

Dual Descriptor Method for Biological Sequence Analysis: A Revisit

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1. Introduction

Dual Descriptor Method was originally proposed in the master's thesis of Bin-Guang Ma (Ma, 2003) and partially described in two articles (Ma, 2007; Ma, 2008). In this article, we revisit and refine its formulation and apply this methodology to more sequence processing problems.

2. Methodology

2.1. Definition of Dual Descriptor

As elaborated in Ma (2008), for a character set $C = \{c_1, c_2, \dots, c_i, \dots, c_n\}$ ($n \geq 2$), we use C^* to represent the set of the sequences composed of the characters in C and with finite lengths. On C^* , Dual Descriptor (DD) is defined as a two-element set:

$$DD = \{M, P\} \quad (1)$$

where M is the Composition Weight Map (CWM) and P is the Position Weight Function (PWF) which are used jointly to reflect the two aspects of information of a character sequence: composition and permutation.

M is a map from the character set C to a real number set X , i.e., $M: C \rightarrow X$, $X = \{x_1, x_2, \dots, x_i, \dots, x_n \mid (x_i \in \mathbb{R} - \{0\})\}$. P is a real-valued function of position k in the character sequence s ; $P(k)$ reflects the endowed weight to the position k .

2.1.1. Pattern Description Function

For a sequence s composed of the characters in C with length L , under the map $M: C \rightarrow X$, it can be converted into a real number sequence x , namely:

$$\begin{aligned}
s &= [s[1], s[2], \dots, s[k], \dots, s[L]] \\
&\Downarrow \\
x &= [x[1], x[2], \dots, x[k], \dots, x[L]]
\end{aligned} \tag{2}$$

where $x[k] = x_i$ if $s[k] = c_i$ ($k = 1, 2, \dots, L$; $x_i \in X, c_i \in C$).

For the character sequence s , its pattern description function is defined as:

$$N(k) = P(k) \times x[k] \quad (k = 1, 2, \dots, L) \tag{3}$$

where the coefficient $P(k)$ before $x[k]$ is the position weight function.

2.1.2. Dual Formula

The sum of the first l items of $N(k)$ is

$$S(l) = \sum_{k=1}^l N(k) = \sum_{k=1}^l P(k)x[k] = \sum_{x_i \in X} x_i \sum_{k_{x_i}} P(k_{x_i}) \tag{4}$$

where k_{x_i} represents the position k where x_i appears. $S(l)$ indicates some kind of dual relation and thus is called Dual Formula or Dual Variable. Let $P_{x_i} = \sum_{k_{x_i}} P(k_{x_i})$; P_{x_i} ($x_i \in X$) is the position-weighted frequencies when it is normalized by the sequence length L , which constitutes the “permutation part” of dual variable. x_i ($x_i \in X$) are called Composition Weight Factors (CWF), which constitute the “composition part” of dual variable. These two parts are interdependent on each other and jointly reflect the information of a character sequence.

2.1.3. Target Pattern and Standard Pattern

When $P(k) = \text{constant}$ and $x[k] = \text{constant}$, the pattern description function is also a constant: $N(k) = P(k)x[k] = \text{constant} = t$ ($k = 1, 2, \dots, L$), and t is called Target Pattern. When $t = 1$, namely, $N(k) = 1$ ($k = 1, 2, \dots, L$), it is called Standard Pattern.

2.2. Training DD to describe patterns of character sequence

Dual Descriptor can be trained on datasets. The training process of DD is the process of feature extraction from character sequence, which is implemented by minimizing the pattern deviation of a character sequence from a target pattern.

2.2.1. Pattern Deviation Function

To describe the pattern deviation of a sequence, we defined the Pattern Deviation Function (PDF) as:

$$d = \frac{1}{L} \sum_{k=1}^L (N(k) - t)^2 \quad (5)$$

which represents the deviation of a sequence (whose pattern is described by $N(k)$) from a target pattern t . when $t=1$, d represents the deviation of the sequence from the standard pattern: $N(k)=1 \quad (k=1, 2, \dots, L)$.

2.2.2. Minimization of Pattern Deviation Function

The training of a DD is to minimize d . Substitute Eq. (3) into Eq. (5), we get

$$d = \frac{1}{L} \sum_{k=1}^L (P(k)x[k] - t)^2. \quad (6)$$

$P(k)$ can be expanded on a set of basis functions $b_h(k) \quad (h=1, 2, \dots, o)$, i.e.,

$$P(k) = \sum_h a_h b_h(k) \quad (h=1, 2, \dots, o) \quad (7)$$

in which a_h is independent of k and $b_h(k) \quad (h=1, 2, \dots, o)$ is the o items of the basis functions. The coefficients (a_h) in the expanded form of the position weight function $P(k)$ are abbreviated as PWC (Position Weight Coefficients).

One-step training from C: For a given CWM, $x_i \quad (x_i \in X_0)$ are constants. To minimize d , from $\frac{\partial d}{\partial a_h} = 0$, we get

$$\begin{aligned}
u_{hg} &= \sum_{k=1}^L b_h(k) b_g(k) x[k]^2 \\
v_h &= t \sum_{k=1}^L b_h(k) x[k]
\end{aligned}
\quad (h, g = 1, 2, \dots, o) \tag{8}$$

where $b_h(k)$ and $b_g(k)$ are the h -th and g -th basis functions, respectively, and $x[k] \in X_0$ is the number at the k -th position in the real number sequence x . The coefficients of $P(k)$ can be written as a vector \mathbf{a} which can be obtained from the matrix \mathbf{u} and the vector \mathbf{v} :

$$\mathbf{a} = \mathbf{u}^{-1} \mathbf{v} \tag{9}$$

where $\mathbf{a} = (a_1, a_2, \dots, a_h, \dots, a_o)$ and the matrix \mathbf{u} and the vector \mathbf{v} are composed of the elements u_{hg} and v_h .

One-step training from P: For a given PWF ($P_0(k)$), $a_h(k)$ ($h=1, 2, \dots, o$)

are constants. To minimize d , from $\frac{\partial d}{\partial x_i} = 0$, we arrive at:

$$x_i = \frac{t \sum_{k_{x_i}} P_0(k_{x_i})}{\sum_{k_{x_i}} P_0^2(k_{x_i})} \tag{10}$$

where k_{x_i} represents the position k in the real number sequence x where x_i appears.

2.2.3. Extracting common features of multiple sequences

For the situation of multiple sequences, to extract the common features of these sequences, the PDF for the ensemble of these sequences is defined as the mean value of the PDF values of these sequences:

$$D = \frac{1}{N} \sum_{j=1}^N d_j \tag{11}$$

where N is the number of the sequences, and $d_j = \frac{1}{L_j} \sum_{k=1}^{L_j} (N_j(k) - t)^2$ is the PDF

value for the j -th sequence with the length L_j , and $N_j(k)$ is the pattern description function of the j -th sequence.

One-step training from C: For a given CWM, from $\frac{\partial D}{\partial a_h} = \sum_{j=1}^N \frac{\partial d_j}{\partial a_h} = 0$, we arrive

at:

$$\begin{aligned} U_{hg} &= \sum_{j=1}^N u_{hg}^j \\ V_h &= \sum_{j=1}^N v_h^j \end{aligned} \quad (h, g = 1, 2, \dots, o). \quad (12)$$

At this time, the coefficient vector \mathbf{a} is given by

$$\mathbf{a} = \mathbf{U}^{-1} \mathbf{V} \quad (13)$$

where the matrix \mathbf{U} and the vector \mathbf{V} are the sums of \mathbf{u} and \mathbf{v} (that are for single sequence), respectively.

One-step training from P: Similarly, for a given PWF, from $\frac{\partial D}{\partial x_i} = \sum_{j=1}^N \frac{\partial d_j}{\partial x_i} = 0$,

we arrive at:

$$x_i = \frac{t \sum_j \sum_{k_{x_i}} P_0(k_{x_i})}{\sum_j \sum_{k_{x_i}} P_0^2(k_{x_i})}. \quad (14)$$

2.2.4. Alternate training process

The alternate training process for a DD on a sequence (or a set of sequences) consists of the following steps:

Step (1): Preparing a dataset composed of one or multiple sequences; set the maximum step number T_{\max} .

Step (2): Randomly construct a CWM, i.e, assign a random real number to each of the characters in C and these real numbers constitute the set of x_i ($x_i \in X$), and

then use the minimization condition in Eq. (9) or Eq. (13) to obtain a corresponding PWF, namely, a set of coefficients $a_h(k)$ ($h=1, 2, \dots, o$).

Step (3): With the set of coefficients $a_h(k)$ ($h=1, 2, \dots, o$), use the minimization condition in Eq. (10) or Eq. (14) to obtain a CWM, namely, a set of x_i ($x_i \in X$); Generally speaking, the set of x_i ($x_i \in X$) obtained in this step is not the same as those used in Step (1).

Step (4): Repeat Step (2) and Step (3) until the stop condition is satisfied.

Stop condition: the minimum d (or D) is achieved, or the maximum step number T_{\max} is reached.

In the training process, d (or D) becomes smaller and smaller. When d (or D) reaches its minimum value, the training process stops and an optimum DD is obtained on the dataset of the sequences used. Dual descriptor method can be viewed as a kind of machine-learning approach. Different from other machine-learning approaches where local minimums are ubiquitous and cannot be tackled readily, the DD method does not yield local minimum in principle because the PDF (Eq. (5)) is a quadric function and has only a unique global minimum. An object-oriented implementation of Dual Descriptor (the DD class written in Python language), which wraps the training algorithm, is freely available at GitHub ([Link here](#)).

2.2.5. Choice of the basis functions

Basis functions in Eq. (7) are usually chosen as periodic functions, such as trigonometric function

$$P(k) = \sum_h a_h \cos\left(\frac{2\pi k}{h}\right) \quad (h=1 \text{ or } 2, 3, \dots, o) \quad (20)$$

or

$$P(k) = e^{k \bmod h} \quad (h = 1 \text{ or } 2, 3, \dots, o) \quad (21)$$

because periodicity is a main difference between an ordered and a random sequence. Note that h starts from 1 (usually for one-step training) or 2 (usually for alternate training). Except for trigonometric functions, basis functions can also be other types of functions like wavelet functions, radial basis function, sigmoid functions, *etc.*, depending on question contexts.

2.2.6. Gradient-based training process

In addition to the alternate training process where DD is trained by solving closed-form equation systems, DD can also be trained by commonly used gradient descent method, particularly for large systems (big n and o) or the vectorized form of DD (see below).

2.3. The vector form of DD

2.3.1. Encoding vectors and position weight function matrix

As described in Ma (2003), The CWM $M : C \rightarrow X$ can be generalized into $M : C \rightarrow \mathbf{X}$, where $\mathbf{X} = \{\mathbf{x}_1, \mathbf{x}_2, \dots, \mathbf{x}_i, \dots, \mathbf{x}_n \mid \mathbf{x}_i \in R^m\}$ is a set of m -dimensional real vectors. The vectors in the vector set \mathbf{X} are column vectors, referred to as "encoding vectors". Arranging these n column vectors of dimension m from the vector set \mathbf{X} together forms a matrix $M_{m \times n}$, referred to as the "encoding matrix", i.e.,

$$M_{m \times n} = \begin{bmatrix} x_{11} & x_{12} & \cdots & x_{1i} & \cdots & x_{1n} \\ x_{21} & x_{22} & \cdots & x_{2i} & \cdots & x_{2n} \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ x_{j1} & x_{j2} & \cdots & x_{ji} & \cdots & x_{jn} \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ x_{m1} & x_{m2} & \cdots & x_{mi} & \cdots & x_{mn} \end{bmatrix} \quad (x_{ji} \in R - \{0\}; i = 1, 2, \dots, n, j = 1, 2, \dots, m).$$

Each column in this matrix corresponds to one character in the character set C , and each row corresponds to one component of the vectors. To reduce information redundancy, the components should be mutually independent, meaning the row vectors of the "encoding matrix" should be linearly independent from each other; ideally, they should be mutually orthogonal. However, this principle is not an absolute requirement.

Under the map $M : C \rightarrow \mathbf{X}$, a character sequence of length L is transformed into a sequence of m -dimensional real vectors:

$$\begin{aligned} s &= [s[1], s[2], \dots, s[k], \dots, s[L]] \quad (s[k] \in C, k = 1, 2, \dots, L) \\ &\Downarrow \\ \mathbf{x} &= [\mathbf{x}[1], \mathbf{x}[2], \dots, \mathbf{x}[k], \dots, \mathbf{x}[L]], \quad (\mathbf{x}[k] \in \mathbf{X}) \end{aligned}$$

The position-weighted sum its first l terms, i.e., the dual formula, is as follows:

$$\mathbf{s}(l) = \sum_{k=1}^l \mathbf{P}(k) \mathbf{x}[k] \quad (l = 1, 2, \dots, L) \quad (22)$$

in which

$$\mathbf{P}(k) = \begin{bmatrix} P_{11}(k) & P_{12}(k) & \cdots & P_{1q}(k) & \cdots & P_{1m}(k) \\ P_{21}(k) & P_{22}(k) & \cdots & P_{2q}(k) & \cdots & P_{2m}(k) \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ P_{p1}(k) & P_{p2}(k) & \cdots & P_{pq}(k) & \cdots & P_{pm}(k) \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ P_{m1}(k) & P_{m2}(k) & \cdots & P_{mq}(k) & \cdots & P_{mm}(k) \end{bmatrix}_{m \times m} \quad (23)$$

is the Position Weight Function Matrix (PWFM, an m square matrix), where each element $P_{pq}(k)$ is a positional weight function. $\mathbf{x}[k]$ is the k -th vector (of dimension m) in the vector sequence \mathbf{x} , corresponding to the k -th character in the character sequence s :

$$\mathbf{x}[k] = \mathbf{x}_i \quad \text{if } (s[k] = c_i) \quad (k = 1, 2, \dots, L; \mathbf{x}_i \in \mathbf{X}, c_i \in C).$$

From Eq. (22), when l varies from 1 to L , a sequence \mathbf{s} of dual variables $\mathbf{s}(l)$ is obtained. This is also a vector sequence, namely, $\mathbf{s} = [\mathbf{s}[1], \mathbf{s}[2], \dots, \mathbf{s}[l], \dots, \mathbf{s}[L]]$. This sequence is the position-weighted sum sequence of the first l terms of the encoding vector sequence \mathbf{x} .

2.3.2. The vector form of PDF

In the vector form of DD, the PDF is defined as:

$$d = \frac{1}{L} \sum_{k=1}^L \|\mathbf{N}(k) - \mathbf{t}\|^2 = \frac{1}{L} \sum_{k=1}^L \|\mathbf{P}(k)\mathbf{x}[k] - \mathbf{t}\|^2 \quad (24)$$

where $\mathbf{P}_{m \times m}(k)$ is the position weight function matrix Eq. (23) mentioned earlier, in which each element $P_{pq}(k)$ is a position weight function, and can be expanded into a sum of o terms using the basis $b(k)$ as follows:

$$P_{pq}(k) = \sum_{h=1}^o a_h^{pq} b_h^{pq}(k) \quad (25)$$

and $\mathbf{x}[k]$ is the k -th vector (of dimension m) in the vector sequence \mathbf{x} ; \mathbf{t} is the target vector, an m -dimensional constant vector.

2.3.3. Alternate Training of vector DD

If the position weight function matrix $\mathbf{P}_{m \times m}(k)$ is known, from $\frac{\partial d}{\partial \mathbf{x}_i} = 0$ we

obtain

$$\mathbf{x}_i = \mathbf{w}^{-1} \mathbf{y} \quad (26)$$

where the elements of matrix \mathbf{w} and vector \mathbf{y} are

$$\begin{aligned} w_{pq} &= \sum_{k_{x_i}} \sum_{f=1}^m P_{fp}(k_{x_i}) P_{fq}(k_{x_i}) \\ y_p &= \sum_{k_{x_i}} \sum_{f=1}^m t_f P_{fp}(k_{x_i}) \end{aligned} \quad (f, p, q = 1, 2, \dots, m). \quad (27)$$

If $M : C \rightarrow \mathbf{X}$ is known, from $\frac{\partial d}{\partial \mathbf{a}_f} = 0$ we obtain

$$\mathbf{a}_f = \mathbf{u}_f^{-1} \mathbf{v}_f \quad (28)$$

where \mathbf{a}_f represents the total coefficient row vector for the expansion of all elements in the f -th row of the position weight function matrix. This row vector contains $m \times o$ components. These components are grouped every o elements, belonging respectively to the m elements of the f -th row. The elements of matrix \mathbf{u}_f and vector \mathbf{v}_f are given by:

$$\begin{aligned} u_{pq}^f &= \sum_{k=1}^L b_{hg}^f(k) b_{h'g'}^f(k) x[k]_s x[k]_t \\ v_p^f &= t_f \sum_{k=1}^L b_{hg}^f(k) x[k]_s \end{aligned} \quad (f, p, q = 1, 2, \dots, m) \quad (29)$$

where

$$\begin{aligned} h &= \left\lceil \frac{p}{o} \right\rceil & g &= \delta(p \bmod o) \cdot o + p \bmod o \\ h' &= \left\lceil \frac{q}{o} \right\rceil & g' &= \delta(q \bmod o) \cdot o + q \bmod o . \\ s &= \left\lceil \frac{p}{o} \right\rceil & t &= \left\lceil \frac{q}{o} \right\rceil \end{aligned} \quad (30)$$

Here, $\lceil \bullet \rceil$ denotes taking the smallest integer not less than " \bullet ", and

$$\delta(\bullet) = \begin{cases} 1 & \text{if } \bullet = 0 \\ 0 & \text{if } \bullet \neq 0 \end{cases}.$$

In the case of multiple sequences, let the number of sequences be N , and

$D = \frac{1}{N} \sum_{j=1}^N d_j$, then we have

$$\begin{aligned} \mathbf{W} &= \sum_{j=1}^N \mathbf{w}_j & \mathbf{Y} &= \sum_{j=1}^N \mathbf{y}_j \\ \mathbf{U}^f &= \sum_{j=1}^N \mathbf{u}_j^f & \mathbf{V}^f &= \sum_{j=1}^N \mathbf{v}_j^f \end{aligned} \tag{31}$$

All the matrices above are symmetric matrices. Formally, if all components are mutually independent, the position weight function matrix simplifies to a diagonal matrix of $m \times m$.

2.3.4. Implementations of vector DD

There can be several different implementation forms for vector DD depending on how to deal with PWFM. These implementation forms are special cases of the vector DD.

Form 1: Tensor form: In this form, PWFM is implemented as a 3D tensor $\mathbf{P} \in R^{m \times m \times o}$ and each element in the tensor is a coefficient of a basis function $b(k)$. \mathbf{P} is randomly initialized. There are totally $n \times m + m \times m \times o = m(n + m \times o)$ trainable parameters in this form of vector DD, where n is the size of character set C , m is the dimension of encoding vector, and o is the number of bases in each expanded position weight function (totally $m \times m$ PWFs).

Form 2: P matrix form: In this form, PWFM is implemented as a 2D matrix $\mathbf{P} \in R^{m \times m}$ and each element in the matrix is a coefficient of a basis function $b(k)$. \mathbf{P} is randomly initialized and trainable. In this case, there are totally $n \times m + m \times m = m(n + m)$ trainable parameters, where n and m have the same meaning as in **Form 1**. Indeed, \mathbf{P} matrix form is the 2D tensor form.

Form 3: AB matrix form: In this form, PWFm is implemented as a product of two matrixes $\mathbf{A} \in R^{m \times L}$ and $\mathbf{B} \in R^{L \times m}$, where \mathbf{A} is the coefficient matrix and \mathbf{B} is the basis weight matrix and L is the length of the character sequence to be described. For multiple sequences, L can be set as the maximum sequence length. \mathbf{A} is randomly initialized. \mathbf{B} is initialized by computing basis function weights. For example, the elements in \mathbf{B} can be calculated as $B[k, i] = b_i(k) = \cos(2\pi \cdot k / i)$ where k is row index ($k = 1, \dots, L$) and i is the column index ($i = 1, \dots, m$). In this case, there are totally $m(n + L)$ parameters, where n and m have the same meaning as in **Form 1** and L is the maximum sequence length. Indeed, L is adjustable and can be regarded as a hidden dimension for controlling parameter numbers.

Form 4: Random AB matrix form: In this form, PWFm is implemented as a product of two matrixes $\mathbf{A} \in R^{m \times L}$ and $\mathbf{B} \in R^{L \times m}$, and both \mathbf{A} and \mathbf{B} are randomly initialized and trainable. In this case, there are totally $m(n + 2L)$ parameters where n, m, L have the same meaning as in **Form 3**.

2.4. Rank definition of DD

Now consider the set formed by double-letter permutations from the character set C , that is, the second direct power of C : $C \times C = C^2$, where " \times " represents the Cartesian product of sets. Since C has n elements (characters), C^2 has n^2 elements, all of which are (concatenated) strings of length 2, so $C^2 \subset C^*$. These n^2 elements can be regarded as n^2 new characters. The DD of rank-2 refers to the DD formed by the composition weight factors corresponding to the elements in C^2 and the introduced corresponding position weight functions. Generally, for the set formed by r -letter

permutations (r -pers) from the character set C , that is, the r -th direct power of C :

$\times_{i=1}^r C_i = C^n$, the DD of rank- r can be defined. The pattern description function and

pattern deviation function of high-rank DD can be defined in the same way as for the

DD of rank-1 (corresponding to letters in character set C). The keys in the CWM of

high-rank DDs are called r -pers (permutations of length r), semantically identical to

k -mers that are widely acknowledged in the context of biological sequence analysis.

High-rank DDs consider the local associations within the character sequence,

increasing the number of CWFs.

2.5. Description modes of high-rank DD

When describing a character sequence using high-rank DD, there are two description methods depending on how the subsequences are extracted: "linear" description and "nonlinear" description.

Linear description mode: Linear description uses a technique called the "sliding window". Moving from left to right, it slides one character each time. Thus, linear description has the highest information redundancy.

Nonlinear description mode: Using a tiling (or covering) approach, characters already used are not reused. Thus, it takes every r (rank) characters each time in the description. The nonlinear description does not reuse characters from the original sequence; thus, the description is non-redundant.

Customized description mode: In addition to the above two extreme modes, there can be something in between, which are called user customized description mode. In this mode, the moving step is between 1 and rank, i.e., $1 < \text{step_size} < \text{rank}$.

2.6. Combined use of multiple DDs

Multiple DDs refer to a group of DDs used jointly to describe sequence characteristics. These descriptors can be of the same rank or different ranks. Each descriptor describes a part of the sequence's characteristics; together they provide a relatively complete description of the sequence.

2.7. Numeric DD

To directly deal with real number or vector sequences, the composition part (map M) of DD can be generalized into a matrix $\mathbf{M}^{m \times m}$, and the mapping operation from a character to an m -dimensional vector can be generalized as a transformation of the input m -dimensional vector via left-multiplying the vector by \mathbf{M} . The permutation part P of DD remains the same as in the vector form of DD. Correspondingly, there are four implementation forms of numeric DD (nDD).

2.8 Hierarchical DD

As mentioned in Ma (2003), DD can be used recursively to give a hierarchical description of character sequence. Based on numeric DD, hierarchical DD (hDD) can be defined. hDD recursively use numeric DD to transform the input vector sequence into different dimension and/or length (by using Linker matrix). In hDD, each layer is a numeric vector DD. To support deeper layers, tricks from modern deep-learning methods such as pre-layer normalization and residual connection can be adopted.

2.9 DD network

DD network (DDN) is defined as a combination of DD (especially hDD) with other machine learning modules such as multilayer perceptron (MLP), convolutional

neural network (CNN), recurrent neural network (RNN), transformers and so on.

DDN enhances modeling ability by combining the capabilities of these modules.

3. Applying DD to sequence problems

3.1 using DD for feature extraction

3.2 using DD for identification

3.3 using DD for classification

3.4 using DD for regression

3.5 using DD for generation

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