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Transfer Function Design Toolbox for Full-Color Volume Datasets

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ABSTRACT

In this paper, we tackle the challenge of effective Transfer Function (TF) design for Direct Volume Rendering (DVR) of full-color datasets. We propose a novel TF design toolbox based on color similarity which is used to adjust opacity as well as replacing colors. We show that both CIE $L^*u^*v^*$ chromaticity and the chroma component of $YCbCr$ are equally suited as underlying color space for the TF widgets. In order to maximize the area utilized in the TF editor, we renormalize the color space based on the histogram of the dataset. Thereby, colors representing a higher share of the dataset are depicted more prominently, thus providing a higher sensitivity for fine-tuning TF widgets. The applicability of our TF design toolbox is demonstrated by volume ray casting challenging full-color volume data including the visible male cryosection dataset and examples from 3D histology.

Index Terms: Computer Graphics [I.3.3]: Picture/Image Generation—Display algorithms Computer Graphics [I.3.6]: Methodology and Techniques Computer Graphics [I.3.7]: Three-Dimensional Graphics and Realism Computer Graphics [I.3.8]: Applications

1 INTRODUCTION

Histology, a subfield of pathology, deals with the medical analysis at microscopic level of tissue specimen from the human body. The tissue samples are studied on the cellular scale. Digitization of the colored microscopy images opens new exciting possibilities. The resulting 3D stacks of collections of histology images build large-scale full-color volume datasets with typically $100,000 \times 100,000 \times 100$ voxels. The development of intuitive tools for the exploration of these data by domain experts is important to exploit the full capacity of this new data.

Direct Volume Rendering (DVR) is a key visualization technique providing exploratory capabilities to many application domains. The most common scenario is having a scalar dataset as input, which is turned into a color rendering mapping the scalar values to color and transparency using an appropriate transfer function. Interactive design of the transfer function (TF) enables the exploration of the data and provides a means to integrate domain knowledge to generate meaningful visualizations. Thereby, the design of the TF can be a challenging task and much work has been done with this respect [13]. Multivariate input datasets, with several feature dimensions, are also a recurring task for DVR methods. However, full color volume data have not received much attention in previous research. RGB datasets

Figure 1: Our approach for designing a TF for full color volumes. By picking a color in the slice view of the volume, the user creates a matching TF widget in the interaction panel, i.e., a projection of the color space, which he then can adjust. The TF widgets are evaluated during volume ray casting creating the final rendering.

have their specific characteristics which have to be considered when designing a transfer function. In histology, color has a direct connection to the microscopic interpretation of the data and should not be altered too much for the final visualization. This adds additional requirements and constraints to the TF function design.

In this work, we are concerned with the visualization of such full-color datasets. Automatic segmentation is typically not an option since interactive adjustments are needed and preprocessing times are excessive. Therefore, an interactive TF design is the preferred approach. Since the input space for the TF design is already three-dimensional, traditional TF widgets are not sufficient. And TF design for DVR of color volumes has previously not been thoroughly explored. The goal of this paper is to close this gap and provide an interactive TF design interface which supports an effective exploration of full-color data using a two-dimensional interaction panel. Specific challenges and requirements to such an interaction panel are:

- (i) It should provide a meaningful embedding of the 3D color space in the 2D interaction panel.
- (ii) It should support a direct link to the colors in the volume data and keep the color changes low.
- (iii) Areas of interest are often related to peaks in the color histogram within small areas. For these areas, a high sensitivity is required to allow a fine tuned differentiation. However, peaks also appear for background colors where high sensitivity is not required and should hence not overemphasized. Thus, the

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interaction panel has to provide a working solution for both cases.

- (iv) Often there are also large areas in the color space which are not covered by the data. These colors should be mostly eliminated from the user interface since they distract from the region of focus and use much of the interaction panel space.

To meet these requirements we have developed an interaction panel interface specifically designed for interactive full-color TF design. In summary the major contributions are:

- Sensitive TF space using a non-linear histogram equalization in a reduced color space providing high sensitivity in regions of interest while minimizing color distortion.
- TF widgets operating in this space supporting picking with flexible radius fall off. Applying logical operations between the resulting transfer functions facilitates a large variety of design options.
- Integrating the TF widgets and TF space in an intuitive easy to use TF design interface which supports opacity specification and color replacement for effective volume rendering of full-color datasets.
- We demonstrate the proposed methods through volume ray casting of four challenging full-color volume cases, the visible male cryosection dataset from the Visible Human Project (VHP) and three cases from 3D histology.

The paper is structured as follows. In Section 2, the most related work is summarized. Section 3 provides an overview of our TF design toolbox. In Section 4, we describe the construction of the interaction panel. The TF-widgets are explained in Section 5 and their implementation and utilization in DVR is discussed in Section 6. The next section, Section 7, describes four scenarios for the use of our system. We conclude with a summary in Section 8.

2 RELATED WORK

TF design has been central in DVR research from the beginning [2]. TF primitives or widgets, defining range and mapping to the resulting output, have been a cornerstone for many years in DVR for scalar data [1] and for multi-variate data [10], where the additional attribute typically is gradient magnitude. Different TF primitives were proposed for such 2D TFs, ranging from simple boxes and polygons to more complex shapes like arcs [11]. The main difference to full-color volume datasets is that the primitives cannot be easily extended into the third dimension. As an example, Kniss et al. [11] apply a multi-dimensional TF to full-color data by considering only two axes of the RGB color space at a time.

Ebert et al. [3, 4] and Morris & Ebert [15] presented work on DVR of the cryosection data from VHP. Their approach focused on emphasizing boundary regions and suppressing homogeneous regions using the first and second order derivatives in the chromaticity subspace of the CIE $L^*u^*v^*$ color space to modulate the opacity of the volume samples. In the present work, the authors have chosen both CIE $L^*u^*v^*$ and the $YC_B C_R$ color space [8] and provide justification for its suitability.

The user interface concept of sampling the attribute space of the data on slice views has been presented by Tzeng et al. [19] and Kohlman et al. [12]. Samples picked or strokes painted in the slice view generate input to either a neural network training [19] or automated selection of preset TFs [12]. For the approach in this paper the samples picked on the slice view generate initial parameters for a TF widget by analyzing a small neighborhood at the point of selection.

Color volume TF design is also related to general classification in multi-dimensional data. One example of many is to use Independent Component Analysis (ICA) to transform the input RGB data into

a space more suitable for differentiation [17]. An early color clustering approach using Principal Component Analysis (PCA), in the CIE $L^*a^*b^*$ color space, for image segmentation was presented by Tominaga [18]. In this paper we present preliminary comparisons for PCA, related to different color spaces.

The construction of 3D histology datasets is a laborious process offering challenges to normalize staining and to perform slice registration [16]. Visualization of 3D histology has so far been done with traditional TF design [14, 16] limiting the exploratory possibilities. DVR of massive microscopy data streams has been previously addressed [5], but not with focus on TF design or color data volumes.

3 TF DESIGN TOOLBOX – OVERVIEW

Figure 1 depicts an overview of our approach addressing the TF design for full-color volume datasets. The interface exposed to the user is composed of a browsable slice view showing original full-color images from the volume, the interaction panel for TF design where an arbitrary number of TF widgets can be defined, and a view of the resulting 3D rendering. In the interaction panel, i.e., the TF editor, the color space is shown and a voxel value histogram of the volume at hand can be overlaid in black. Logical operations are supported by combining the widgets including additive and subtractive TF widgets. This provides the option to gradually build up a rendering by adding and subtracting features from the rendered full volume, respectively. Our DVR approach is ray casting of the RGB volume utilizing the interactively composed TF.

The key idea of this TF design approach is that each TF widget assigns an opacity to a color range defined by a central color and its neighborhood consisting of all colors being sufficiently similar. At a basic level this approach relates to chroma keying, a technique well-known from the movie industry, also known as green screen. To make this TF design intuitive and easy to use an elaborate configuration of the interaction panel and a color similarity measure is essential. The interaction panel must support the generation of fine tuned TF in color regions of interest which often correspond to small areas of the color space. The two basic parts of the design toolbox, the interaction panel and the TF widgets, will be described in the following sections.

4 INTERACTION PANEL DESIGN

The goal of the interaction panel design is to provide an interface that allows the user to navigate in the familiar color set from the applications which often has a distinct meaning. Thereby, the interaction space should be used in an optimal way. This means removing unused colors from the panel, providing more space for sensitive color regions while keeping the color changes minimal.

Thus, the first fundamental question is the choice of the color space in which the TF widgets reside. In order to make widget shape and size changes consistent, and to provide the user with an intuitive notion of color similarity, we suggest a perceptually calibrated color space. The CIE $L^*u^*v^*$ space is arguably the best choice in that respect [4], but the $YC_B C_R$ space is also a suitable candidate. In particular, $YC_B C_R$ offers a linear transformation from RGB as well as a good approximation of perceptually uniform color distances. For our applications we observed that both color spaces, CIE $L^*u^*v^*$ as well as $YC_B C_R$, are equally well-suited for this task as discussed in Section 4.1. Therefore our TF interaction panel supports both options.

Figure 2 shows the steps for constructing our interaction panel. It is based on a 2D color plane (requirement (i)) of a perceptually-uniform/-based color space (requirement (ii)). To obtain a high sensitivity in interesting areas, we employ a spring-mass system which is used to perform a non-linear histogram equalization (requirements (iii) and (iv)). In the following, we detail the histogram projection and the non-linear histogram equalization with the spring-mass system. The goal of these methods is to maximize the interaction space

Figure 2: Steps for creating our proposed interaction panel for TF design of full-color volume datasets. The volume histogram is projected on either the chromaticity u^*v^* of the CIE $L^*u^*v^*$ color space or the chroma plane of $YC_B C_R$. A spring-mass system is used to perform a histogram equalization in order to create a sensitive and space-efficient TF design space.

Figure 3: Comparing color distances between CIE $L^*u^*v^*$ chromaticity and $YC_B C_R$. (a) equidistant contours around D65 white. (b) D65 white mapped from CIE $L^*u^*v^*$ to $YC_B C_R$. (c) D65 white mapped from $YC_B C_R$ to CIE $L^*u^*v^*$. (d) purple mapped from CIE $L^*u^*v^*$ to $YC_B C_R$. (e) purple mapped from $YC_B C_R$ to CIE $L^*u^*v^*$.

for the TF design while providing the original context as well as removing unused colors, which can be very distracting. We consider the techniques described in Section 4.1 and Section 4.2 to be optional under this respect. The proposed TF widgets based on color distances in either CIE $L^*u^*v^*$ and $YC_B C_R$ could also be used without this mapping.

4.1 Histogram Projection

When finding similar colors in an image using a threshold, perception-based color spaces offer a huge advantage. In order to make the TF widgets intuitive for the user, distances in the TF interaction panel should align with perceptual differences.

Dimensionality reduction of the three-dimensional histogram of the full-color volume dataset is achieved by projecting each entry onto the u^*v^* chromaticity plane of the CIE $L^*u^*v^*$ color space or the chroma plane of $YC_B C_R$, thereby addressing requirements (i) and (ii). Lightness (CIE $L^*u^*v^*$) and luminance ($YC_B C_R$) values of the colors are often only of minor importance in many applications. By maintaining color hues when using this embedding eases the users' cognition and color variations are kept at a minimum. In addition, this mapping fits perfectly with the stain design used in histology datasets. Here, the stains are designed to be clearly separable using color deconvolution [6, 9] and the stains are, typically, differentiated using hue and not luminance or lightness. In datasets where luminance might bear additional information, e.g., the dark-red blood vessels in the visible male cryosection dataset, we noted that the projection to chromaticity is nonetheless yielding respectable results. In cases where more control is necessary, like the extraction of blood vessels in cryogenic data, we allow the user to restrict the luminance range for certain colors as described in Section 5.

Although CIE $L^*u^*v^*$ is considered to be *perceptually uniform* regarding human vision, using $YC_B C_R$, being a *perception-based* color space, yields similar performance in the context of our work. As you can see in Figure 3 when comparing color distances in

CIE $L^*u^*v^*$ and $YC_B C_R$, transformed contours are only marginally distorted while keeping the equidistance close to the original. In our tests, the practical differences between using either of the two color spaces as underlying color space were hardly discernible. However, $YC_B C_R$ performs slightly better for the visible male cryosection dataset while CIE $L^*u^*v^*$ appears to be better suited for histology data.

Although being quite similar, the slight distortions between the two color spaces (cf. Figure 3) appear to have a minor influence on the TF design process. In particular, when looking at the histogram of the Visible Male in CIE $L^*u^*v^*$ (Figure 2, second image), the blue region is rather elongated. Considering the histogram in $YC_B C_R$ (e.g., Figures 7 and 9), however, the blue area is covered more homogeneously. Likewise for the histology datasets which are more in alignment with the CIE $L^*u^*v^*$ color space. One could argue that by adjusting the anisotropy and the orientation of the TF widget the color space distortions can be compensated but at the cost of additional user interaction.

4.2 Non-Linear Histogram Equalization

The non-linear histogram equalization addresses requirement (iii) by maximizing the sensitivity for color selection. It can be observed that color histograms of typical datasets only cover a small area of the entire color space, exhibiting strong peaks in very small areas, see Figure 1, top right. A consequence is that much of the interaction space is wasted to non-used colors. These colors dominate the color space and make it difficult to relate to the colors of interest. A fine tuned navigation in the regions of interest is hardly possible. To overcome this limitation we construct a color panel that first eliminates large parts of the dispensable color space (requirement (iv)) and then transforms it by equalizing the histogram (requirement (iii)). The explicit choice for the color transformation has been guided by these goals while keeping the distortion small and simple.

The most obvious way to reduce the color space would be to

Figure 4: Histogram equalization in CIE $L^*u^*v^*$ using a spring mass system (shown in the lower right). The convex hull of the area of the projected histogram is depicted in white. (a) initial, undistorted CIE $L^*u^*v^*$ color space. (b) moderate histogram influence. (c) a smoothed histogram yields a more uniform deformation. (d) increased histogram influence.

compute the convex hull of the histogram and then map it to a rectangular shape. However, this already introduces strong non-intuitive deformations of the color space. We experimented with other alternatives and concluded that a simple axis-aligned box works best and keeps color-space distortions at a minimum. We expand this box slightly to provide some space to increase the overall contrast without altering colors much.

In a second step, we perform a non-linear histogram equalization within this bounding box using a spring-mass system. The spring-mass system is set up as a regular grid in the color space with a uniform, constant mass m per node. The nodes at the boundary are fixed. The force is composed of the oscillatory spring force and a damping force.

$$F = -k(x)(\Delta x) - cv + F_{\text{ext}}$$

A fixed damping constant is set to $c = 0.5$, which leads to a quick and stable convergence of the system. We apply a constant additional external force F_{ext} field based on the histogram gradient. It pulls the nodes towards areas with higher density. The closer the nodes get together the larger the enclosed area will be depicted in the interaction panel. The free parameters of the system are the sampling density for the grid, the specification of the spring rate $k(x)$, and the strength of the external force.

We modify the spring rate or elasticity of the springs based on the histogram density at the center of the spring (location between two nodes). Higher values cause an increase in elasticity which in turn will pull the nodes together. The spring rate is updated in each iteration step with reset to the current node location. In areas of high frequency in the histogram this can lead to strong changes in the spring rate. In order to avoid such a behavior we use a weighted average of the current and previous value for each spring. To reduce the dominance of single spikes in the histogram, e.g., background color or cryogenic fluid (see Section 7), we always work with a logarithmically scaled histogram. A possible weighting function for springs is displayed in Figure 5 which equalizes the histogram more or less uniformly. It is defined as a polynomial of order γ for values between a minimum and a maximum density value $f(x) = ((x - t_1)/(t_2 - t_1))^\gamma$. The basic element of the mapping in Figure 5 for the histogram equalization is the definition of a minimum and a maximum density threshold t_1 and t_2 , respectively. The maximum t_2 is necessary to not overemphasize a dominant background color. The simplest transition between these values would be a linear transition, which works fine. The polynomial definition increases the flexibility of the mapping either focusing on the dominant color or rather outlier colors.

The histogram equalization is depicted for a single slice image of a histology dataset in Figure 4. To better illustrate the deformation of the color space a grid was superimposed. A preset of default

Figure 5: Weighting function for spring elasticity using a minimum and maximum threshold for the histogram density. In between we raise the normalized density value to the power of γ , a user-adjustable exponent. The parameter is set to a default values $\gamma = 4$, which worked well for all of our examples.

values for the spring mass system proved to be quite universal in our experiments with multiple datasets and produced good initial results despite the varying shapes of the histograms. If necessary, the parameters of the spring mass system can be further tweaked for fine adjustments, e.g., increasing the influence of the external force. A variation of this force can balance the emphasis of the histogram peaks (see Figure 4(d), also cf. requirement (iii)). Note the increasing size of the histogram peak around the white point which will provide more color sensitivity in this area during user interaction. The resolution of the first histogram has also an influence of the result. Smoothing the histogram lead to more uniform histogram equalization (Figure 4(c)).

5 CHROMATICITY-BASED TF WIDGETS

In contrast to the TF design for density, i.e., scalar data, a color mapping is not needed for full-color volume data since color values can directly be used for visualization. The opacity information, however, is usually lacking and the volume will be rendered as a solid block. We therefore propose a TF design supporting logical operations with respect to opacity. In subtractive mode, we begin with a solid volume, i.e., an opacity value of one everywhere, and remove different materials like background and other unwanted parts step by step. The additive mode resembles the traditional TF design with everything being initially invisible and assigning opacity values to parts which should appear. Figure 6 depicts an example rendered with both design modes.

To provide a high level of flexibility and ease of use, we use

Figure 6: Our TF widgets feature positive and negative opacity values enabling two design modes. (a) subtractive TF design: the structure is carved out of a solid block by removing material, i.e., assigning negative opacity. (b) additive TF design: the structure is built up by combining several TF widgets for different materials with positive opacity similar to regular TF design.

individual TF widgets and set the concept of a single unified TF aside. Each primitive is associated with one color and will only affect similar colors based on perceptual color distances regarding chromaticity similar to chroma keying. During volume rendering the widgets are evaluated and the results are combined (see Section 6).

Figure 7 shows all parameters of a single TF widget, located inside the interaction panel, and the associated editor. The user can create a TF widget either by using a color picker tool, e.g., picking a point in a 2D slice of the volume or directly selecting a color in the interaction panel. The position of the TF widget corresponds to its matching color together with a circular extent in the chromaticity plane. This extent restricts the influence of the primitive, i.e., only similar colors within a certain range will be affected. The size can be adjusted by a radius and an anisotropy parameter.

Figure 7: The TF widget and its parameters in the TF editor (here depicted for $YCbCr$). The widget position, i.e., its location in the chromaticity plane, is shown on the left in the interaction panel together with the influenced area. The equalized histogram of the dataset is shown in background for reference.

To support additive and subtractive TF design, the opacity value of the TF widget accepts both positive and negative values thereby enabling logical operations including unions, intersections, etc. The overall effect of the widget is then given by the product of opacity and fall-off function. The different available fall-off functions are depicted in Figure 8. Optionally, the user can also assign a replacement color to emphasize or highlight certain areas.

6 DVR INTEGRATION AND IMPLEMENTATION

Direct volume rendering techniques like ray casting can be adapted with minor modifications to render full-color volume datasets while

Figure 8: The effect of different fall-off functions for a TF widget with positive opacity (left) and negative opacity (right). (a) box function with smooth fall-off at edges. (b) linear fall-off from center. (c) Gaussian fall-off with three standard deviations inside the range. A single TF widget was used with $C_B = -0.14$, $C_R = 0.07$, and $r = 0.13$.

utilizing our proposed TF design. It is important to note that the non-linear histogram equalization is only used in the context of the interaction panel when designing the TF in order to provide higher sensitivity. The TF widgets themselves are directly embedded in the underlying color space and, thus, no transformations are required during rendering.

In order to apply DVR to full-color volumes, the classification step, i.e., the TF mapping for each volume sample, needs to be replaced with the evaluation of all TF widgets. Algorithm 1 outlines the ray casting loop resulting from the replacement.

// DVR ray casting loop

foreach sampling position along ray do

```

 $c_{RGB} \leftarrow$  sample RGB volume;
// initialize  $\alpha$  depending on TF design mode
 $c_{TF} \leftarrow$  convert  $c_{RGB}$  to either CIE  $L^*u^*v^*$  or  $YCbCr$ ;
 $\alpha \leftarrow 0$  if additive TF design; 1 otherwise;
foreach TF widget do
     $d \leftarrow$  compute chromaticity distance between  $c_{TF}$  and
        color of the TF widget;
    opacity  $\leftarrow$  evaluate TF fall-off function  $f(d)$ ;
     $\alpha \leftarrow \alpha + \text{opacity}$ ;
     $\alpha \leftarrow \text{clamp } \alpha \text{ to } [0,1]$ ;
    // optional color replacement
    if TF widget replaces color then
         $c_{RGB} \leftarrow \text{mix } c_{RGB} \text{ and } c_{\text{new}} \text{ by } |\text{opacity}|$ ;
    end
end
// optional shading step
 $c_{RGB} \leftarrow \text{localShading}(c_{RGB}, \text{luminance gradient})$ 
regular compositing with  $c_{RGB}$  and  $\alpha$ ;

```

end

Algorithm 1: Main loop for RGB volume ray casting utilizing our TF widgets for color similarity.

After the volume data has been sampled at the current ray position, the sample color c_{RGB} is converted to a color c_{TF} in the TF design color space. Additionally, the alpha value α of the sample

Figure 9: Designing a TF step-by-step for extracting the head of the visible male dataset from cryogenic fluid using three TF widgets and subtractive TF design in $Y C_B C_R$. (a) solid RGB volume. (b) removal of ice. (c) removal of liquid inside body and at ear lobe. (d) remove patina on skin. (e) final TF design.

Figure 10: Slide images of cryogenic datasets might suffer from artifacts like missing tissue or frosting on top of the slide (a). The artifacts can be suppressed with additional TF widgets besides the ones used for background removal. (b) background removal. (c) removal of slide frosting. (d) final TF design.

is initialized based on the chosen TF design mode, i.e., $\alpha = 1$ for subtractive TFs and $\alpha = 0$ for additive TFs. For each TF widget, we compute the color distance d between the widget color and the converted sample color c_{TF} . The color distance computation for 2D primitives, the default, considers only chromaticity while neglecting luminance values of both colors. If luminance matching is enabled, all three dimensions are considered when computing the color distance.

The distance is normalized with respect to the radius and the fall-off function is applied. The resulting opacity is then added to α . Please note that the opacity can be negative to allow for subtractive TFs. In case the TF widget is supposed to replace matching colors, the absolute value of the opacity is used to mix c_{RGB} with the replacement color by linear interpolation.

After all primitives have been evaluated, we perform regular front-to-back compositing using c_{RGB} and α clamped to zero and one. To allow for local shading of each sample, we compute the gradient of corresponding grayscale values. This can be done while sampling the RGB volume data and calculating the respective luminance of the samples. The Phong model with a single light source was used for some of the volume renderings in this paper.

We implemented the above ray casting algorithm in OpenGL using GLSL. The TF widgets are stored in a uniform buffer and the evaluation takes place within a loop. Similarly, the fall-off functions are implemented in GLSL instead of pre-computed 1D lookup tables. The spring-mass system used in the interaction panel is CPU-bound and utilizes the Verlet integration scheme for increased stability. In most cases, 50 to 100 integration steps were sufficient to obtain a converging histogram equalization.

7 RESULTS

7.1 Visible Male Dataset

This dataset is probably one of the best-known examples of a full-body scan in volume rendering. It was created in the Visible Human Project run by the National Library of Medicine. Besides the full-body CT scan, the dataset also contains full-color RGB slice images of the entire body.

The images were obtained by taking photographs of cryosections. The body was frozen in a mixture of water and gelatin and then thin slices, about 1 mm thick, were shaved off before a picture was taken of the next slice. The full-color dataset consists of 1,880 images, each with a resolution of 2,048 pixel by 1,216 pixel corresponding to 0.33 mm per pixel. Due to the large size of the data, we loaded only parts of the dataset into a RGBA texture used for ray casting.

The feet shown in Figure 6 were extracted from 180 slices. In a subtractive TF (Figure 6(a)), a large negative opacity is assigned to all parts which are to be removed, e.g., the cryogenic fluid surrounding the body. This leaves the remaining structures unchanged and fully opaque. By using small negative opacities, materials affected by the TF widget become semitransparent and reveal internal structures like blood vessels embedded in the skin. On the other hand, additive TF design (Figure 6(b)) is more modular and combines areas where the user assigns positive opacity values, in this case muscles and vessels and a slight hint of skin.

The step-by-step process of designing a TF is shown in Figure 9. Adding TF widgets with negative opacity results in a subtractive TF which extracts the head from the ice (170 slices). To remove the cryogenic fluid (a), we pick a gray-blue color in the ice creating TF

Figure 11: Cross-section of the head of the visible male dataset (left) with the same TF as in Figure 9. Adjusting the opacity of TF₂ reveals the fluid inside the head while the background remains transparent (right).

Figure 12: Barrett's esophagus dataset with H&E stain consisting of 100 microscope slide images. Single slide image showing digitization artifacts (top), volume rendering of the entire slide stack with background removed (center), and extracted purple boundary structures (bottom).

widget TF_1 (b), which gets rid of almost all fluid. Another, smaller primitive TF_2 is added to remove the remaining, slightly differently colored liquids at the ear lobe and inside the head (c). The third primitive TF_3 , with a Gaussian fall-off, is used to get rid of the green layer on top of the skin. Figure 9(e) depicts the final TF.

Combining TF widgets with negative and positive opacity values provides a great flexibility and allows for fine-tuning. Figure 11 depicts a cross-section of the extracted head in Figure 9(c). Assigning a positive opacity to the light blue TF widget (TF_2) next to two negative primitives brings back the details of fluid being inside the head without affecting the cryogenic fluid which has been removed before.

Sometimes, cryosection data features artifacts on single slice images. These might be due to miss-alignment, overlaps, or missing tissue or problems related to the cryogenic fluid like frosting or glazing. Slice 4505 of the visible male is such an example (Figure 10). To suppress these artifacts, we add three additional TF widgets besides the two used for removing the background leaving only a slight tint on the top while preserving the details.

7.2 3D Histology

Histology is concerned with studying tissues and cells on a microscopic scale. After collecting a tissue sample, the sample is fixated and cut into thin slices. Once put on a microscope slide, the slices are typically stained with specific dyes increasing contrast and highlighting certain characteristics like nuclei. The slides are then studied using a microscope or they are digitized with specialized scanners resulting in high-resolution slide images.

In 3D histology, multiple of these microscope slide images from the same sample are coregistered and then put back together into a single image stack or volume. Investigating the data in three dimensions can provide some additional insights like spatial connectivity which one can barely grasp by looking at 2D slide images. On the other hand, a TF is required to be able to look inside the volume. To demonstrate the applicability of our approach to 3D histology, we apply our chromaticity-based TF widgets in CIE $L^*u^*v^*$ to datasets covering three different medical conditions.

Figure 13: Highlighting nuclei (purple) in the Barrett's esophagus dataset. Volume rendering of original data (top), and replacing purple with cyan using one TF widget (bottom).

7.2.1 Barrett's esophagus

Barrett's esophagus is a medical condition where cells change in abnormal ways due to stomach acid. If not treated, this condition might result in cancer. The dataset consists of 100 slide images obtained from a biopsy of the lower esophagus with a Leica Aperio AT2 Scanner. The slides were stained with haematoxylin and eosin (H&E stain) and the images have each a resolution of $64,000 \text{ pixel} \times 40,000 \text{ pixel}$ stored with JPEG2000 compression.

For the purpose of this paper, we extracted an overview volume dataset containing a down-sampled version of the slide images and a second excerpt at full resolution. The volume resolutions are $2,048 \times 900 \times 102$ and $2,048 \times 1,200 \times 102$, respectively.

The overview volume is depicted in Figure 12 along with one of the microscope slide images. The slide image features some typical stripe artifacts which can occur during scanning. Despite the variation, a single TF widget is sufficient to remove the background including JPEG artifacts and, thus, revealing the boundaries of the tissue sample (center). To extract the purple boundaries we use one TF widget and the additive TF design (bottom).

As pointed out earlier, the TF widgets can also be used to replace certain colors for highlighting. In Figure 13, the white background is removed first and then a second TF widget is added replacing purple with light blue, thereby emphasizing the positions of nuclei.

7.2.2 Liver Cirrhosis

The second histology dataset stems from a patient suffering from alcoholic cirrhosis. Cirrhosis causes scarring of the liver, forming nodules of liver cells bounded by fibrous tissue. Different distributions and shapes of cirrhosis may be observed depending on the stage and cause of the disease. A 1 cm by 1 cm by 1 cm tissue sample was obtained from the liver and sectioned into 100 slices, which are $5 \mu\text{m}$ apart. The downsampled slide images have a resolution of $1,248 \text{ pixel} \times 1,114 \text{ pixel}$ and are stained with Sirius red, which marks collagen in red and liver cells in brown.

The solid slide stack is depicted in Figure 14(a). By using one TF widget we can remove the white background revealing the hollow vessels. However, replacing white with a semitransparent black color adds a depth cue emphasizing cavities (Figure 14(b)). These depth cues become even more apparent and also helpful when removing

Figure 14: Liver cirrhosis. (a) stack of slide images from a liver cirrhosis; cells are colored in brown and scar tissue in red. (b) one TF widget is used to replace the white background with transparent black to emphasize internal structures. (c) another TF widget is used to remove liver cell nodules.

Figure 15: Early stage of a colorectal adenocarcinoma stained with keratin immunohistochemistry. (a) single slide image with the resection being visible in the top left. (b) stack of slide images with background removal; the epithelium is colored in brown. (c) cropped subsection at the highest available resolution. (d) one TF widget is used to replace the white background with transparent black to emphasize internal structures. (e) interaction panel with histogram in CIE $L^*u^*v^*$.

the brown interior of all cells with another TF widget as shown in Figure 14(c).

7.2.3 Colorectal Polyp

This dataset of a colorectal polyp depicts an early colorectal adenocarcinoma. It is stained with keratin immunohistochemistry to show the epithelium in brown (Figure 15(a)). The stalk of the polyp where it has been resected is visible in the top-right corner of Figure 15(b). The data comprises 47 slide images, each with a resolution of 60,000 pixel by 60,000 pixel where one pixel represents 0.5 μm and the slides being 20 μm apart.

The entire slide stack is depicted in Figure 15(b) while (c) depicts a subregion including the background. Using one TF widget enables us to remove the white background in order to reveal internal structures. When white is replaced with a black color, internal structures become visible allowing for a better understanding of whether glands are interconnected (Figure 14(a), (d)).

7.3 PCA Comparison

An alternative to TF design in a pre-defined color space would be a data-driven approach which could, for example, be based on dimensionality reduction schemes. In the context of histology, color deconvolution [6, 9] is used since the utilized stains are designed in a way to be easily distinguishable by color analysis. Data-driven dimensionality reductions can be rather computationally expensive in contrast to the elementary color space transformations used in this paper.

In the following, we chose the principal component analysis (PCA) as one representative approach of the reduction schemes. The principal components can be thought of defining the most relevant color space axes. When comparing the PCA results with the YCbCr space, Figure 16 shows that for the Barrett's esophagus data the first principal component coincides almost fully with luma, which is also the case for the visible male data. Thus, the second and third components span the chroma plane, even though those axes are not the same for the two datasets. These results indicate that a data-driven

color space selection has limited additional value compared to using YCbCr . In addition, a pre-defined color space like CIE $L^*u^*v^*$ or YCbCr has the advantages of low computational overhead and dataset independence.

Figure 16: Principal component analysis of the visible male (a) and Barrett's esophagus (b) in YCbCr color space. The first eigenvector of both results coincides with luma whereas the second and third eigenvectors lie in the chroma plane.

8 CONCLUSION

In this paper, we presented a TF design toolbox for full-color volume data utilizing a 2D TF interaction panel. This TF interaction panel embeds the underlying color space and provides a direct link to the data values of the volume dataset. By means of a non-linear histogram equalization we achieve a high sensitivity for positioning TF widgets in areas of particular interest. We suggest the use of either CIE $L^*u^*v^*$ or YCbCr as both color spaces are well-suited for a consistent user experience with respect to color similarity. This enables us to define color similarity in an intuitive way by means of chromaticity differences. In most cases, 2D chromaticity is sufficient for similarity selection and luminance information can be discarded, thus reducing the complexity when creating new TF widgets.

The TF widgets support opacity manipulation and color replacement as well as logical operators. Subtractive TF design is of particular interest when dealing with full-color volumes to remove

unwanted materials like the background of microscope slide images or frozen water in cryo datasets.

We have demonstrated the usefulness and applicability of our approach with examples from 3D histology and cryosection data. Using TF widgets based on chromaticity provides a high level of robustness for inhomogeneous, but similarly colored, areas like noisy data or cryogenic fluids.

For future research, we want to explore how the concepts of our TF design can benefit DVR of other types of multi-variate data.

For example, the 2D gradient-magnitude density domain could be used for scalar volumetric data instead of a color space. This should produce results similar to those obtained when segmenting the intensity-gradient histograms [7]. Regarding 3D histology, we are thinking of using a custom color space similar to ISpace [17], since the dyes used for staining samples are designed for maximum color separations, are relatively constant, and have a direct biological interpretation.

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