Improved nearest neighbor interpolators based on confidence region in medical image registration

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ABSTRACT

In order to reduce artifacts in match metric and improve the registration speed in medical image registration, three types of improved nearest neighbor (NN) interpolators based on confidence region (CR) are studied. These improved NN interpolators include: (1) NN based on deterministic confidence region (DCR), DCRNN; (2) NN based on stochastic confidence region (SCR), SCRNN; (3) NN based on confidence region integrating deterministic information and stochastic information (DSCR), DSCRNN. The values of normalized mutual information (NMI) are deterministic and accurate at any grid translation position when any improved NN interpolator is used. The smoothness of the NMI curves is compared by applying DCRNN, SCRNN, and DSCRNN interpolators to rigid medical image registration with different numbers of intensity bins and random variables. The results of tests show that the new DSCRNN interpolator outperforms DCRNN and SCRNN in curve smoothness and anti-micro-fluctuation, and outperforms the conditional NN, PVI and LI interpolators in convergence performance and noise immunity.

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1. Introduction

A major inaccuracy in medical image registration stems from interpolation artifacts when automatic intensity-based registration methods are used [1,2]. The common similarity metrics of image registration are squared differences (SSD) [3,4], mutual information (MI) [5–7], and normalized mutual information (NMI) [8]. Recently some improved similarity metrics are used such as conditional mutual information [12], residual complexity [14], Tsallis entropy [15] and Havrda–Charvát–Tsallis entropy [16]. The simplest and most commonly used interpolators are nearest neighbor (NN), linear (LI) and partial volume interpolation (PVI). They have faster computational speed, but also cause more interpolation artifacts. In order to reduce the artifacts in the mutual information similarity metric, Puium et al. [9] proposed a re-sampled scheme to diminish the impact of artifacts; Tsao [1] observed that the artifacts were reduced substantially when the periodicities of the pixel grids were abolished with strategies such as jittered sampling, or when histogram blurring techniques were used; or when one image was rotated or re-sampled relative to the other image; Hua-mei Chen and Varshney [10] extended PVI to generalized partial volume estimation (GPVE), which employed higher order B-spline kernels during the estimation of the joint histogram and this scheme reduced the abrupt change of the joint histogram dispersion caused by the PVI method; Thévenaz et al. [11] solved both grid effect and overlap issues by estimating the joint histogram by quasi-random sampling; Rohde et al. [2] clearly demonstrated interpolation artifacts in terms of the energy of the interpolated signal, and combined ‘low pass filtering the data prior to computations’, ‘higher degree and sinc interpolation’ and ‘stochastic sampling’ approaches to mitigate oscillations.

The aforementioned interpolation methods in medical image registration can be classified into three types. The first type is to use low pass filter to blur the registering images before registration or to filter the joint histogram in the process of registration. The second group uses interpolators of longer supporting kernel, e.g., high degree B-spline interpolator, windowed sinc function and high order GPVE. The third type employs random sampling method including random re-sampling, Halton sampling and jittered sampling.

The common shortcoming of the former two types of interpolators is that the joint information between registering images is reduced because some high frequency information is filtered out at non-grid positions. When the second interpolation method is involved in aligning images, the computational complexity will be increased as more supporting pixels are required for interpolation. The shortcoming of using the third type is that the uncertainty of random sampling will produce micro-fluctuation in measure’s curve. Therefore a reasonable direction for developing a better interpolation scheme is to take into consideration of
2. Theories

2.1. Confidence region

In the real world, the gray value often varies abruptly at the edge of one object or between the boundaries of two different objects, but it is often nearly constant or slowly changed inside the object. The registering images to be processed by computers are discretely sampled versions, so the gray values at the non-grid positions need to be estimated by the gray values at the neighboring grid positions. When the interpolators based on finite supporting interval are used, some high frequency information is inevitably lost, and the estimation of gray values near the edge of the object is inaccurate. To solve this problem, we introduce the definition of confidence region (CR). The CR of one pixel is defined as the largest possible area around that pixel where the gray value is unchanged. The distances between the edge of CR and the corresponding pixel are smaller than one pixel.

There are a number of factors that determine the CR. Firstly, the intensity probability density function (pdf) can be estimated by histogram or Parzen window techniques [6]. The pdf value of each intensity bin in one image is constant, so the ratio between the area of the same intensity pixels and that of the total pixels is constant. According to probability theory, if the intensity pdf value of a pixel is large, the probability of having the same intensity around that pixel is large, and then the CR of that pixel is large. Some mathematical formulas about CR are introduced in the following section.

Let $M \times N$ denote the size of image $A$, and $(m, n)$ be the coordinate of a pixel inside the image where $1 \leq m \leq M, 1 \leq n \leq N$. Firstly, the pdf of $A$ is calculated, which is denoted as $p(x) = [p(x_1) p(x_2) \cdots p(x_N)]$ where $x_i$ is the intensity value in $A$. Secondly, the pdf is sorted in descending order. Thirdly, the nonzero parts of the sorted pdf are divided into $U$ categories by Eq. (1), and they are denoted as $[q(0), q(1), \ldots q(y)]$ where $q(0)$ equals the largest value in $p(x)$, and $q(y)$ equals the smallest non-zero value in $p(x)$. And lastly each grid $(m, n)$ is assigned to a new value by formula (2).

\[
f(A(m, n)) = 1 + \left[\frac{y}{U} (U - 1) + 0.5\right]
\]

\[
g(m, n) = \frac{U + 1 - f(A(m, n))}{U}
\]

The resulting image $A_1$ is obtained when Eqs. (1) and (2) are cycling-calculated for all pixels in image $A$, and the value at grid $(m, n)$ in $A_1$ is assigned according to formula (2).

Image $A_2$ is the result of element-by-element multiplication between $A_1$ and random image $r$.

\[
A_2 = A_1 \circ r
\]

where $r$ is a random image with the same size as $A_1$, and the values of elements in $r$ are uniformly distributed in the interval $(0, 1)$. The symbol '$\circ$' denotes element-by-element multiplication, or array multiplication, or Hadamard multiplication.

From formula (3), it can be seen that $A_2$ includes deterministic information $A_1$ and stochastic information $r$. The space among neighboring pixels is seamlessly segmented by CR of these pixels. Therefore CR at grid $(m, n)$ not only is related to $A_2(m, n)$, but also is related to its neighboring grids $A_2(m+1, n)$, $A_2(m-1, n)$, $A_2(m, n-1)$ and $A_2(m, n+1)$. The up, down, left and right CR of a pixel will be defined in the following section to show its relationship to the corresponding neighboring pixels.

From Image $A_2$ and the following formula (4), we can obtain the up CR image $A_U$, the down CR image $A_D$, the left CR image $A_L$ and the right CR image $A_R$. The sketch of $A_U(m, n), A_L(m, n), A_D(m, n)$ and $A_R(m, n)$ is shown in Fig. 1.

\[
A_{U}(m, n) = A_{U}(m, n) + A_{U}(m, n+1)
\]

\[
A_{D}(m, n) = A_{D}(m, n) + A_{D}(m, n-1)
\]

\[
A_{L}(m, n) = A_{L}(m, n) + A_{L}(m-1, n)
\]

\[
A_{R}(m, n) = A_{R}(m, n) + A_{R}(m+1, n)
\]

If one pixel in formula (4) lies outside image $A_2$, then it will be replaced by the nearest pixel, e.g., $A_{U}(0, n) = A_{U}(1, n), A_{R}(M+1, n) = A_{R}(M, n), A_{U}(m, 0) = A_{U}(m, 1), A_{R}(m, N+1) = A_{R}(m, N)$.

According to formula (4), the following formula (5) can be obtained.

\[
A_{L}(m, n-1) + A_{L}(m, n) = 1, \quad A_{D}(m, n-1) + A_{D}(m, n) = 1
\]

If any one of $A_U$ and $A_D$ is known, the other can be calculated using formula (5). Similarly, we need to calculate only one of $A_U$ and $A_D$ by formula (4), so the amount of computation of formula (4) is reduced by 50%.

Sometimes there are overlaps or gaps among the up, down, left and right CRs of the four neighboring pixels. To avoid this, these CRs need to be modified. The modifications are discussed under nine situations, which are shown in Fig. 2.

In Fig. 2, $P_1, P_2, P_3$ and $P_4$ are four neighboring pixels. According to the CRs’ sizes among adjacent pixels, the modifications are classified into nine cases corresponding to nine sub-graphs in Fig. 2. There are $A_R(P_1) < A_R(P_3)$ and $A_D(P_1) > A_D(P_3)$ in Fig. 2 (a); $A_R(P_1) < A_R(P_3)$ and $A_D(P_1) > A_D(P_3)$ in Fig. 2 (b); $A_R(P_1) > A_R(P_3)$ and $A_D(P_1) < A_D(P_3)$ in Fig. 2 (c); $A_R(P_1) > A_R(P_3)$ and $A_D(P_1) < A_D(P_3)$ in Fig. 2 (d); $A_R(P_1) < A_R(P_3)$ and $A_D(P_1) > A_D(P_3)$ in Fig. 2 (e).

\[ A_0(P_1) > A_0(P_2) \text{ and } A_0(P_1) = A_0(P_3) \text{ in Fig. 2 (f); } A_0(P_1) = A_0(P_3) \text{ and } A_0(P_1) > A_0(P_2) \text{ in Fig. 2 (g); } A_0(P_1) = A_0(P_3) \text{ and } A_0(P_1) < A_0(P_2) \text{ in Fig. 2 (h); } A_0(P_1) = A_0(P_3) \text{ and } A_0(P_1) = A_0(P_2) \text{ in Fig. 2 (i). From Eq. (5), it can be derived that the relationships among these parameters are: } A_0(P_1) + A_0(P_2) = 1, A_0(P_3) + A_0(P_4) = 1, A_0(P_1) + A_0(P_2) = 1 \text{ and } A_0(P_2) + A_0(P_4) = 1. \]

The modifications of CR follow the three rules: (1) the same color region (see Fig. 2) around pixel \( P_L \) is its CR; (2) the X region (see Fig. 2(a–d)) belongs to the biggest region among its four neighbors. For example, the areas of the four regions can be obtained by the following equations: \( S_1 = A_0(P_1) \times A_0(P_2), S_2 = (1 - A_0(P_1)) \times (1 - A_0(P_2)), S_3 = (1 - A_0(P_1)) \times (1 - A_0(P_4)) \) and \( S_4 = A_0(P_3) \times A_0(P_4). \) If \( S_1 \) is the sole maximum, then the region X belongs to the CR of \( P_L. \) If \( S_1 \) is one of the maxima, then the region X is randomly set to belong to one of the adjacent maximal regions; (3) the boundary between two CRs is randomly set to belong to one of two CRs.

After the above modifications to CR, any point in image belongs to the CR of its adjacent pixels. The DSCR of a pixel is constructed by its modified up, down, left and right CR with formula (1–4) and the above three modification rules. The stochastic information includes two parts: (1) random image \( r \) in formula (3); (2) the randomness of region X and boundaries.

If formula (3) is changed to \( A_2 = A_1, \) then \( A_2 \) only includes deterministic information. Using a processing method similar to that of DSCR, the DCR can be constructed.

If formula (3) is changed to \( A_2 = r, \) then \( A_2 \) is stochastic image which only includes stochastic information. Similar to the construction of DSCR, the SCR can be constructed.

### 2.2. Nearest neighbor interpolator based on confidence region

In this section, CR will be integrated with the conditional NN interpolator. Let \( Q_l \) be a pixel in a floating image \( F \) and its coordinate be \((m, n). \) After applying geometric transformation \( T \) to \( F, \) the point \( Q_2 \) in the reference image \( R \) corresponds to \( Q_l \) and its coordinate is \((i + \Delta i, j + \Delta j) \) (see Fig. 3). The joint histogram of \( R \) and transformed \( F \) is updated by the following formula (6) and (7).

\[
\begin{align*}
\beta^0(i + \Delta i, j + \Delta j, i + k, j + l) &= 1 & \text{if } Q_2(i + \Delta i, j + \Delta j) \in C_0(i + k, j + l) \\
&= 0 & \text{elsewhere}
\end{align*}
\]

From formula (6) and (7), when \( Q_2 \) is located in the CR of a neighboring pixel \( Q_l, \) the joint histogram \( h_T(F(Q_1), R(Q_2)) \) would increase by 1. When \( C_0(i + k, j + l) \) represents DSCR of pixel \((i + k, j + l) \) of \( R, \) formula (6) corresponds to DCRNN interpolator. If \( C_0(i, j) \) is DCR of pixel \((i, j) \) of \( R, \) formula (6) corresponds to DCRNN interpolator.

Specifically when \( C_0(i + k, j + l) \) denotes a unit square with the center located in pixel \((i + k, j + l), \) then \( \beta^0(i + \Delta i, j + \Delta j, i + k, j + l) = f_1(i + \Delta i - (i + k)) \times f_1(j + \Delta j - (j + l)) = f_1(\Delta i - k) \times f_1(\Delta j - l) \) where \( f_1(x) \) equals to 1 when \(-0.5 \leq x < 0.5\) otherwise it equals zero, and then formula (6) corresponds to the conditional NN interpolator that is zero-order GPVE [10]. The unit square region with the center located at the grid is defined as CR of the conditional NN interpolator (NNCR), which is a special case of DCRNN interpolator with \( U = 1 \) (see Theorem 3).

The following properties of the kernel function \( \beta^0(x, y, m, n) \) can be derived where \( x, y \in \mathbb{R} \) and \( m, n \in \mathbb{Z}. \)

\[
\begin{align*}
(1) \ & \beta^0(x, y, m, n) \text{ only equals } 0 \text{ or } 1. \\
(2) \ & \beta^0(x, y, m, n) = \begin{cases} 
1 & (x - m) = 0 \text{ and } (y - n) = 0 \\
0 & (x - m) \in \mathbb{Z} \text{ and } ((x - m) \neq 0 \text{ or } (y - n) \neq 0)
\end{cases} \\
(3) \ & \sum_{i, j \in \mathbb{Z}} \beta^0(i + x, j + y, m, n) = 1.
\end{align*}
\]
Property (1) guarantees that the renormalization of the joint histogram is non-negative. Property (2) assures that the joint histogram is not filtered if it is re-sampled on the grid. Property (3) means that the direct current (DC) amplification will be unity or the energy of the joint histogram remains unchanged for any displacement. Therefore regardless of outlier, we always have \( \sum h_i(F, R) = c \) where \( c \) is the total pixel numbers in the floating images.

2.3. Optimal geometric transformation and NMI

According to theories of the joint histogram, the joint probability distribution \( p_T(a, b) \) and marginal probability distribution are calculated as the following.

\[
p_T(a, b) = \frac{h_T(a, b)}{\sum_{a, b} h_T(a, b)} \tag{8}
\]

\[
p_T(a) = \sum_{b} p_T(a, b) \tag{9}
\]

\[
p_T(b) = \sum_{a} p_T(a, b) \tag{10}
\]

Substituting formula (8), (9) and (10) to the following NMI formula, formula (14) can be obtained.

\[
NMI_T(F, R) = \frac{H(F) + H(R)}{H(F, R)} \tag{11}
\]

where

\[
H(F) = - \sum_{a} p_T(a) \log p_T(a),
\]

\[
H(F, R) = - \sum_{a, b} p_T(a, b) \log p_T(a, b),
\]

Hence

\[
NMI_T(F, R) = \frac{- \sum_{a} p_T(a) \log p_T(a) - \sum_{b} p_T(b) \log p_T(b)}{- \sum_{a, b} p_T(a, b) \log p_T(a, b)}. \tag{14}
\]

Considering that NMI measure can reduce sensitivity to image overlap statistics in contrast to MI measure [8], we used NMI measure in this study.

When two images are absolutely aligned, geometric transformation \( T \) is named as the optimal geometric transformation \( T^* \), and NMI measure reaches its maximum. \( T^* \) is searched by formula (15)

\[
T^* = \arg \max_{(T)} NMI_T(F, R) \tag{15}
\]

2.4. Frequency analysis

The other forms of formula (6) and (7) are

\[
R(i + \Delta i, j + \Delta j) = \sum_{m, k} R(i + m, j + k) \beta_0(i + \Delta i, j + \Delta j, i + k, j + l) \tag{16}
\]

\[
h_T(F(m, n), R(i + \Delta i, j + \Delta j)) = h_T(F(m, n), R(i + \Delta i, j + \Delta j)) + 1. \tag{17}
\]

Eq. (16) is described as the convolution in space domain, so it is in product form in frequency domain.

When the region \( C_k(i + k, j + l) \) is rectangle, \( \beta_0(i + \Delta i, j + \Delta j, i + k, j + l) \) is the product of two separable interpolation kernels

\[
\beta_0(i + \Delta i, j + \Delta j, i + k, j + l) = \beta_0(\Delta i - k) \times \beta_0(\Delta j - l) \tag{18}
\]

where \( \beta_0(\Delta i - k) = \begin{cases} 
1 & x_1 \leq \Delta i - k < x_2 \\
0 & \text{elsewhere}
\end{cases} \) and \( \beta_0(\Delta j - l) = \begin{cases} 
1 & y_1 \leq \Delta j - l < y_2 \\
0 & \text{elsewhere}
\end{cases} \)

Let \( x_1 \) and \( x_2 \) denote the difference between the \( x \) values at the left and right edge of \( C_k(i + k, j + l) \) and the integer \( i + k \) respectively, \( y_1 \) and \( y_2 \) represent the difference between the \( y \) values at the up and down edge of \( C_k(i + k, j + l) \) and the integer \( j + l \) respectively. Obviously we have \(-\Delta k \leq x_1, y_1 < 0 \) and \(0 < x_2, y_2 < 1\). We analyze interpolation kernels by the Fourier transform (FT) only when \( x_2 = x_1 \). For scenarios when \( x_2 \neq x_1 \), the FT can be calculated with the time-shift property. When \( x_2 = x_1 = \tau \), the FT \( B(\omega) \) of \( \beta_0(\omega) \) is

\[
B(\omega) = \int_{-\infty}^{+\infty} \beta_0(\omega)e^{-j\omega x} dx = \int_{-\tau}^{+\tau} e^{-j\omega x} dx = \frac{2\sin(\omega\tau)}{\omega} \tag{19}
\]

The curves of \( B(\omega)/(2\tau) \) are shown in Fig. 4 when \( \tau = 0.1 \), \( \tau = 0.5 \) and \( \tau = 0.9 \).

From Fig. 4 it can be seen that the pass band of frequency increases as \( \tau \) decreases, which implies that the corresponding CR also decreases. By using the NN interpolator based on CR, the spectrum of pixels with high pdf (e.g. background) contains a smaller portion of high-frequency components in comparison with the spectrum with low pdf. Therefore the CR of pixels with high pdf will be larger than the CR of those with low pdf.

2.5. Relationships among DSCR, DCR and SCR

The following three theorems describe the relationships among DSCR, DCR and SCR, and then the relationships among DSCRRN, DCRNN and SCRNN.

Theorem 1. Let \( X_1, X_2, \ldots, X_n \) be an infinite sequence of i.i.d. (independent and identically distributed) integrable random variables
who are uniformly distributed in the interval \((0, 1)\), and \(Y_n = (1/n) \sum_{k=1}^{n} X_k\), then for any \(\varepsilon > 0\),
\[
\lim_{n \to \infty} \left\{ Y_n - \frac{1}{2} \right\} < \varepsilon = 1.
\]

**Proof.** Since \(X_i\) is uniformly distributed in the interval \((0, 1)\), we obtain its probability density

\[
f(x) = \begin{cases} 1 & 0 < x < 1 \\ 0 & \text{else} \end{cases}
\]

And since \(X_1, X_2, \ldots, X_n\) are independent and have the same distributions, we know that their expected values and variances are

\[
E(X_i) = \int_{-\infty}^{+\infty} xf(x) \, dx = \int_{0}^{1} x \, dx = \frac{1}{2},
\]
and

\[
D(X_i) = E(X_i^2) - [E(X_i)]^2 = \int_{-\infty}^{+\infty} x^2 f(x) \, dx - \left( \frac{1}{2} \right)^2 = \int_{0}^{1} x^2 \, dx - \left( \frac{1}{2} \right)^2 = \frac{1}{12},
\]

where \(i = 1, 2, \ldots, n\).

Then the expected values and variances of \(Y_n\) are

\[
E(Y_n) = E\left( \frac{1}{n} \sum_{k=1}^{n} X_k \right) = \frac{1}{n} \sum_{k=1}^{n} E(X_k) = \frac{1}{n} \times n \times E(X) = \frac{1}{2},
\]
and

\[
D(Y_n) = D\left( \frac{1}{n} \sum_{k=1}^{n} X_k \right) = \frac{1}{n^2} \sum_{k=1}^{n} D(X_k) = \frac{1}{n^2} \times n \times D(X) = \frac{1}{12n}.
\]

Using Chebyshev’s Inequality, for any \(\varepsilon > 0\),

\[
1 \geq P \left\{ Y_n - \frac{1}{2} \right\} < \varepsilon \geq 1 - \frac{1}{12n\varepsilon^2}.
\]

Thus, for fixed \(\varepsilon\), as \(n \to +\infty\)
\[
\lim_{n \to \infty} \left\{ Y_n - \frac{1}{2} \right\} < \varepsilon = 1.
\]

\[ \Box \]

**Theorem 1** shows that \(Y_n \overset{p}{\to} (1/2)\), which is a special case of the Law of Large Numbers. This implies that large sample mean of a random variable approaches a constant. So if every pixel in one noise image \(r\) is regarded as a random sample, the mean of many random noise images approach deterministic image, which is proven in **Theorem 2**.

**Theorem 2.** Let \(r_k (k = 1, 2, \ldots, n)\) be random noise images whose values are uniformly distributed in the interval \((0, 1)\) and their sizes are the same as those of image \(A_1\), the following formula (20) is held.

\[
\lim_{n \to \infty} \frac{1}{n} \sum_{k=1}^{n} A_1 \circ r_k = A_1 \frac{1}{2}
\]

\[
(20)
\]

**Proof.** Let \(r_i(i, j)\) be the gray value of pixel \((i, j)\) in image \(r\). Let \(M \times N\) be the size of \(A_1\). Let random variable \(X_{kij}\) denote \(r_i(i, j)\), and random variable \(Y_{nij}\) denote \(Y_n(i, j)\) where

\[
Y_{nij} = \frac{1}{n} \sum_{k=1}^{n} r_i(i, j)
\]

and

\[
\lim_{n \to \infty} \frac{1}{n} \sum_{k=1}^{n} r_i(i, j) = A_1\frac{1}{2}.
\]

Thus, \(Y_{nij} \to A_1\frac{1}{2}\) when \(n \to \infty\) for pixel \((i, j)\) in image \(r\).

**Theorem 3.** For any image \(A\) with the size \(M \times N\), if \(U = 1\) in Eq. (1), then \(A_1 = (1)_{M \times N}\).

Let

\[
B_n = \frac{1}{n} \sum_{k=1}^{n} A_1 \circ r_k
\]

and \(B_{n, U}, B_{n, D}, B_{n, L}, B_{n, R}\) denote the up, down, left, right CR of \(B_n\), respectively, then

\[
\lim_{n \to \infty} B_{n, U} = \lim_{n \to \infty} B_{n, D} = \lim_{n \to \infty} B_{n, L} = \lim_{n \to \infty} B_{n, R} = \left( \frac{1}{2} \right)_{M \times N}
\]

**Proof.** Since \(U = 1\), then by Eq. (1), for \((i, j)\) is a pixel grid of \(A\), we get

\[
f(A_i, j) = 1
\]

Substituting the above result to Eq. (2) gives

\[
g(i, j) = \frac{U + 1 - f(A_i, j)}{U} = \frac{1 + 1 - 1}{1} = 1.
\]

Thus, \(A_1 = (1)_{M \times N}\).
Since $B_n = \frac{1}{2} \sum_{k=1}^{n} A_1 \circ r_k$, we can apply Theorem 2. We obtain
\[
\lim_{n \to \infty} B_n = \left( \frac{1}{2} \right)_{M \times N}.
\]

The following section will prove \( \lim_{n \to \infty} B_n \rightarrow U = \left( \frac{1}{2} \right)_{M \times N} \).

By Eq. (4), \( B_n(i, j) = \frac{B_n(i, j)}{B_n(i, j) + B_n(i-1, j)} \) where \( B_n(i, j) \) denotes the value of \( B_n \) at any grid \( (i, j) \).

As \( n \to \infty \), we get
\[
\lim_{n \to \infty} B_n(i, j) = \left( \frac{1}{2} \right)_{M \times N}. \]

Thus, \( B_n \rightarrow U = \left( \frac{1}{2} \right)_{M \times N} \). \( \square \)

Similarly, we can prove \( \lim_{n \to \infty} B_n(i, j) = \lim_{n \to \infty} B_n(i, j) = \lim_{n \to \infty} B_n(i, j) = \lim_{n \to \infty} B_n(i, j) = \left( \frac{1}{2} \right)_{M \times N} \).

The number \( n \) in Eq. (21) stands for the number of random variables. When \( U = 1 \), \( n = 1 \) by using DCR \( (A_2 = A_1) \) and Theorem 3 we obtain \( A_2 = A_1 = (1)_{M \times N} \), and then by using Eq. (4) we obtain \( B_n(i, j) \), \( B_n(i, j) \) is NCNR and DCRNN interpolator is the conditional NN interpolator. When \( U = 1 \), \( n = 1 \) and using DSCR \( (A_2 = A_1 = r_1), \) from Theorem 3 we obtain \( A_2 = (1)_{M \times N} \), which implies that A2 is stochastic, so under the conditions of \( U = 1 \), \( n = 1 \), and \( A_2 = (1)_{M \times N} \), DSCR and DSCRRNN interpolator is the CRNN interpolator.

3.3. Comparison of NMI curves under different Us with DSCRRNN interpolator

The other conditions are the same as those in Section 3.2 except that the interpolator changes from DCRNN to DSCRRNN. In Fig. 7(a) the translation range in x direction is \([-33] \) and its translation step is 0.002 pixel. Fig. 7(b) is the zoomed version of Fig. 7(a) in the translation range \([323] \). In Fig. 7(c) the rotation range around the center is \([14.16] \) degrees and its rotation step is 0.002 degree.

Comparing those in Fig. 6, the curves of NMI similarity measure in Fig. 7 are smoother in a body, which implies that integrating stochastic information can improve the overall smoothness. In Fig. 6(b) we can see that NMI curves change from micro-fluctuation to smooth shape as \( U \) increases from 1 to 239. From Fig. 7(c) it is also seen that MI curves becomes slowly smoother shape under rotation transform as \( U \) increases. When \( U = 1 \) the DSCRRNN is SCRNN, i.e., the image \( A_2 = r \) (see formula (3) and Theorem 3) and only includes stochastic information, so there are more micro-fluctuations in the translation curve of NMI similarity measure. The values of NMI at grid translation in Fig. 6(a) are deterministic and independent of \( U \).

3.4. Comparison among NN, DSCRNN, SCRNN interpolator under bias field distortion

The smoothness of NMI curves is compared in this section when the interpolators NN, DSCRRNN and SCRNN are used. The last two interpolators are used with \( U = 239 \) that is the number of the original non-zero intensity bin. The reference image is also Fig. 5(a), but the floating image (see Fig. 8(a)) is distorted with a second-degree multiplication bias field \( ax^2 + bxy + cx + dy^2 + e \), with \( a \) to \( e \) uniformly sampled from \([-0.75, -0.25], [0.25, 0.75] \). [12]. Fig. 8(b) plots the pdf of the reference image and the floating image. In Fig. 8(c) the translation range is \([0] \) in x direction with a step of 0.002 pixel. Fig. 8(d) is the zoomed in version of Fig. 8(c) in the translation range \([2.23] \). In Fig. 8(e) the rotation range is \([14.16] \) degree around the center with a rotation step of 0.002 degree.

When the multiplication bias field is added to the floating image, intensity variations in the same tissue and intensity overlap in different tissues can be observed, as is shown in Fig. 8(a). In Fig. 8(b) one can see that whereas there is an obvious peak in the pdf of the original image, no corresponding peak exists in the pdf of the distorted floating image. The curves of NMI similarity measure in Fig. 8(c) are completely lower than those in Fig. 7(a), which is the result of less joint information between the two registering images corrupted by additional bias field. From Fig. 8(d) and (e) it is seen that the smoothness of NMI curve with DSCRNN interpolator is better than those with the conditional NN interpolator and SCRNN interpolator. The values of NMI at grid translation in Fig. 8(c) are also deterministic with the three interpolators.

3.5. Relationship between DCRNN and SCRNN

The registering images are the same as in Section 3.2. The curves of NMI similarity measure are plotted in Fig. 9 with \( U = 1 \) and \( n \) in Formula (21) is 1, 2, 3, 7 and approaches to \( \infty \) respectively. The translation range of Fig. 9(a) in x direction is \([-33]\) and its translation step is 0.1 pixel. The rotation range of Fig. 9(b) around the center is \([-66]\) degree and its rotation step is 0.5 degree.

From Theorem 3 we know that the DSCRNN interpolator is SCRNN and DCRNN interpolator is the conditional NN interpolator when \( U = 1 \) and \( n = 1 \), and the SCRNN interpolator is the conditional NN interpolator when \( U = 1 \) and \( n \to +\infty \). As \( n \) increases from 1 to \( +\infty \), the randomness of CR decreases and CR changes from SCR to
NNCR. From Fig. 9(a) it is seen that as \( n \) increases from 1 to \( +\infty \) the overall smoothness of NMI curve decreases and eventually the curve is transformed into the ladder shape of the conditional NN interpolator. From Fig. 9(b) it is also seen that for rotation transform the NMI curves transit to the rough shape of the conditional NN interpolator. The values of NMI at grid translation in Fig. 9(a) are deterministic and independent of the number \( n \).

3.6. Comparison using different interpolators such as NN, DSCRNN, LI, PVI and high-order GPVE

The curves of NMI similarity measure are plotted in Fig. 10 using different interpolators such as the conditional NN, DSCRNN (\( U = 239 \) and \( n = 1 \)), LI, PVI and high-order GPVE. The translation range and step are the same as those in Section 3.5. For Fig. 10(a), we also use Fig. 5(a) as the reference and floating images. But the floating image for Fig. 10(b) is acquired by adding white noise of zero mean and 0.02 normalized variance to Fig. 5(a).

Fig. 10(a) and (b) show that the smoothness of NMI curve using DSCRNN interpolator is better than that using the conditional NN, PVI and LI, and is similar to that using high-order GPVE. In contrast to PVI and LI interpolators, DSCRNN interpolator has better anti-noise ability, which is manifested by the concave or convex shape of PV and LI in Fig. 10(b). The values of NMI measures using DSCRNN are higher than those using high-order (second, third, fourth, fifth) GPVE, which implied that some high-frequency information is filtered by high-order GPVE, but it can be retained at grid positions by DSCRNN interpolator.

The convergence of NMI measure is characterized by area of function attraction (AFA) [13] and local maximum number (LMN). AFA counts the number of points from which the global maximum can be reached by a maximum gradient method. LMN counts the number of local maximal point. The higher AFA and the less LMN, the better of convergence is. With the translation range \([-44, 44]\)
pixels in x and y direction and a translation step of 0.1 pixel, the results using different interpolators are shown in Table 1.

From Table 1, it can be seen that the convergence of NMI measure using DSCRNN interpolator is better than that using the conditional NN, PVI and LI interpolator because the AFA of DSCRNN is the largest and its LMN is only one. DSCRNN, second- and third-order GPVE have the equal AFA and LMN, but DSCRNN has faster interpolation speed because it is zero-order interpolator.

Table 1

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Interpolators</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NN</td>
</tr>
<tr>
<td>LMN</td>
<td>100</td>
</tr>
<tr>
<td>AFA</td>
<td>6461</td>
</tr>
</tbody>
</table>

When the registering images are changed to CT images as is shown in Fig. 11(a), the resulting NMI curves using different interpolators are shown in Fig. 11(b) and (c). The other conditions are the same as those in Fig. 10. We can conclude the similar conclusions from Fig. 11 as those from Fig. 10: In CT images registration, NMI measure also has better anti-noise ability and better smoothness of curves by using DSCRNN interpolator than by using the conditional NN, PVI and LI interpolators; DSCRNN interpolator can retain more joint information of two images than high-order GPVE interpolators.

4. Discussions and conclusions

The classifications of CR and the improved NN interpolators are relative to the used information. The improved NN interpolators include three types: DCRNN, SCRNN and DSCRNN. If $A_2$ in Eq. (3) only contains deterministic information, i.e., $A_2 = A_1$, then the

DCR is obtained. The improved NN interpolator based on DCR is DCRNN interpolator. If \( A_2 \) in Eq. (3) only contains stochastic information, i.e., \( A_2 = r \), then the SCR can be obtained. The improved NN interpolator based on SCR is SCRNN interpolator. If \( A_2 \) in Eq. (3) contains deterministic information and stochastic information at the same time, i.e., Eq. (3) is unchanged, then the DSCR can be obtained. The improved NN interpolator based on DSCR is DSCRNN interpolator. When the number of the intensity bin \( U = 1 \) and the number of the random variable \( n = 1 \), DCRNN interpolator is the conditional NN interpolator, and DSCRNN interpolator is SCRNN interpolator. When \( U = 1 \) and \( n \to +\infty \) the SCRNN interpolator is the conditional NN interpolator.

The interpolation kernel in this study is the function \( \beta^q \), which belongs to zero order function. We have known that the conditional NN interpolator can be expanded to PVI interpolator, linear interpolator or higher-order interpolator when the order of interpolation kernel function is increased. Similarly, if the boundary of two neighboring CR is regarded as the center line of the two corresponding pixels and the order of interpolation kernel is improved, the improved NN interpolator can also be extended to higher-order improved interpolator. Similarly, the improved NN interpolators can also be extended to three-dimensional image interpolation when the three-dimensional CRs are constructed. The three-dimensional CRs can also be modified by the similar rules as two-dimensional CRs: the overlap or gap spaces belong to the biggest adjacent 3D CRs. If there are two or more equal adjacent biggest CRs, then the overlaps or gaps randomly belong to one of them. However, as space is limited, we leave implementing our proposed interpolator to the 3D applications to our future work.

From Sections 3.2–3.4, we can conclude that DSCRNN interpolator outperforms SCRNN and DCRNN in terms of smoothness of NMI curve under translation or rotation transform. CRs of the reference image are obtained before registration and are only calculated once, which are not changed in the process of registration, so the CRs’ computation has no obvious effect on registration speed. As is shown in Fig. 7(b), there are less micro-fluctuations in the curves of NMI similarity measure when the number \( U \) of intensity bin becomes larger, therefore \( U \) is suggested to choose the number of the original non-zero intensity bin.

The experiments in Section 3.5 compare the NMI curves with different interpolator and \( n \) (see in Eq. (21)) only when \( U = 1 \). When \( U \) is assigned to a larger integer, some similar results are observed, i.e., when \( n \) increases from 1 to \( +\infty \) the total smoothness of NMI curve decreases, and the curve’s shape approaches to ladder, and the stochastic information in CR decreases, in contrast, the deterministic information in CR increases. Therefore the best total smoothness of NMI curve can be achieved when \( n = 1 \) in Eq. (21), which is also the definition of Eq. (3).

We conclude that by assigning \( U \) to the number of the original non-zero intensity bin’s number and \( n \) to one, DSCRNN interpolator has the similar registration speed as the conditional NN interpolator without compromising the smoothness of NMI curve, which is crucial to registration accuracy. We also conclude that the values of NMI at grid translation are deterministic when any improved NN interpolator based on CR is used. The DSCRNN
interpolator outperforms the conditional NN, PVI and LI interpolators in convergence performance and noise immunity, and outperforms high-order GPVE interpolators in interpolation speed.

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References
