{\hat{z}}^{I^+S}(k,l)]\\ &- \mu\hat{z}^2[(1-\mu'')e^{-ik}[e^{il}\phi_{\hat{z}}^{SI^+}(k,l) + e^{-il}\phi_{\hat{z}}^{I^+S}(k,l)]\\ &+ (1-\mu')(\phi_{\hat{z}}^{SD^+}(k,l) + \phi_{\hat{z}}^{D^+S}(k,l))]\}.\end{aligned} \tag{A30}$$

We now continue with the rest:

$$\begin{aligned}\phi_{\hat{z}}^{SD}(x_1,x_2) &= v\hat{z}^2[\mu\phi_{\hat{z}}^{SS^+}(x_1,x_2-2) + (\nu-\mu)\phi_{\hat{z}}^{SD^+}(x_1,x_2-2)\\ &- \mu(1-\mu'')\phi_{\hat{z}}^{SI^+}(x_1,x_2-2)]\\ &+ \phi_{\hat{z}}^{DD}(x_1,x_2) + \phi_{\hat{z}}^{ID}(x_1,x_2),\end{aligned}$$

$$\begin{aligned}\phi_{\hat{z}}^{SD}(k,l) &= \phi_{\hat{z}}^{DD}(k,l) + \phi_{\hat{z}}^{ID}(k,l)\\ &+ v\hat{z}^2e^{-ik+il}[\mu\phi_{\hat{z}}^{SS^+}(k,l) + (\nu-\mu)\phi_{\hat{z}}^{SD^+}(k,l)\\ &- \mu(1-\mu'')\phi_{\hat{z}}^{SI^+}(k,l)],\end{aligned} \tag{A31}$$

and similarly

$$\begin{aligned}\phi_{\hat{z}}^{DS}(k,l) &= \phi_{\hat{z}}^{DD}(k,l) + \phi_{\hat{z}}^{DI}(k,l) + v\hat{z}^2e^{-ik-il}[\mu\phi_{\hat{z}}^{S^+S}(k,l)\\ &+ (\nu-\mu)\phi_{\hat{z}}^{D^+S}(k,l) - \mu(1-\mu'')\phi_{\hat{z}}^{I^+S}(k,l)].\end{aligned} \tag{A32}$$

$$\begin{aligned}\phi_{\hat{z}}^{SD^+}(x_1,x_2) - \mu\delta_{x_1,0}\delta_{x_2,0} &= \mu[\phi_{\hat{z}}^{SS}(x_1,x_2) - \delta_{x_1,0}\delta_{x_2,0}]\\ &+ (\nu-\mu)\phi_{\hat{z}}^{SD}(x_1,x_2)\\ &- \mu(1-\mu'')\phi_{\hat{z}}^{SI}(x_1,x_2),\end{aligned}$$

$$\begin{aligned}\phi_{\hat{z}}^{SD^+}(x_1,x_2) &= \mu\phi_{\hat{z}}^{SS}(x_1,x_2) + (\nu-\mu)\phi_{\hat{z}}^{SD}(x_1,x_2)\\ &- \mu(1-\mu'')\phi_{\hat{z}}^{SI}(x_1,x_2),\end{aligned}$$

$$\phi_{\hat{z}}^{SD^+}(k,l) = \mu\phi_{\hat{z}}^{SS}(k,l) + (\nu-\mu)\phi_{\hat{z}}^{SD}(k,l) - \mu(1-\mu'')\phi_{\hat{z}}^{SI}(k,l), \tag{A33}$$

and similarly

$$\begin{aligned}\phi_{\hat{z}}^{D^+S}(x_1,x_2) - \mu\delta_{x_1,0}\delta_{x_2,0} &= \mu[\phi_{\hat{z}}^{SS}(x_1,x_2) - \delta_{x_1,0}\delta_{x_2,0}]\\ &+ (\nu-\mu)\phi_{\hat{z}}^{DS}(x_1,x_2)\\ &- \mu(1-\mu'')\phi_{\hat{z}}^{IS}(x_1,x_2),\end{aligned}$$

$$\begin{aligned}\phi_{\hat{z}}^{D^+S}(x_1,x_2) &= \mu\phi_{\hat{z}}^{SS}(x_1,x_2) + (\nu-\mu)\phi_{\hat{z}}^{DS}(x_1,x_2)\\ &- \mu(1-\mu'')\phi_{\hat{z}}^{IS}(x_1,x_2),\end{aligned} \tag{A34}$$

$$\phi_{\hat{z}}^{D^+S}(k,l) = \mu\phi_{\hat{z}}^{SS}(k,l) + (\nu-\mu)\phi_{\hat{z}}^{DS}(k,l) - \mu(1-\mu'')\phi_{\hat{z}}^{IS}(k,l).$$

We now go for the *SI* combinations:

$$\phi_{\hat{z}}^{SI}(k,l) = \phi_{\hat{z}}^{DI}(k,l) + \phi_{\hat{z}}^{II}(k,l) + v\hat{z}^2[\mu\phi_{\hat{z}}^{SS^+}(k,l) + (\nu-\mu)\phi_{\hat{z}}^{SI^+}(k,l) - \mu(1-\mu')\phi_{\hat{z}}^{SD^+}(k,l)], \tag{A35}$$

$$\phi_{\hat{z}}^{IS}(k,l) = \phi_{\hat{z}}^{ID}(k,l) + \phi_{\hat{z}}^{II}(k,l) + v\hat{z}^2[\mu\phi_{\hat{z}}^{S^+S}(k,l) + (\nu-\mu)\phi_{\hat{z}}^{I^+S}(k,l) - \mu(1-\mu')\phi_{\hat{z}}^{D^+S}(k,l)], \tag{A36}$$

$$\phi_{\hat{z}}^{SI^+}(k,l) = e^{ik-il}[\mu\phi_{\hat{z}}^{SS}(k,l) + (\nu-\mu)\phi_{\hat{z}}^{SI}(k,l) - \mu(1-\mu')\phi_{\hat{z}}^{SD}(k,l)], \tag{A37}$$

$$\phi_{\hat{z}}^{I^+S}(k,l) = e^{ik+il}[\mu\phi_{\hat{z}}^{SS}(k,l) + (\nu-\mu)\phi_{\hat{z}}^{IS}(k,l) - \mu(1-\mu')\phi_{\hat{z}}^{DS}(k,l)], \tag{A38}$$

$$\phi_{\hat{z}}^{DD}(k,l) = \hat{z}e^{-ik}\{\mu^2[\phi_{\hat{z}}^{SS}(k,l) + (1-\mu'')^2\phi_{\hat{z}}^{II}(k,l) - (1-\mu'') \times(\phi_{\hat{z}}^{SI}(k,l) + \phi_{\hat{z}}^{IS}(k,l))] + (\nu-\mu)^2\phi_{\hat{z}}^{DD}(k,l) + \mu(\nu-\mu)[\phi_{\hat{z}}^{SD}(k,l) + \phi_{\hat{z}}^{DS}(k,l) - (1-\mu'')(\phi_{\hat{z}}^{ID}(k,l) + \phi_{\hat{z}}^{DI}(k,l))]\}, \tag{A39}$$

$$\phi_{\hat{z}}^{II}(k,l) = \hat{z}e^{ik}\{\mu^2[\phi_{\hat{z}}^{SS}(k,l) + (1-\mu')^2\phi_{\hat{z}}^{DD}(k,l) - (1-\mu') \times(\phi_{\hat{z}}^{SD}(k,l) + \phi_{\hat{z}}^{DS}(k,l))] + (\nu-\mu)^2\phi_{\hat{z}}^{II}(k,l) + \mu(\nu-\mu)[\phi_{\hat{z}}^{SI}(k,l) + \phi_{\hat{z}}^{IS}(k,l) - (1-\mu')(\phi_{\hat{z}}^{ID}(k,l) + \phi_{\hat{z}}^{DI}(k,l))]\}, \tag{A40}$$

$$\phi_{\hat{z}}^{ID}(k,l) = \hat{z}e^{il}\{\mu^2\phi_{\hat{z}}^{SS}(k,l) + (\nu-\mu)^2\phi_{\hat{z}}^{ID}(k,l) + \mu^2(1-\mu')(1-\mu'')\phi_{\hat{z}}^{DI}(k,l) + \mu(\nu-\mu)[\phi_{\hat{z}}^{SD}(k,l) + \phi_{\hat{z}}^{IS}(k,l)] - \mu^2(1-\mu'')\phi_{\hat{z}}^{SI}(k,l) - \mu^2(1-\mu')\phi_{\hat{z}}^{DS}(k,l) - \mu(\nu-\mu) \times[(1-\mu')\phi_{\hat{z}}^{DD}(k,l) + (1-\mu'')\phi_{\hat{z}}^{II}(k,l)]\}, \tag{A41}$$

$$\phi_{\hat{z}}^{DI}(k,l) = \hat{z}e^{-il}\{\mu^2\phi_{\hat{z}}^{SS}(k,l) + (\nu-\mu)^2\phi_{\hat{z}}^{DI}(k,l) + \mu^2(1-\mu')(1-\mu'')\phi_{\hat{z}}^{ID}(k,l) + \mu(\nu-\mu)[\phi_{\hat{z}}^{SI}(k,l) + \phi_{\hat{z}}^{DS}(k,l)] - \mu^2(1-\mu'')\phi_{\hat{z}}^{IS}(k,l) - \mu^2(1-\mu')\phi_{\hat{z}}^{SD}(k,l) - \mu(\nu-\mu) \times[(1-\mu')\phi_{\hat{z}}^{DD}(k,l) + (1-\mu'')\phi_{\hat{z}}^{II}(k,l)]\}. \tag{A42}$$

In real calculations, it seems worthwhile to utilize linear combinations of these variables instead of the ones defined originally. Furthermore, since we ultimately are only interested in the case when the center of mass momentum $k=0$, we might as well set $k=0$ from this point on. We therefore will abbreviate $\phi_{\hat{z}}^{XX}(k=0,l)$ by ϕ^{XX}. The new linear combinations we will adopt are as follows:

$$S_p = \phi^{SS^+} + \phi^{S^+S},$$

$$S_m = \phi^{SS^+} - \phi^{S^+S},$$

$$D_p = \phi^{SD^+} + \phi^{D^+S},$$

$$D_m = \phi^{SD^+} - \phi^{D^+S},$$

$$I_p = e^{il}\phi^{SI^+} + e^{-il}\phi^{I^+S},$$

$$I_m = e^{il}\phi^{SI^+} - e^{-il}\phi^{I^+S},$$

$$\phi_p^{SD} = \phi^{SD} + \phi^{DS},$$

$$\phi_m^{SD} = \phi^{SD} - \phi^{DS},$$

$$\phi_p^{SI} = \phi^{SI} + \phi^{IS},$$

$$\phi_m^{SI} = \phi^{SI} - \phi^{IS},$$

$$\psi_p^{DI} = e^{il}\phi^{DI} + e^{-il}\phi^{ID},$$

$$\psi_m^{DI} = e^{il}\phi^{DI} - e^{-il}\phi^{ID}.$$

From the definitions of ϕ^{XX}, we have

$$S_p = \frac{(1+\hat{z}v\cos l)D_p + (\cos l + \hat{z}v)I_p - i(I_m - \hat{z}vD_m)\sin l}{1-\hat{z}^2v^2},$$

$$S_m = \frac{(1-\hat{z}v\cos l)D_m + (\cos l - \hat{z}v)I_m - i(I_p + \hat{z}vD_p)\sin l}{1-\hat{z}^2v^2},$$

$$D_p = 2\mu\phi^{SS} + (\nu-\mu)\phi_p^{SD} - \mu(1-\mu'')\phi_p^{SI},$$

$$D_m = (\nu-\mu)\phi_m^{SD} - \mu(1-\mu'')\phi_m^{SI},$$

$$I_p = 2\mu\phi^{SS} + (\nu-\mu)\phi_p^{SI} - \mu(1-\mu')\phi_p^{SD},$$

$$I_m = (\nu-\mu)\phi_m^{SI} - \mu(1-\mu')\phi_m^{SD},$$

and

$$\phi^{SI^+} + \phi^{I^+S} = I_p\cos l - iI_m\sin l,$$

$$\phi^{SI^+} - \phi^{I^+S} = I_m\cos l - iI_p\sin l,$$

$$\phi^{DI} + \phi^{ID} = \psi_p^{DI}\cos l - i\psi_m^{DI}\sin l,$$

$$\phi^{DI}-\phi^{ID}=\psi_m^{DI}\cos l-i\psi_p^{DI}\sin l.$$

We can also invert the relations and express $\phi_{p(m)}^{SD(I)}$s in terms of D_p,D_m,I_p,I_m, and ϕ^{SS}. Explicitly, we have

$$\phi_p^{SD}=\frac{\nu-\mu}{(\nu-\mu)^2-\mu^2(1-\mu')(1-\mu'')}(D_p-2\mu\phi^{SS})+\frac{\mu(1-\mu'')}{(\nu-\mu)^2-\mu^2(1-\mu')(1-\mu'')}(I_p-2\mu\phi^{SS}),$$

$$\phi_m^{SD}=\frac{\nu-\mu}{(\nu-\mu)^2-\mu^2(1-\mu')(1-\mu'')}D_m+\frac{\mu(1-\mu'')}{(\nu-\mu)^2-\mu^2(1-\mu')(1-\mu'')}I_m,$$

$$\phi_p^{SI}=\frac{\mu(1-\mu')}{(\nu-\mu)^2-\mu^2(1-\mu')(1-\mu'')}(D_p-2\mu\phi^{SS})+\frac{\nu-\mu}{(\nu-\mu)^2-\mu^2(1-\mu')(1-\mu'')}(I_p-2\mu\phi^{SS}),$$

$$\phi_m^{SI}=\frac{\mu(1-\mu')}{(\nu-\mu)^2-\mu^2(1-\mu')(1-\mu'')}D_m+\frac{\nu-\mu}{(\nu-\mu)^2-\mu^2(1-\mu')(1-\mu'')}I_m.$$

With these new definitions, we can rewrite the equations of interest in a slightly more compact fashion. For example, we now write the following:

$$\phi^{SS}=1+v^2\hat{z}^2\phi^{SS}+\Delta\hat{z}^2\phi_{\hat{z}}^{SS}(y=0)+\frac{1}{2}(\phi_p^{SD}+\phi_p^{SI})+\frac{v}{2}\hat{z}^2\{\mu[(1+\cos l)S_p+iS_m\sin l-(1-\mu'')I_p-(1-\mu')D_p]+(\nu-\mu)[(D_p+I_p)\cos l+i(D_m-I_m)\sin l]\},$$

$$\phi_p^{SD}=2\phi^{DD}+\psi_p^{DI}\cos l-i\psi_m^{DI}\sin l+v\hat{z}^2\{[\mu S_p+(\nu-\mu)D_p]\cos l+i[\mu S_m+(\nu-\mu)D_m]\sin l-\mu(1-\mu'')I_p\},$$

$$\phi_m^{SD}=-\psi_m^{DI}\cos l+i\psi_p^{DI}\sin l+v\hat{z}^2\{[\mu S_m+(\nu-\mu)D_m]\cos l+i[\mu S_p+(\nu-\mu)D_p]\sin l-\mu(1-\mu'')I_m\},$$

$$\phi_p^{SI}=2\phi^{II}+\psi_p^{DI}\cos l-i\psi_m^{DI}\sin l+v\hat{z}^2\{\mu S_p+(\nu-\mu)\times[I_p\cos l-iI_m\sin l]-\mu(1-\mu')D_p\},$$

$$\phi_m^{SI}=\psi_m^{DI}\cos l-i\psi_p^{DI}\sin l+v\hat{z}^2\{\mu S_m+(\nu-\mu)[I_m\cos l-iI_p\sin l]-\mu(1-\mu')D_m\},$$

$$\phi^{DD}=\hat{z}\{\mu^2[\phi^{SS}+(1-\mu'')^2\phi^{II}-(1-\mu'')\phi_p^{SI}]+(\nu-\mu)^2\phi^{DD}+\mu(\nu-\mu)[\phi_p^{SD}-(1-\mu'')(\psi_p^{DI}\cos l-i\psi_m^{DI}\sin l)]\},$$

$$\phi^{II}=\hat{z}\{\mu^2[\phi^{SS}+(1-\mu')^2\phi^{DD}-(1-\mu')\phi_p^{SD}]+(\nu-\mu)^2\phi^{II}+\mu(\nu-\mu)[\phi_p^{SI}-(1-\mu')(\psi_p^{DI}\cos l-i\psi_m^{DI}\sin l)]\},$$

$$\psi_p^{DI}=\hat{z}\{2\mu^2\phi^{SS}+[(\nu-\mu)^2+\mu^2(1-\mu')(1-\mu'')]\times[\psi_p^{DI}\cos l-i\psi_m^{DI}\sin l]+\mu(\nu-\mu)[\phi_p^{SI}+\phi_p^{SD}]-\mu^2(1-\mu'')\phi_p^{SI}-\mu^2(1-\mu')\phi_p^{SD}-2\mu(\nu-\mu)[(1-\mu')\phi^{DD}+(1-\mu'')\phi^{II}]\},$$

$$\psi_m^{DI}=\hat{z}\{[(\nu-\mu)^2-\mu^2(1-\mu')(1-\mu'')][\psi_m^{DI}\cos l-i\psi_p^{DI}\sin l]+\mu\nu[\phi_m^{SI}-\phi_m^{SD}]+\mu^2[\mu'\phi_m^{SD}-\mu''\phi_m^{SI}]\}.$$

A common quantity that constantly appears is $S_p\cos l+iS_m\sin l$ together with $S_m\cos l+iS_p\sin l$. These two quantities can be readily expressed in terms of D_p,D_m,I_p, and I_m:

$$S_p\cos l+iS_m\sin l=\{(\cos l+\hat{z}v)D_p+(1+\hat{z}v\cos l)I_p-i\hat{z}vI_m\sin l+iD_m\sin l\}/(1-\hat{z}^2v^2),$$

$$S_m\cos l+iS_p\sin l=\{iD_p\sin l+i\hat{z}vI_p\sin l+(\cos l-\hat{z}v)D_m+(1-\hat{z}v\cos l)I_m\}/(1-\hat{z}^2v^2).$$

One thing that jumps out is the combination of $S_p+S_p\cos l+iS_m\sin l$ and $S_m+S_m\cos l+iS_p\sin l$, which then give us

$$(1+\cos l)S_p+iS_m\sin l=(1+\hat{z}v)[(1+\cos l)(D_p+I_p)+i(D_m-I_m)\sin l]/(1-\hat{z}^2v^2),$$

$$(-1+\cos l)S_p+iS_m\sin l=(1-\hat{z}v)[(-1+\cos l)(D_p-I_p)+i(D_m+I_m)\sin l]/(1-\hat{z}^2v^2),$$

$$(1+\cos l)S_m+iS_p\sin l=(1-\hat{z}v)[(1+\cos l)(D_m+I_m)+i(D_p-I_p)\sin l]/(1-\hat{z}^2v^2),$$

$$(-1+\cos l)S_m+iS_p\sin l=(1+\hat{z}v)[(-1+\cos l)(D_m-I_m)+i(D_p+I_p)\sin l]/(1-\hat{z}^2v^2).$$

APPENDIX B: THE THREE SPECIALIZED CASES

In this appendix, we describe some more details of how to obtain Eqs. (108)–(110) for the three specialized cases.

1. The $\mu'=\mu''=1$ case

In this case, the equations can be greatly simplified

$$\phi^{SS}=1+v^2\hat{z}^2\phi^{SS}+\Delta\hat{z}^2\phi_{\hat{z}}^{SS}(y=0)+\tfrac{1}{2}(\phi_p^{SD}+\phi_p^{SI})+\frac{v}{2}\hat{z}^2\{\mu[(1+\cos l)S_p+iS_m\sin l]+(\nu-\mu)[(D_p+I_p)\cos l+i(D_m-I_m)\sin l]\},$$

$$\phi_p^{SD} = 2\phi^{DD} + \psi_p^{DI} \cos l - i\psi_m^{DI} \sin l + v\hat{z}^2\{[\mu S_p + (\nu-\mu)D_p]\cos l + i[\mu S_m + (\nu-\mu)D_m]\sin l\},$$

$$\phi_m^{SD} = -\psi_m^{DI} \cos l + i\psi_p^{DI} \sin l + v\hat{z}^2\{[\mu S_m + (v-\mu)D_m]\cos l + i[\mu S_p + (v-\mu)D_p]\sin l\},$$

$$\phi_p^{SI} = 2\phi^{II} + \psi_p^{DI} \cos l - i\psi_m^{DI} \sin l + v\hat{z}^2\{\mu S_p + (v-\mu) \times [I_p \cos l - iI_m \sin l]\},$$

$$\phi_m^{SI} = \psi_m^{DI} \cos l - i\psi_p^{DI} \sin l + v\hat{z}^2\{\mu S_m + (\nu-\mu)[I_m \cos l - iI_p \sin l]\},$$

$$\phi^{DD} = \hat{z}\{\mu^2\phi^{SS} + (\nu-\mu)^2\phi^{DD} + \mu(\nu-\mu)\phi_p^{SD}\},$$

$$\phi^{II} = \hat{z}\{\mu^2\phi^{SS} + (\nu-\mu)^2\phi^{II} + \mu(\nu-\mu)\phi_p^{SI}\},$$

$$\psi_p^{DI} = \hat{z}\{2\mu^2\phi^{SS} + (\nu-\mu)^2[\psi_p^{DI} \cos l - i\psi_m^{DI} \sin l] + \mu(\nu-\mu)[\phi_p^{SI} + \phi_p^{SD}]\},$$

$$\psi_m^{DI} = \hat{z}\{(\nu-\mu)^2[\psi_m^{DI} \cos l - i\psi_p^{DI} \sin l] - \mu(\nu-\mu)[\phi_m^{SD} - \phi_m^{SI}]\}.$$

Furthermore, the relations between ϕ^{XX} and $D(I)_{p(m)}$ are very simple. In particular, we have

$$\phi_p^{SD} = \frac{D_p - 2\mu\phi^{SS}}{\nu-\mu},$$

$$\phi_m^{SD} = \frac{D_m}{\nu-\mu},$$

$$\phi_p^{SI} = \frac{I_p - 2\mu\phi^{SS}}{\nu-\mu},$$

$$\phi_m^{SI} = \frac{I_m}{\nu-\mu}.$$

We now note that if we call $A_p \equiv D_p + I_p$ and $B_m \equiv D_m - I_m$, we may simplify the calculation when solving for ϕ^{SS}. In fact, upon using the new variables the equations do simplify and we only need $\phi^{DD} + \phi^{II} \equiv \phi$, and $\cos l\ \psi_p^{DI} - i \sin l\ \psi_m^{DI} \equiv \tilde{\phi}^{DI}$, and $\cos l\ \psi_m^{DI} - i \sin l\ \psi_p^{DI} \equiv \phi^{DI}$. We end up having three fewer equations:

$$\phi^{SS} = 1 + v^2\hat{z}^2\phi^{SS} + \Delta\hat{z}^2\phi_{\hat{z}}^{SS}(y=0) + \left[\frac{1}{2(\nu-\mu)} + \frac{\mu\hat{z}^2 v}{2(1-\hat{z}v)}\right]A_p - 2\frac{\mu}{\nu-\mu}\phi^{SS} + \frac{v}{2}\hat{z}^2\left\{\left[\frac{\mu\hat{z}v}{1-\hat{z}v} + \nu\right][A_p \cos l + iB_m \sin l]\right\},$$

$$\frac{1}{\nu-\mu}A_p = 4\frac{\mu}{\nu-\mu}\phi^{SS} + \frac{\mu v\hat{z}^2}{1-\hat{z}v}A_p + 2(\phi + \tilde{\phi}^{DI}) + v\hat{z}^2\left[\nu + \frac{\mu\hat{z}v}{1-\hat{z}v}\right][A_p \cos l + iB_m \sin l],$$

$$\frac{1}{\nu-\mu}B_m = -2\phi^{DI} - \frac{\mu v\hat{z}^2}{1-\hat{z}v}B_m + v\hat{z}^2\left[\nu + \frac{\mu\hat{z}v}{1-\hat{z}v}\right][B_m \cos l + iA_p \sin l],$$

$$\phi = \hat{z}\{(\nu-\mu)^2\phi + \mu A_p - 2\mu^2\phi^{SS}\},$$

$$\cos l\ \tilde{\phi}^{DI} + i \sin l\ \phi^{DI} = \hat{z}\{(\nu-\mu)^2\tilde{\phi}^{DI} + \mu(A_p - 2\mu\phi^{SS})\},$$

$$\cos l\ \phi^{DI} + i \sin l\ \tilde{\phi}^{DI} = \hat{z}\{(\nu-\mu)^2\phi^{DI} - \mu B_m\}.$$

The first two equations actually imply

$$\phi^{SS} = 1 + v^2\hat{z}^2\phi^{SS} + \Delta\hat{z}^2\phi_{\hat{z}}^{SS}(y=0) + \frac{1}{(\nu-\mu)}A_p - 4\frac{\mu}{\nu-\mu}\phi^{SS} - \phi - \tilde{\phi}^{DI}. \tag{B1}$$

From these equations, we see that the dimensions of $\hat{z} \sim 1/v$ and the dimensions of $v \sim \mu^2$, while μ and ν have the same dimensions. We therefore find it more straightforward to use the dimensionless coefficients defined in Eq. (107). After defining the lower case a_p and b_m such that $a_p = A_p/\mu$ and $b_m = B_m/\mu$, we have

$$\phi^{SS} = 1 + \tilde{\Delta}z^2\phi^{SS} + z^2\phi^{SS}(y=0) + \frac{1}{\alpha}a_p - 4\frac{1}{\alpha}\phi^{SS} - \phi - \tilde{\phi}^{DI},$$

$$\frac{1}{\alpha}a_p = 4\frac{1}{\alpha}\phi^{SS} + \frac{\beta z^2}{1-z}a_p + 2(\phi + \tilde{\phi}^{DI}) + \beta z^2\left[\alpha + \frac{1}{1-z}\right] \times [a_p \cos l + ib_m \sin l],$$

$$\frac{1}{\alpha}b_m = -2\phi^{DI} - \frac{\beta z^2}{1-z}b_m + \beta z^2\left[\alpha + \frac{1}{1-z}\right][b_m \cos l + ia_p \sin l],$$

$$\phi = \beta z\{\alpha^2\phi + a_p - 2\phi^{SS}\},$$

$$\cos l\ \tilde{\phi}^{DI} + i \sin l\ \phi^{DI} = \beta z\{\alpha^2\tilde{\phi}^{DI} + (a_p - 2\phi^{SS})\},$$

$$\cos l\ \phi^{DI} + i \sin l\ \tilde{\phi}^{DI} = \beta z\{\alpha^2 \phi^{DI} - b_m\}.$$

After a tedious calculation with $G^1_{\exp}$ given by Eq. (111), we obtain

$$\phi^{SS} = [G^1_{\exp} + G^2 + G^3][1 + \tilde{\Delta} z^2 \phi^{SS}(y=0)], \qquad \text{(B2)}$$

where

$$G^2 = \frac{(1-\alpha^2\beta z)^2[1-(1-2\alpha\beta-\alpha^2\beta)z-\alpha^2\beta z^2]}{(1+\alpha-\alpha z)D^a(z)[H^2_{d0}-H^2_{d1}\cos l]}, \qquad \text{(B3)}$$

$$G^3 = \frac{2\alpha(1-\alpha(1+\alpha)\beta z)(1+\alpha^2\beta z^2)N^a_3(z)}{(1+\alpha+\alpha z)D^a(z)[H^3_{d0}-H^3_{d1}\cos l]}, \qquad \text{(B4)}$$

where $D^a(z)$ is given by Eq. (114) and

$$H^2_{d0} = 1 - 2(1+\beta)z + [1+(\alpha+2)^2\alpha^2\beta^2]z^2 - 2(\alpha+2)\alpha^3\beta^2 z^3 + \alpha^4\beta^2 z^4,$$

$$H^2_{d1} = 2\beta z[(\alpha+1)^2 - 2\alpha(\alpha+1)z + \alpha^2 z^2],$$

$$H^3_{d0} = 1 + (1-2\alpha\beta-\alpha^2\beta)z - \alpha(2+\alpha)\beta z^2 + 2\alpha^2\beta^2 z^3 + \alpha^3(\alpha+2)\beta^2 z^4 + \alpha^4(1-2\alpha\beta-\alpha^2\beta)\beta^2 z^5 - \alpha^6\beta^3 z^6,$$

$$H^3_{d1} = 2\alpha[1+\alpha+\alpha[1-(\alpha+1)^2\beta]z - \alpha^2(\alpha+1)\beta z^2]\beta z^2.$$

Using $\phi^{SS}(y=0) = (1/\pi)\int_0^\pi \phi^{SS} dl$ and integrating both sides of Eq. (B2) over l from 0 to π, we can then solve for $\phi^{SS}(y=0)$. It is straightforward, with notations defined in Eqs. (115)–(118), to verify that

$$\sqrt{(H^2_{d0})^2 - (H^2_{d1})^2} = \sqrt{(1-\alpha^2\beta z)F^a_2(z)}[1-(1-2\alpha\beta-\alpha^2\beta)z - \alpha^2\beta z^2],$$

$$\sqrt{(H^3_{d0})^2 - (H^3_{d1})^2} = \sqrt{N^a_3(z)F^a_{31}(z)F^a_{32}(z)}(1+\alpha^2\beta z^2),$$

which then lead to Eqs. (108)–(113).

2. The $\mu' = \mu'' = 0$ case

When $\mu' = \mu'' = 0$, the recursions still have the $D(I)$ symmetry which we will exploit. We have

$$\phi^{SD}_p = \frac{\nu-\mu}{\nu(\nu-2\mu)}(D_p - 2\mu\phi^{SS}) + \frac{\mu}{\nu(\nu-2\mu)}(I_p - 2\mu\phi^{SS}),$$

$$\phi^{SD}_m = \frac{\nu-\mu}{\nu(\nu-2\mu)}D_m + \frac{\mu}{\nu(\nu-2\mu)}I_m,$$

$$\phi^{SI}_p = \frac{\mu}{\nu(\nu-2\mu)}(D_p - 2\mu\phi^{SS}) + \frac{\nu-\mu}{\nu(\nu-2\mu)}(I_p - 2\mu\phi^{SS}),$$

$$\phi^{SI}_m = \frac{\mu}{\nu(\nu-2\mu)}D_m + \frac{\nu-\mu}{\nu(\nu-2\mu)}I_m.$$

With these new definitions, we can rewrite the equations of interest in a slightly more compact fashion. For example, we now write the following:

$$\phi^{SS} = 1 + \upsilon^2\hat{z}^2\phi^{SS} + \Delta\hat{z}^2\phi^{SS}_{\hat{z}}(y=0) + \tfrac{1}{2}(\phi^{SD}_p + \phi^{SI}_p) + \frac{\upsilon}{2}\hat{z}^2\{\mu[(1+\cos l)S_p + iS_m \sin l - I_p - D_p] + (\nu-\mu)[(D_p+I_p)\cos l + i(D_m - I_m)\sin l]\},$$

$$\phi^{SD}_p = 2\phi^{DD} + \psi^{DI}_p \cos l - i\psi^{DI}_m \sin l + \upsilon\hat{z}^2\{[\mu S_p + (\nu-\mu)D_p]\cos l + i[\mu S_m + (\nu-\mu)D_m]\sin l - \mu I_p\},$$

$$\phi^{SD}_m = -\psi^{DI}_m \cos l + i\psi^{DI}_p \sin l + \upsilon\hat{z}^2\{[\mu S_m + (\nu-\mu)D_m]\cos l + i[\mu S_p + (\nu-\mu)D_p]\sin l - \mu I_m\},$$

$$\phi^{SI}_p = 2\phi^{II} + \psi^{DI}_p \cos l - i\psi^{DI}_m \sin l + \upsilon\hat{z}^2\{\mu S_p + (\nu-\mu)\times[I_p \cos l - iI_m \sin l] - \mu D_p\},$$

$$\phi^{SI}_m = \psi^{DI}_m \cos l - i\psi^{DI}_p \sin l + \upsilon\hat{z}^2\{\mu S_m + (\nu-\mu)[I_m \cos l - iI_p \sin l] - \mu D_m\},$$

$$\phi^{DD} = \hat{z}\{\mu^2[\phi^{SS} + \phi^{II} - \phi^{SI}_p] + (\nu-\mu)^2\phi^{DD} + \mu(\nu-\mu)[\phi^{SD}_p - (\psi^{DI}_p \cos l - i\psi^{DI}_m \sin l)]\},$$

$$\phi^{II} = \hat{z}\{\mu^2[\phi^{SS} + \phi^{DD} - \phi^{SD}_p] + (\nu-\mu)^2\phi^{II} + \mu(\nu-\mu)[\phi^{SI}_p - (\psi^{DI}_p \cos l - i\psi^{DI}_m \sin l)]\},$$

$$\psi^{DI}_p = \hat{z}\{2\mu^2\phi^{SS} + [(\nu-\mu)^2 + \mu^2][\psi^{DI}_p \cos l - i\psi^{DI}_m \sin l] + \mu(\nu-2\mu)[\phi^{SI}_p + \phi^{SD}_p] - 2\mu(\nu-\mu)[\phi^{DD} + \phi^{II}]\},$$

$$\psi^{DI}_m = \hat{z}\{[(\nu-\mu)^2 - \mu^2][\psi^{DI}_m \cos l - i\psi^{DI}_p \sin l] + \mu[\nu\phi^{SI}_m - \nu\phi^{SD}_m]\}.$$

We now note that if we call $A_p \equiv D_p + I_p$ and $B_m \equiv D_m - I_m$, we may simplify the calculation when solving for ϕ^{SS}. Note that

$$\phi^{SD}_p + \phi^{SI}_p = \frac{1}{\nu-2\mu}(D_p + I_p - 4\mu\phi^{SS}),$$

$$\phi^{SD}_m - \phi^{SI}_m = \frac{1}{\nu}(D_m - I_m).$$

With the observation above, the equations do simplify when we further introduce $\phi^{DD} + \phi^{II} \equiv \phi$, and $\cos l\ \psi^{DI}_p - i \sin l\ \psi^{DI}_m \equiv \tilde{\phi}^{DI}$, and $\cos l\ \psi^{DI}_m - i \sin l\ \psi^{DI}_p \equiv \phi^{DI}$. Using these new definitions, we ended up having three fewer equations:

$$\phi^{SS} = 1 + v^2\hat{z}^2\phi^{SS} + \Delta\hat{z}^2\phi^{SS}_{\hat{z}}(y=0) + \left[\frac{1}{2(\nu-2\mu)} + \frac{\mu\hat{z}^3v^2}{2(1-\hat{z}v)}\right]A_p - 2\frac{\mu}{\nu-2\mu}\phi^{SS} + \frac{v}{2}\hat{z}^2\left\{\left[\frac{\mu\hat{z}v}{1-\hat{z}v}+\nu\right] \times[A_p\cos l + iB_m\sin l]\right\},$$

$$\left[\frac{1}{\nu-2\mu} - \frac{\mu\hat{z}^3v^2}{1-\hat{z}v}\right]A_p = 4\frac{\mu}{\nu-2\mu}\phi^{SS} + 2(\phi+\tilde{\phi}^{DI}) + v\hat{z}^2\left[\nu+\frac{\mu\hat{z}v}{1-\hat{z}v}\right] \times[A_p\cos l + iB_m\sin l],$$

$$\left[\frac{1}{\nu} + \frac{\mu\hat{z}^3v^2}{1-\hat{z}v}\right]B_m = -2\phi^{DI} + v\hat{z}^2\left[\nu+\frac{\mu\hat{z}v}{1-\hat{z}v}\right][B_m\cos l + iA_p\sin l],$$

$$\phi = \hat{z}\{[(\nu-\mu)^2+\mu^2]\phi + \mu A_p - 2\mu(\nu-\mu)\tilde{\phi}^{DI}\} - 2\hat{z}\mu^2\phi^{SS},$$

$$\cos l\ \tilde{\phi}^{DI} + i\sin l\ \phi^{DI} = \hat{z}\{[(\nu-\mu)^2+\mu^2]\tilde{\phi}^{DI} + \mu(A_p - 2\mu\phi^{SS}) - 2\mu(\nu-\mu)\phi\},$$

$$\cos l\ \phi^{DI} + i\sin l\ \tilde{\phi}^{DI} = \hat{z}\{[(\nu-\mu)^2-\mu^2]\phi^{DI} - \mu B_m\}.$$

Similar reasoning leads us to use the definition (107) to lighten the notation. Again a_p and b_m are defined through $a_p = A_p/\mu$ and $b_m = B_m/\mu$. We then have

$$\phi^{SS} = 1 + z^2\phi^{SS} + \tilde{\Delta}z^2\phi^{SS}(y=0) + \frac{1}{2}\left[\frac{1}{\alpha-1} + \frac{\beta z^3}{1-z}\right]a_p - \frac{2}{\alpha-1}\phi^{SS} + \frac{1}{2}z^2\beta\left[\frac{1}{1-z}+\alpha\right][a_p\cos l + ib_m\sin l],$$

$$\left[\frac{1}{\alpha-1} - \frac{\beta z^3}{1-z}\right]a_p = \frac{4}{\alpha-1}\phi^{SS} + 2(\phi+\tilde{\phi}^{DI}) + z^2\beta\left[\alpha+\frac{1}{1-z}\right][a_p\cos l + ib_m\sin l],$$

$$\left[\frac{1}{\alpha+1} + \frac{\beta z^3}{(1-z)}\right]b_m = -2\phi^{DI} + z^2\beta\left[\alpha+\frac{1}{1-z}\right] \times[b_m\cos l + ia_p\sin l],$$

$$\phi = z\beta\{[\alpha^2+1]\phi + a_p - 2\alpha\tilde{\phi}^{DI}\} - 2z\beta\phi^{SS},$$

$$\cos l\ \tilde{\phi}^{DI} + i\sin l\ \phi^{DI} = z\beta\{[\alpha^2+1]\tilde{\phi}^{DI} + a_p - 2\phi^{SS} - 2\alpha\phi\},$$

$$\cos l\ \phi^{DI} + i\sin l\ \tilde{\phi}^{DI} = z\beta\{[\alpha^2-1]\phi^{DI} - b_m\}.$$

The first two equations actually tell us that

$$\phi^{SS} = 1 + \left[z^2 - \frac{4}{(\alpha-1)}\right]\phi^{SS} + \tilde{\Delta}z^2\phi^{SS}(y=0) + \frac{1}{\alpha-1}a_p - \phi - \tilde{\phi}^{DI}, \quad \text{(B5)}$$

and the five equations relating $a_p, b_m, \phi, \phi^{DI}$, and $\tilde{\phi}^{DI}$ can be turned into

$$\left[\frac{1}{\alpha-1} - \frac{\beta z^3}{(1-z)} - \beta z^2\left(\alpha+\frac{1}{1-z}\right)\cos l\right]a_p - i\sin l\ \beta z^2\left[\alpha+\frac{1}{1-z}\right]b_m - 2(\phi+\tilde{\phi}^{DI}) = \frac{4}{\alpha-1}\phi^{SS},$$

$$-i\sin l\ \beta z^2\left[\alpha+\frac{1}{1-z}\right]a_p + \left[\frac{1}{\alpha+1} + \frac{\beta z^3}{1-z} - \beta z^2\left(\alpha+\frac{1}{1-z}\right)\cos l\right]b_m + 2\phi^{DI} = 0,$$

$$-\beta z\ a_p + [1-\beta z(\alpha^2+1)]\phi + 2\beta z\alpha\ \tilde{\phi}^{DI} = -2\beta z\ \phi^{SS},$$

$$-\beta z\ a_p + 2\beta z\alpha\ \phi + [\cos l - \beta z(\alpha^2+1)]\tilde{\phi}^{DI} + i\sin l\ \phi^{DI} = -2\beta z\ \phi^{SS},$$

$$\beta z\ b_m + i\sin l\ \tilde{\phi}^{DI} + [\cos l - \beta z(\alpha^2-1)]\phi^{DI} = 0.$$

Subtracting the fourth equation above by the third equation, we obtain the new fourth equation and thus

$$[\beta z(\alpha+1)^2 - 1]\phi + [\cos l - \beta z(\alpha+1)^2]\tilde{\phi}^{DI} + i\sin l\phi^{DI} = 0. \quad \text{(B6)}$$

Consequently, we have

$$\left[\frac{1}{\alpha-1} - \frac{\beta z^3}{(1-z)} - \beta z^2\left(\alpha+\frac{1}{1-z}\right)\cos l\right]a_p - i\sin l\ \beta z^2\left[\alpha+\frac{1}{1-z}\right]b_m - 2(\phi+\tilde{\phi}^{DI}) = \frac{4}{\alpha-1}\phi^{SS},$$

$$-i\sin l\ \beta z^2\left[\alpha+\frac{1}{1-z}\right]a_p + \left[\frac{1}{\alpha+1} + \frac{\beta z^3}{1-z} - \beta z^2\left(\alpha+\frac{1}{1-z}\right)\cos l\right]b_m + 2\phi^{DI} = 0,$$

$$-\beta z\ a_p + [1-\beta z(\alpha^2+1)]\phi + 2\beta z\alpha\ \tilde{\phi}^{DI} = -2\beta z\ \phi^{SS},$$

$$[\beta z(\alpha+1)^2 - 1]\phi + [\cos l - \beta z(\alpha+1)^2]\tilde{\phi}^{DI} + i\sin l\ \phi^{DI} = 0,$$

$$\beta z\, b_m + i \sin l\, \tilde{\phi}^{DI} + [\cos l - \beta z(\alpha^2-1)]\phi^{DI} = 0.$$

After a tedious calculation with $G^1_{\rm exp}$ given by Eq. (111), we obtain an equation of similar form to Eq. (B2) but with

$$G^2 = \frac{(1-(1+\alpha)^2\beta z)^2[1-(1-(\alpha+1)^2\beta)z]}{(1+\alpha-\alpha z)D^b(z)[H^2_{d0}-H^2_{d1}\cos l]}, \quad \text{(B7)}$$

$$G^3 = \frac{2[\alpha+(1-\alpha)(1+\alpha)^2\beta z][1-(1-\alpha^2)\beta z^2]N_3^b(z)}{(1+\alpha+\alpha z)D^b(z)[H^3_{d0}-H^3_{d1}\cos l]}, \quad \text{(B8)}$$

where

$$H^2_{d0} = 1-2z+[1+(\alpha+1)^4\beta^2]z^2 - 2[1-(1-\alpha^2)(1+\alpha)^2\beta]\beta z^3 + (1-\alpha^2)^2\beta^2 z^4,$$

$$H^2_{d1} = 2\beta(1+\alpha-\alpha z)^2 z,$$

$$H^3_{d0} = 1+[1-(1+\alpha)^2\beta]z - (1+\alpha)^2\beta z^2 - 2\beta z^3 - (1-\alpha)(1+\alpha)^3\beta^2 z^4 + (1-\alpha^2)^2[1-(1+\alpha)^2\beta]\beta^2 z^5 + (1-\alpha^2)^3\beta^3 z^6,$$

$$H^3_{d1} = 2\beta\{\alpha(1+\alpha)+[\alpha^2+2\alpha(1-\alpha^2)\beta+(1-\alpha^4)\beta]z + \alpha(1-\alpha)(1+\alpha^2)z^2\}z^2.$$

Using $\phi^{SS}(y=0)=(1/\pi)\int_0^\pi \phi^{SS} dl$ and integrating both sides of (B2) over l from 0 to π, we can then solve for $\phi^{SS}(y=0)$. It is straightforward, with notations defined in Eqs. (122)–(125), to verify that

$$\sqrt{(H^2_{d0})^2-(H^2_{d1})^2} = \sqrt{(1-(1+\alpha)^2\beta z)F^b_2(z)} \times [1-[1-(\alpha+1)^2\beta]z],$$

$$\sqrt{(H^3_{d0})^2-(H^3_{d1})^2} = \sqrt{N^{\,b}_{\,3}(z)F^{\,b}_{\,31}(z)F^{\,b}_{\,32}(z)}[1-(1-\alpha^2)\beta z^2],$$

which then leads to Eqs. (108)–(111), (119), and (120).

3. The $\mu'=1$ and $\mu''=0$ case

Here, we will consider a specialized case where $\mu'=1$. This, in fact, is the case we commonly used in numerical work. As one may readily observe, it changes six out of the nine equations in the general development displayed near the end of Appendix A, giving

$$\phi^{SS} = 1 + v^2\hat{z}^2\phi^{SS} + \Delta\hat{z}^2\phi^{SS}_{\hat{z}}(y=0) + \tfrac{1}{2}(\phi^{SD}_p+\phi^{SI}_p) + \frac{v}{2}\hat{z}^2\{\mu[(1+\cos l)S_p + iS_m\sin l - I_p] + (\nu-\mu)[(D_p+I_p)\cos l + i(D_m-I_m)\sin l]\},$$

$$\phi^{SD}_p = 2\phi^{DD} + \psi^{DI}_p\cos l - i\psi^{DI}_m\sin l + v\hat{z}^2\{[\mu S_p+(\nu-\mu)D_p]\cos l + i[\mu S_m+(\nu-\mu)D_m]\sin l - \mu I_p\},$$

$$\phi^{SD}_m = -\psi^{DI}_m\cos l + i\psi^{DI}_p\sin l + v\hat{z}^2\{[\mu S_m+(\nu-\mu)D_m]\cos l + i[\mu S_p+(\nu-\mu)D_p]\sin l - \mu I_m\},$$

$$\phi^{SI}_p = 2\phi^{II} + \psi^{DI}_p\cos l - i\psi^{DI}_m\sin l + v\hat{z}^2\{\mu S_p+(\nu-\mu)[I_p\cos l - iI_m\sin l]\},$$

$$\phi^{SI}_m = \psi^{DI}_m\cos l - i\psi^{DI}_p\sin l + v\hat{z}^2\{\mu S_m+(\nu-\mu)[I_m\cos l - iI_p\sin l]\},$$

$$\phi^{DD} = \hat{z}\{\mu^2[\phi^{SS}+\phi^{II}-\phi^{SI}_p] + (\nu-\mu)^2\phi^{DD} + \mu(\nu-\mu)[\phi^{SD}_p - (\psi^{DI}_p\cos l - i\psi^{DI}_m\sin l)]\},$$

$$\phi^{II} = \hat{z}\{\mu^2\phi^{SS} + (\nu-\mu)^2\phi^{II} + \mu(\nu-\mu)\phi^{SI}_p\},$$

$$\psi^{DI}_p = \hat{z}\{2\mu^2\phi^{SS} + (\nu-\mu)^2[\psi^{DI}_p\cos l - i\psi^{DI}_m\sin l] + \mu(\nu-\mu)\times[\phi^{SI}_p+\phi^{SD}_p-2\phi^{II}] - \mu^2\phi^{SI}_p\}, \quad \text{(B9)}$$

$$\psi^{DI}_m = \hat{z}\{(\nu-\mu)^2[\psi^{DI}_m\cos l - i\psi^{DI}_p\sin l] + \mu[\nu\phi^{SI}_m - (\nu-\mu)\phi^{SD}_m]\}.$$

Now it looks more promising to work with the combinations of the variables $\phi^{DD},\phi^{II},\psi^{DI}_p,\psi^{DI}_m,D_p,D_m,I_p,I_m$. Basically, we can transform the equations into those variables depending on ϕ^{SS}. Explicitly, we will also need to use

$$\phi^{SD}_p = \frac{1}{\nu-\mu}(D_p-2\mu\phi^{SS}) + \frac{\mu}{(\nu-\mu)^2}(I_p-2\mu\phi^{SS}),$$

$$\phi^{SD}_m = \frac{1}{\nu-\mu}D_m + \frac{\mu}{(\nu-\mu)^2}I_m,$$

$$\phi^{SI}_p = \frac{1}{\nu-\mu}(I_p-2\mu\phi^{SS}),$$

$$\phi^{SI}_m = \frac{1}{\nu-\mu}I_m.$$

We further note that

$$S_p = \frac{(1+\hat{z}v\cos l)D_p + (\cos l+\hat{z}v)I_p - i(I_m-\hat{z}vD_m)\sin l}{1-\hat{z}^2v^2} = \frac{(1+\hat{z}v\cos l)(D_p+I_p) + i\hat{z}v(D_m-I_m)\sin l}{1-\hat{z}^2v^2} - \frac{(1-\cos l)I_p + iI_m\sin l}{1+\hat{z}v},$$

$$S_m = \frac{(1-\hat{z}v\cos l)D_m + (\cos l - \hat{z}v)I_m - i(I_p + \hat{z}vD_p)\sin l}{1-\hat{z}^2v^2}$$
$$= \frac{(1-\hat{z}v\cos l)(D_m - I_m) - i\hat{z}v(D_p+I_p)\sin l}{1-\hat{z}^2v^2} + \frac{(1+\cos l)I_m - iI_p\sin l}{1+\hat{z}v}. \tag{B10}$$

We then turn those nine equations in Eq. (B9) first into

$$\phi^{SS} = 1 + v^2\hat{z}^2\phi^{SS} + \Delta\hat{z}^2\phi_{\hat{z}}^{SS}(y=0) + \frac{1}{2}(\phi_p^{SD}+\phi_p^{SI}) - \frac{\mu v\hat{z}^2}{2}I_p + \frac{v}{2}\hat{z}^2\left\{\left[\frac{\mu}{1-\hat{z}v}(1+\cos l) + (\nu-\mu)\cos l\right](D_p+I_p) + i\sin l\left[\frac{\mu}{1-\hat{z}v}+\nu-\mu\right](D_m-I_m)\right\},$$

$$\phi_p^{SD}+\phi_p^{SI} = 2[\phi^{DD}+\phi^{II}+\psi_p^{DI}\cos l - i\psi_m^{DI}\sin l] - \mu v\hat{z}^2 I_p + v\hat{z}^2\left\{\left[\frac{\mu}{1-\hat{z}v}(1+\cos l)+(\nu-\mu)\cos l\right]\times(D_p+I_p) + i\sin l\left[\frac{\mu}{1-\hat{z}v}+\nu-\mu\right]\times(D_m-I_m)\right\},$$

$$\phi_p^{SI} = 2\phi^{II} + \psi_p^{DI}\cos l - i\psi_m^{DI}\sin l + v\hat{z}^2\left\{\frac{\mu(1+\hat{z}v\cos l)}{1-\hat{z}^2v^2}\times(D_p+I_p) + i\frac{\mu\hat{z}v\sin l}{1-\hat{z}^2v^2}(D_m-I_m) - \frac{\mu}{1+\hat{z}v}I_p + \left(\nu-\mu+\frac{\mu}{1+\hat{z}v}\right)(I_p\cos l - iI_m\sin l)\right\},$$

$$\phi_m^{SD}-\phi_m^{SI} = -2[\psi_m^{DI}\cos l - i\psi_p^{DI}\sin l] - \mu v\hat{z}^2 I_m + v\hat{z}^2\left\{\left[\frac{\mu}{1-\hat{z}v}(-1+\cos l)+(\nu-\mu)\cos l\right]\times(D_m-I_m) + i\sin l\left[\frac{\mu}{1-\hat{z}v}+\nu-\mu\right]\times(D_p+I_p)\right\},$$

$$\phi_m^{SI} = \psi_m^{DI}\cos l - i\psi_p^{DI}\sin l + v\hat{z}^2\left\{\frac{\mu(1-\hat{z}v\cos l)}{1-\hat{z}^2v^2}(D_m-I_m) - i\frac{\mu\hat{z}v\sin l}{1-\hat{z}^2v^2}(D_p+I_p) + \frac{\mu}{1+\hat{z}v}I_m + \left(\nu-\mu+\frac{\mu}{1+\hat{z}v}\right)(I_m\cos l - iI_p\sin l)\right\},$$

$$\phi^{DD} = \hat{z}\{\mu^2\phi^{II} + (\nu-\mu)^2\phi^{DD} + \mu[D_p - \mu\phi^{SS}] - \mu(\nu-\mu)\times[\psi_p^{DI}\cos l - i\psi_m^{DI}\sin l]\},$$

$$\phi^{II} = \hat{z}\{\mu[I_p - \mu\phi^{SS}] + (\nu-\mu)^2\phi^{II}\},$$

$$\psi_p^{DI} = \hat{z}\{2\mu^2\phi^{SS} + (\nu-\mu)^2[\psi_p^{DI}\cos l - i\psi_m^{DI}\sin l] - 2\mu(\nu-\mu)\phi^{II} + \mu[I_p + D_p - 4\mu\phi^{SS}]\},$$

$$\psi_m^{DI} = \hat{z}\{(\nu-\mu)^2[\psi_m^{DI}\cos l - i\psi_p^{DI}\sin l] + \mu[I_m - D_m]\}.$$

Given these equations, it is easier for calculation's purpose to use

$$A_p \equiv (D_p + I_p),$$

$$I_p,$$

$$B_m \equiv (D_m - I_m),$$

$$I_m,$$

$$\tilde{\phi}^{DI} \equiv \psi_p^{DI}\cos l - i\psi_m^{DI}\sin l,$$

$$\phi^{DI} \equiv \psi_m^{DI}\cos l - i\psi_p^{DI}\sin l,$$

$$\phi^{II},$$

$$\phi \equiv \phi^{DD} + \phi^{II},$$

as independent variables. The equation for ϕ^{SS} can be slightly simplified to reinforce our introducing new notations.

$$\phi^{SS} = 1 + \Delta\hat{z}^2\phi_{\hat{z}}^{SS}(y=0) + \left[v^2\hat{z}^2 - 4\frac{\mu}{(\nu-\mu)} - 2\frac{\mu^2}{(\nu-\mu)^2}\right]\phi^{SS} + \frac{1}{(\nu-\mu)}A_p - (\phi + \tilde{\phi}^{DI}) + \frac{\mu}{(\nu-\mu)^2}I_p. \tag{B11}$$

Together with our previous definitions of $D(I)_{p(m)}$, we now have the other eight equations (in the order of $\phi_p^{SD}+\phi_p^{SI}$, ϕ_p^{SI}, $\phi_m^{SD}-\phi_m^{SI}$, ϕ_m^{SI}, $\phi^{DD}+\phi^{II}$, ϕ^{II}, ψ_p^{DI}, ψ_m^{DI}):

$$\frac{A_p}{\nu-\mu}+\frac{\mu I_p}{(\nu-\mu)^2}=2[\phi+\tilde{\phi}^{DI}]-\mu v\hat{z}^2 I_p+2\frac{\mu}{\nu-\mu}\left[2+\frac{\mu}{\nu-\mu}\right]\phi^{SS}$$
$$+v\hat{z}^2\left\{\left[\frac{\mu}{1-\hat{z}v}(1+\cos l)+(\nu-\mu)\cos l\right]A_p+i\sin l\left[\frac{\mu}{1-\hat{z}v}+\nu-\mu\right]B_m\right\},$$

$$\frac{I_p}{\nu-\mu}=2\phi^{II}+\tilde{\phi}^{DI}+v\hat{z}^2\left[\frac{\mu(1+\hat{z}v\cos l)}{1-\hat{z}^2v^2}A_p+i\sin l\frac{\mu\hat{z}v}{1-\hat{z}^2v^2}B_m\right]+2\frac{\mu}{(\nu-\mu)}\phi^{SS}$$
$$+v\hat{z}^2\left\{\left[(\nu-\mu)\cos l+\frac{\mu(-1+\cos l)}{1+\hat{z}v}\right]I_p-i\sin l\left[\nu-\mu+\frac{\mu}{1+\hat{z}v}\right]I_m\right\},$$

$$\frac{B_m}{\nu-\mu}+\frac{\mu I_m}{(\nu-\mu)^2}=-2\phi^{DI}-\mu v\hat{z}^2 I_m+v\hat{z}^2\left\{\left[\frac{\mu}{1-\hat{z}v}(-1+\cos l)+(\nu-\mu)\cos l\right]B_m+i\sin l\left[\frac{\mu}{1-\hat{z}v}+\nu-\mu\right]A_p\right\},$$

$$\frac{I_m}{\nu-\mu}=\phi^{DI}+v\hat{z}^2\left[\frac{\mu(1-\hat{z}v\cos l)}{1-\hat{z}^2v^2}B_m-i\sin l\frac{\mu\hat{z}v}{1-\hat{z}^2v^2}A_p\right]$$
$$+v\hat{z}^2\left\{\left[(\nu-\mu)\cos l+\frac{\mu(1+\cos l)}{1+\hat{z}v}\right]I_m-i\sin l\left[\nu-\mu+\frac{\mu}{1+\hat{z}v}\right]I_p\right\},$$

$$\phi=\hat{z}\{\mu^2\phi^{II}+(\nu-\mu)^2\phi+\mu[A_p-2\mu\phi^{SS}]-\mu(\nu-\mu)\tilde{\phi}^{DI}\},$$

$$\phi^{II}=\hat{z}\{\mu[I_p-\mu\phi^{SS}]+(\nu-\mu)^2\phi^{II}\},$$

$$\tilde{\phi}^{DI}\cos l+i\phi^{DI}\sin l=\hat{z}\{(\nu-\mu)^2\tilde{\phi}^{DI}-2\mu(\nu-\mu)\phi^{II}+\mu[A_p-2\mu\phi^{SS}]\},$$

$$\phi^{DI}\cos l+i\tilde{\phi}^{DI}\sin l=\hat{z}\{(\nu-\mu)^2\phi^{DI}-\mu B_m\}.$$

We again rescale the variables by replacing X (any capital symbol) by μx and using the definition (107) to obtain

$$\frac{a_p}{\alpha}+\frac{i_p}{\alpha^2}=2[\phi+\tilde{\phi}^{DI}]-\beta z^2 i_p+\frac{2}{\alpha}\left[2+\frac{1}{\alpha}\right]\phi^{SS}$$
$$+\beta z^2\left\{\left[\frac{1}{1-z}(1+\cos l)+\alpha\cos l\right]a_p+i\sin l\left[\frac{1}{1-z}+\alpha\right]b_m\right\},$$

$$\frac{i_p}{\alpha}=[2\phi^{II}+\tilde{\phi}^{DI}]+\beta z^2\left[\frac{1+z\cos l}{1-z^2}a_p+i\sin l\frac{z}{1-z^2}b_m\right]+\frac{2}{\alpha}\phi^{SS}$$
$$+\beta z^2\left\{\left[\frac{(-1+\cos l)}{1+z}+\alpha\cos l\right]i_p-i\sin l\left[\alpha+\frac{1}{1+z}\right]i_m\right\},$$

$$\frac{b_m}{\alpha}+\frac{i_m}{\alpha^2}=-2\phi^{DI}-\beta z^2 i_m+\beta z^2\left\{\left[\frac{(-1+\cos l)}{1-z}+\alpha\cos l\right]b_m+i\sin l\left[\frac{1}{1-z}+\alpha\right]a_p\right\},$$

$$\frac{i_m}{\alpha}=\phi^{DI}+\beta z^2\left[\frac{1-z\cos l}{1-z^2}b_m-i\sin l\frac{z}{1-z^2}a_p\right]$$
$$+\beta z^2\left\{\left[\frac{(1+\cos l)}{1+z}+\alpha\cos l\right]i_m-i\sin l\left[\frac{1}{1+z}+\alpha\right]i_p\right\},$$

$$\phi=\beta z\{\phi^{II}+\alpha^2\phi+[a_p-2\phi^{SS}]-\alpha\tilde{\phi}^{DI}\},$$

$$\phi^{II}=\beta z\{[i_p-\phi^{SS}]+\alpha^2\phi^{II}\},$$

$$\tilde{\phi}^{DI}\cos l + i\phi^{DI}\sin l = \beta z\{\alpha^2\tilde{\phi}^{DI} - 2\alpha\phi^{II} + [a_p - 2\phi^{SS}]\},$$

$$\phi^{DI}\cos l + i\tilde{\phi}^{DI}\sin l = \beta z\{\alpha^2\phi^{DI} - b_m\}.$$

Furthermore, the main equation of ϕ^{SS} becomes

$$\phi^{SS} = 1 + \tilde{\Delta}z^2\phi^{SS}(y=0) + \left[z^2 - 4\frac{1}{\alpha} - 2\frac{1}{\alpha^2}\right]\phi^{SS} + \frac{1}{\alpha}a_p - (\phi + \tilde{\phi}^{DI}) + \frac{1}{\alpha^2}i_p. \quad \text{(B12)}$$

Following the previous two cases (1. and 2.) discussed in this appendix, we will order our variables in the following way: $a_p, b_m, \phi, \tilde{\phi}^{DI}, \phi^{DI}, i_p, i_m, \phi^{II}$. That is to say, the first five variables agree with previous definitions. We now arrange the equations as

$$\frac{a_p}{\alpha} + \frac{i_p}{\alpha^2} = 2[\phi + \tilde{\phi}^{DI}] - \beta z^2 i_p + \frac{2}{\alpha}\left[2 + \frac{1}{\alpha}\right]\phi^{SS} + \beta z^2\left\{\left[\frac{1}{1-z}(1+\cos l) + \alpha\cos l\right]a_p + i\sin l\left[\frac{1}{1-z} + \alpha\right]b_m\right\},$$

$$\frac{b_m}{\alpha} + \frac{i_m}{\alpha^2} = -2\phi^{DI} - \beta z^2 i_m + \beta z^2\left\{\left[\frac{(-1+\cos l)}{1-z} + \alpha\cos l\right]b_m + i\sin l\left[\frac{1}{1-z} + \alpha\right]a_p\right\},$$

$$\phi = \beta z\{\phi^{II} + \alpha^2\phi + [a_p - 2\phi^{SS}] - \alpha\tilde{\phi}^{DI}\},$$

$$\tilde{\phi}^{DI}\cos l + i\phi^{DI}\sin l = \beta z\{\alpha^2\tilde{\phi}^{DI} - 2\alpha\phi^{II} + [a_p - 2\phi^{SS}]\},$$

$$\phi^{DI}\cos l + i\tilde{\phi}^{DI}\sin l = \beta z\{\alpha^2\phi^{DI} - b_m\},$$

$$\frac{i_p}{\alpha} = [2\phi^{II} + \tilde{\phi}^{DI}] + \beta z^2\left[\frac{1+z\cos l}{1-z^2}a_p + i\sin l\frac{z}{1-z^2}b_m\right] + \frac{2}{\alpha}\phi^{SS} + \beta z^2\left\{\left[\frac{(-1+\cos l)}{1+z} + \alpha\cos l\right]i_p - i\sin l\left[\alpha + \frac{1}{1+z}\right]i_m\right\},$$

$$\frac{i_m}{\alpha} = \phi^{DI} + \beta z^2\left[\frac{1-z\cos l}{1-z^2}b_m - i\sin l\frac{z}{1-z^2}a_p\right] + \beta z^2\left\{\left[\frac{(1+\cos l)}{1+z} + \alpha\cos l\right]i_m - i\sin l\left[\frac{1}{1+z} + \alpha\right]i_p\right\},$$

$$\phi^{II} = \beta z\{[i_p - \phi^{SS}] + \alpha^2\phi^{II}\}.$$

After a tedious calculation with G^1_{exp} given by Eq. (111), we obtain an equation of similar form to Eq. (B2) but with

$$G^2 = \frac{(1-\alpha(1+\alpha)\beta z)^2[1-(1-(1+\alpha)^2\beta)z - \alpha^2\beta z]}{(1+\alpha-\alpha z)D^c(z)[H^2_{d0} - H^2_{d1}\cos l]}, \quad \text{(B13)}$$

$$G^3 = \frac{2\alpha[1-\alpha(1+\alpha)\beta z](1+\alpha^2\beta z^2)N^c_3(z)}{(1+\alpha+\alpha z)D^c(z)[H^3_{d0} - H^3_{d1}\cos l]}, \quad \text{(B14)}$$

where

$$H^2_{d0} = 1 - 2z + [1 - 2\beta + (\alpha+1)^4\beta^2]z^2 - 2\alpha^2(1+\alpha)^2\beta^2 z^3 + \alpha^4\beta^2 z^4,$$

$$H^2_{d1} = 2\beta(1+\alpha-\alpha z)^2 z,$$

$$H^3_{d0} = 1 + [1-(1+\alpha)^2\beta]z - \alpha(2+\alpha)\beta z^2 + \alpha^3(2+\alpha)\beta^2 z^4 + \alpha^4[1-(1+\alpha)^2\beta]\beta^2 z^5 - \alpha^6\beta^3 z^6,$$

$$H^3_{d1} = 2\alpha\beta\{1+\alpha+\alpha[1-(1+\alpha)^2\beta]z - \alpha^2(1+\alpha)\beta z^2\}z^2.$$

Using $\phi^{SS}(y=0) = (1/\pi)\int_0^\pi \phi^{SS} dl$ and integrating both sides of (B2) over l from 0 to π, we can then solve for $\phi^{SS}(y=0)$. It is straightforward, with notations defined in Eqs. (129)–(133), to verify that

$$\sqrt{(H^2_{d0})^2 - (H^2_{d1})^2} = \sqrt{F^{\,c}_2(z)}[1-(1-(1+\alpha)^2\beta)z - \alpha^2\beta z],$$

$$\sqrt{(H^3_{d0})^2 - (H^3_{d1})^2} = \sqrt{F^{\,c}_{31}(z)F^{\,c}_{32}(z)F^{c}_{33}(z)}(1+\alpha^2\beta z^2),$$

which then leads to Eqs. (108)–(111), and (126) and (127).

[1] D. A. Huse and C. L. Henley, Phys. Rev. Lett. **54**, 2708 (1985).
[2] M. Kardar, Nucl. Phys. B **290**, 582 (1987).
[3] D. S. Fisher and D. A. Huse, Phys. Rev. B **43**, 10 728 (1991).
[4] S. F. Edwards and P. W. Anderson, J. Phys. F: Met. Phys. **5**, 965 (1975).
[5] *Handbook of Mathematical Functions with Formulas, Graphs, and Mathematical Tables*, edited by M. Abramowitz and I. A. Stegun, 9th ed. (Dover, New York, 1972), p. 928.
[6] B. Derrida, Phys. Rev. B **24**, 2613 (1981).
[7] E. Medina and M. Kardar, Phys. Rev. B **46**, 9984 (1992).
[8] R. Friedberg and Yi-Kuo Yu, Phys. Rev. E **49**, 4157 (1994).
[9] D. A. Huse, C. L. Henley, and D. S. Fisher, Phys. Rev. Lett. **55**, 2924 (1985).
[10] J. M. Burgers, *The Nonlinear Diffusion Equation* (Reidel, Boston, 1974).
[11] D. Forster, D. R. Nelson, and M. J. Stephen, Phys. Rev. A **16**, 732 (1977).
[12] M. Kardar, G. Parisi, and Y.-C. Zhang, Phys. Rev. Lett. **56**, 889 (1986).
[13] T. Halpin-Healy and Y.-C. Zhang, Phys. Rep. **254**, 215 (1995).
[14] P. DeLosRios and Y.-C. Zhang, Phys. Rev. Lett. **81**, 1023 (1998).
[15] T. Hwa and M. Lässig, Phys. Rev. Lett. **76**, 2591 (1996).
[16] R. Olsen, R. Bundschuh, and T. Hwa, in *Proceedings of the Seventh International Conference on Intelligent Systems for Molecular Biology*, edited by T. Lengauer *et al.* (AAAI Press, Menlo Park, CA, 1999), pp. 211–222.
[17] M. Q. Zhang and T. G. Marr, J. Theor. Biol. **174**, 119 (1995).
[18] R. Durbin, S. Eddy, A. Krogh, and G. Mitchison, *Biological Sequence Analysis* (Cambridge University Press, New York, 1998).
[19] M. S. Waterman, *Introduction to Computational Biology* (Chapman & Hall, London, UK, 1994).
[20] D. F. Feng and R. F. Doolittle, Methods Enzymol. **266**, 368 (1996).
[21] Yi-Kuo Yu and T. Hwa, J. Comput. Biol. **8**, 249 (2001).
[22] Yi-Kuo Yu, R. Bundschuh, and T. Hwa, Bioinformatics **18**, 864 (2002).
[23] Yi-Kuo Yu, R. Bundschuh, and T. Hwa, in *Biological Evolution and Statistical Physics*, edited by M. Lässig and A. Valeriani (Springer-Verlag, Berlin, 2002), pp. 3–22.
[24] M. Kschischo, M. Lässig, and Yi-Kuo Yu, Bulle. of Mathe. Biol. (to be published).
[25] M. O. Dayhoff, R. M. Schwartz, and B. C. Orcutt, in *Atlas of Protein Sequence and Structure*, edited by M. O. Dayhoff and R. V. Eck (National Biomedical Research Foundation, Washington, DC, 1978), Vol. 5, Suppl. 3, pp. 345–358.
[26] S. Henikoff and J. G. Henikoff, Proc. Natl. Acad. Sci. U.S.A. **89**, 10 915 (1992).
[27] W. R. Pearson, Proc. Natl. Acad. Sci. U.S.A. **85**, 2444 (1988).
[28] S. F. Altschul, W. Gish, W. Miller, E. W. Myers, and D. J. Lipman, J. Mol. Biol. **215**, 403 (1990); S. F. Altschul, T. L. Madden, A. A. Schäffer, J. Zhang, Z. Zhang, W. Miller, and D. J. Lipman, Nucleic Acids Res. **25**, 3389 (1997).
[29] S. B. Needleman and C. D. Wunsch, J. Mol. Biol. **48**, 443 (1970).
[30] T. F. Smith and M. S Waterman, J. Mol. Biol. **147**, 195 (1981)
[31] R. Arratia, P. Morris, and M. S. Waterman, J. Appl. Probab. **25**, 106 (1988).
[32] S. Karlin and S. F. Altschul, Proc. Natl. Acad. Sci. U.S.A. **90**, 5873 (1993).
[33] S. Karlin and S. F. Altschul, Proc. Natl. Acad. Sci. U.S.A. **90**, 5873 (1993).
[34] S. Karin and A. Dembo, Adv. Appl. Probab. **24**, 113 (1992).
[35] E. J. Gumbel, *Statistics of Extremes* (Columbia University Press, New York, 1958).
[36] M. S. Waterman, L. Gordon, and R. Arratia, Proc. Natl. Acad. Sci. U.S.A. **84**, 1239 (1987).
[37] R. Arratia and M. S. Waterman, Ann. Appl. Probab. **4**, 200 (1994).
[38] R. Bundschuh and T. Hwa, in *Proceedings of the Third Annual International Conference on Computational Molecular Biology*, edited by S. Istrail, P. Pevzner, and M. Waterman (ACM Press, 1999), pp. 70–76.
[39] T. Hwa and M. Lassig, in *Proceedings of the 2nd Annual International Conference on Computational Molecular Biology*, edited by S. Istrail, P. Pevzner, and M. Waterman (ACM Press, 1998), pp. 109–116.
[40] D. Drasdo, T. Hwa, and M. Lassig, in *Proceedings of the 6th Annual International Conference on Intelligent Systems for Molecular Biology*, edited by J. I. Glasgow *et al.* (AAAI Press, Menlo Park, CA, 1998), pp. 52–58.
[41] T. F. Smith, M. S. Waterman, and C. Burks, Nucleic Acids Res. **13**, 645 (1985).
[42] J. F. Collins, A. F. W. Coulson, and A. Lyall, CABIOS, Comput. Appl. Biosci. **4**, 67 (1988).
[43] R. Mott, Bull. Math. Biol. **54**, 59 (1992).
[44] M. S. Waterman and M. Vingron, Stat. Sci. **9**, 367 (1994).
[45] M. S. Waterman and M. Vingron, Proc. Natl. Acad. Sci. U.S.A. **91**, 4625 (1994).
[46] S. F. Altschul and W. Gish, Methods Enzymol. **266**, 460 (1996).
[47] V. Chvátal and D. Sankoff, J. Appl. Probab. **12**, 306 (1975).
[48] R. Bundschuh, Phys. Rev. E **65**, 031911 (2002).
[49] R. Mott and R. Tribe, J. Comput. Biol. **6**, 91 (1999).
[50] D. Siegmund and B. Yakir, Ann. Stat. **28**, 657 (2000).
[51] J. L. Thorne, H. Kishino, and J. Felsenstein, J. Mol. Evol. **33**, 114 (1991).
[52] J. F. Thorne, H. Kishino, and J. Felsenstein, J. Mol. Evol. **34**, 3 (1992).
[53] M. Kschischo and M. Lassig, Pac. Symp. Biocomput **5**, 621 (2000).
[54] I. Holmes and R. Durbin, Recomb DNA Tech. Bull. **98**, 102 (1998).
[55] R. Hughey and A. Krogh, CABIOS, Comput. Appl. Biosci. **12**, 95 (1996).
[56] P. Bucher, K. Karplus, N. Moeri, and K. Hoffman, Comput. Chem. (Oxford) **20**, 3 (1996).
[57] C. Barret, R. Hughey, and K. Karplus, CABIOS, Comput. Appl. Biosci. **13**, 191 (1997).
[58] Yi-Kuo Yu, in *Statistical Physics on the Eve of the 21st Century*, edited by M. T. Batchelor and L. T. Wille (World Scientific, Singapore, 1999), pp. 207–218.
[59] M. Lewandowska, H. Mathur, and Yi-Kuo Yu, Phys. Rev. E **64**, 026107 (2001).
[60] C. H. Liu, S. R. Nagel, D. A. Schecter, S. N. Coppersmith, S. Majumdar, O. Narayan, and T. A. Witten, Science **269**, 513 (1995).