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Perceptual Evaluation of Common Line Variables for Displaying Uncertainty on Molecular Surfaces

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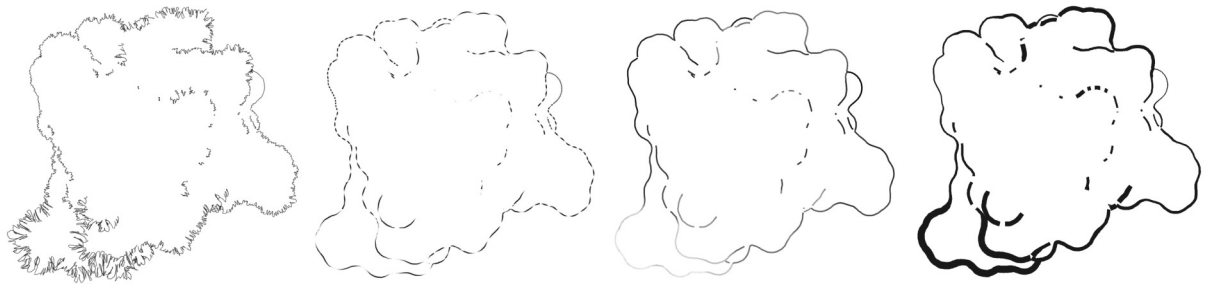


Figure 1: *Line styles for the perceptual evaluation. From left to right: Sketchiness, dashing, grayscale, width.*

Abstract

Data are often subject to some degree of uncertainty, whether aleatory or epistemic. This applies both to experimental data acquired with sensors as well as to simulation data. Displaying these data and their uncertainty faithfully is crucial for gaining knowledge. Specifically, the effective communication of the uncertainty can influence the interpretation of the data and the users' trust in the visualization. However, uncertainty-aware visualization has gotten little attention in molecular visualization. When using the established molecular representations, the physicochemical attributes of the molecular data usually already occupy the common visual channels like shape, size, and color. Consequently, to encode uncertainty information, we need to open up another channel by using feature lines. Even though various line variables have been proposed for uncertainty visualizations, they have so far been primarily used for two-dimensional data and there has been little perceptual evaluation. Therefore, we conducted a perceptual study to determine the suitability of the line variables sketchiness, dashing, grayscale, and width for distinguishing several uncertainty values on molecular surfaces.

CCS Concepts

• ***Human-centered computing*** → ***Empirical studies in visualization; Scientific visualization;*** • ***Computing methodologies*** → *Non-photorealistic rendering;* • ***Applied computing*** → *Imaging;*

1. Introduction

Scientific visualizations rely on the accuracy of the data that the visualization is based on. Unfortunately, errors or data uncertainty can be introduced throughout the whole visualization pipeline, from data acquisition to rasterization. It may even be an inherent property of the object, phenomenon, or process that is encoded in the data, which might be subject to aleatory or epistemic uncertainty. Early work on handling data errors in visualization has been published by Goodchild and Sucharita [GG89] in the domain of Geographic Information Systems (GIS). Uncertainty visualization (UV) is also an active topic in medical visualization [GSWS21]. However, UV is less common in molecular visualization, albeit some work addressing this topic exists (see Section 2.3). We aim to contribute to uncertainty-aware molecular visualization by picking molecular models as an example application for our evaluation.

In molecular visualization, the common visual channels such as coloring the surface, glyphs, etc. are usually occupied with other information. Therefore, we open up another channel by utilizing the feature lines of the molecule. Feature lines are a particularly interesting choice because they occupy very little space, leaving more room for encoding other properties on the molecular surface.

Applying different line styles to encode data associated with the lines is quite independent of the actual lines or curves. The lines need to be stylized according to the underlying data. Additionally, the stylization needs to be updated in a temporally coherent manner, as molecular visualizations are often used in an animated and interactive context. Therefore, we adapted the Active Strokes method [BLC*12] for real-time temporal coherent line stylization to be able to vary the line styles according to uncertainty values.

Several line variables such as *sketchiness*, *dashing*, *grayscale*, *blur*, *wave amplitude* or *wave frequency*, etc. have been proposed for encoding uncertainty in visualizations [SMI99; BBIF12; GHL15; GSWD18]. However, there has been little evaluation on why a chosen line variable is particularly suited in a given context and prior evaluations only considered two-dimensional visualizations [BBIF12; GHL15]. To assess different line variables for their suitability for reading off scalar data, and thus uncertainty, on three-dimensional objects, we conducted a perceptual evaluation of the line variables *sketchiness*, *dashing*, *grayscale*, and *width*. In our study, we analyzed accuracy and response time for these different line variables.

To summarize, our contributions are threefold:

- A novel Uncertainty-aware Visualization for biomolecules that does not use any of the visual channels commonly used in molecular visualization.
- An extension to Active Strokes, allowing the encoding of additional data into line variables.
- A perceptual evaluation on displaying uncertainty using the line variables *sketchiness*, *dashing*, *grayscale* and *width*.

2. Related Work

This section first describes related work in the areas of line generation and line stylization. Next, previous molecular visualizations and particularly molecular *Uncertainty Visualization* (UV) and *Uncertainty-aware Visualization* (UaV) are discussed. Finally, related perceptual experiments are outlined.

2.1. Line Stylization

Line drawings are a type of low-level illustrative visualization. While occupying little space in the rendered image they provide important shape cues and can offer a good first impression of the rendered object. An overview of several types of line drawings can be found in the surveys by Lawonn and Preim [LLPH15] and Lawonn et al. [LVPI18]. Algorithms for generating line drawings can be grouped into object-space, image-space, and hybrid methods [IFH*03]. Object-space methods generate three-dimensional lines directly in object-space and perform visibility computations afterward. They only work for a specific type of underlying model, i.e. polyhedral meshes, but they usually produce high-quality lines. Image-space methods extract the lines from a rendered image. Therefore, they work in a two-dimensional environment and the lines they produce consist of disconnected pixels. They are, however, more interesting to us, as they are generally real-time capable and are independent of the type of underlying model, i.e. they are not restricted to polyhedral meshes. In molecular visualization, a variety of different 3D model types is being used, making image-space approaches particularly interesting. Hybrid approaches combine image-space and object-space techniques.

Most line stylization algorithms are object-space methods [WS94; GTDS04; KH11]. They first extract visible curves from the 3D model, combine them into longer curves, simplify, and finally render them with stroke textures [BH19]. Visualizations of molecules are mostly used animatedly or interactively. Therefore, the stylized lines should have temporal continuity. It is not sufficient to simply compute the lines at every time frame, as this leads to visual artifacts such as popping or sliding [BBT11].

Kalnins et al. [KDMF03] suggested propagating the parameterization of lines frame-to-frame. Their solution ensures temporal coherence, but only works at interactive rates for models with low to medium complexity. Additionally, for models with medium complexity, the approach produces tiny line fragments, making parameter propagation difficult [BLC*12]. If the entire sequence is known beforehand, the method of Buchholz et al. [BFP*11] can be used. It generates a space-time surface to find temporarily coherent parameterizations. Bénard et al. [BLC*12] presented Active Strokes, which use active contours to track and parameterize image-space lines. Then, they generate stylizable brush paths from those contours. The Active Strokes approach is described in more depth in Section 4. Ben-Zvi et al. [BBM*16] use point matching to track curves over time. However, their approach is computationally expensive and thus does not work at interactive frame rates. Another approach to contour parameterization was developed by Lichtenberg and Lawonn [LL20] for tree-like structures that could for example be used to display uncertainty information on vessel trees.

2.2. Perceptual Experiments

Increasingly perceptual experiments are being used not only to evaluate the efficacy of visualization techniques but also to provide insights into how the techniques can be further developed. Cunningham and Wallraven [CW11] gave a thorough overview of experimental (and statistical) methods and how they can be used to study perception in scenes with complex images. Preim et al. [PBC*16]) presented a survey of perceptually motivated medical visualization techniques, including how perceptual effects are studied here. One of the more common techniques used in the study of visualizations is to force viewers or participants to choose which one of two points in a single visualization has more of the desired characteristic. For example, several authors (e.g., [LLPH15; LHL17; LLH17]) have presented a complex 3D object and asked participants which of two points is closer to the viewer. By varying the depth distance between the two points over a series of trials, one can systematically determine the smallest difference that a given visualization technique supports.

Boukhelifa et al. [BBIF12] used several different, common tech-

niques to study four visual line attributes for the depiction of qualitative uncertainty. They specifically examined *sketchiness*, *blur*, *dashing* and *grayscale*, with a focus on *sketchiness*. After initially performing a series of comprehensive qualitative experiments (where participants verbally described their impressions of the visualizations), they ran a quantitative experiment. They presented lines with different amounts of, e.g., blur or dashing, and had participants rate how blurred or dashed the lines were. In the qualitative stage of the experiments, they considered two-dimensional scenarios while for the quantitative experiments they used lines without an accompanying scenario. Findings for two-dimensional scenarios might differ from findings for three-dimensional scenarios as they for example do not deal with occlusion or possible interference with depth perception.

2.3. Molecular Visualization

The visualization of proteins and molecules is an important tool to support the analysis of molecular interactions and processes. However, molecular data is prone to contain errors or some degree of uncertainty (see Section 3.2 for a more detailed discussion). After Richardson [Ric81] motivated the modern way of visualizing molecules and Connolly [Con83] implemented the solvent excluded surface (SES) model, a range of methods emerged, aiming to communicate the properties of molecules via visualization. A specific *line drawing* algorithm for molecules was developed by Lawonn et al. [LKEP14] to highlight salient regions using a hatching-like method. The first UV of proteins was presented by Rheingans and Joshi [RJ99]. To show positional uncertainty, they proposed to either overlay different, semi-transparent configurations of the molecule or to compute a likelihood volume. Similarly, Lee and Varshney [LV02] overlaid semi-transparent molecular surfaces to create a fuzzy surface that shows uncertain parts. Schmidt-Ehrenberg et al. [SBH02] extended the idea of likelihood volumes to show positional uncertainty. However, most modern visualization did not focus on uncertainty in molecular data, as the surveys by Kozlikova et al. [KKF*16] and Krone et al. [KKL*16] show. Different possible states or conformations of proteins are usually shown in ensembles of multiple juxtaposed states [MS16; KJB*17]. This gives an impression of the possible range of conformations that a protein can assume. More recent work by Schulz et al. [SSK*18] addresses UaV (see Section 3.1) of molecular secondary structures. They visualize the data—the result of a secondary structure determination algorithm—and combine it with an uncertainty measure of that data. Maak et al. [MRW*21] propose an all-atom presentation of the atom's positional uncertainty.

3. Background

This section provides background information regarding *Uncertainty-aware Visualization* (Section 3.1) and uncertainty in molecular data (Section 3.2). Here, we clarify why uncertainty information needs to be incorporated in visualizations and what challenges are associated with this task. Further, we motivate our decision to use a molecular visualization scenario for our study.

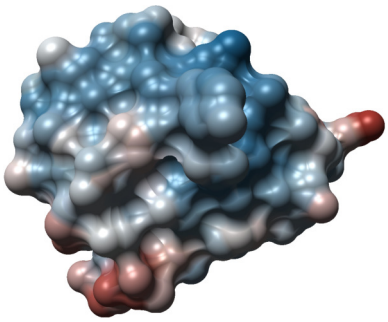


Figure 2: *Solvent Excluded Surface (SES) visualization of a human insulin protein (PDB ID: 3I40) colored by b-factor. Blue areas have low uncertainty while red areas have high uncertainty.*

3.1. Uncertainty-aware Visualization

UV is an important and active topic, as recent publications show [GSWS21; MSH*21; KDJ*21]. A related topic is the visualization of ensembles, i.e., showing multiple possible states of an object to give an impression of the range and occupancy of the whole spectrum of possible states [WHLS19]. The process of creating a visualization usually follows a pipeline that includes the data acquisition, simulation, model transformation, and finally visualization. A common formulation of the visualization pipeline is the one by Haber and McNabb [HM90] that states four steps. The *Data Source* is the result of some data acquisition step. For example, data may be taken via imaging, measurements, or simulation. The *Filtering* follows and may extract and derive additional data from the data source. Then the *Mapping* transforms the data into a renderable representation, e.g., creating actual triangle geometry that can be rendered efficiently by a GPU. Finally, the *Rendering* transforms the renderable data into an image for display to the user.

A problem with visualization is that it imparts information that may be inaccurate, but suggests a level of accuracy and certainty that is not really present in the data. All of the above steps in a rendering pipeline may introduce some error to the final visualization and the viewer may be unaware of that error. *Uncertainty Visualization* attempts to visualize this error explicitly. *Uncertainty-aware Visualization* tries to incorporate these errors or uncertainties into the visualization, e.g., augmenting the visualization of data with the uncertainty associated with it (see the requirements of UaV stated by Gillman et al. [GSWS21]). This is not an easy task, as the uncertainty has to be quantified first and then added to a visualization using a separate information channel. Since common channels—such as color, size, shape, texture, or transparency—are usually occupied by the actual data visualization, stylized lines may provide a way to encode uncertainty. *Visualization of uncertainty* follows the same visualization pipeline where the *Data Acquisition* provides the uncertainty data. Consequently the *visualization of uncertainty* itself introduces an *uncertainty of visualization* that is associated with the last three steps of the pipeline [BAL12].

3.2. Uncertainty in Molecular Data

As mentioned in Section 2.3, uncertainty did not gain much attention in the molecular visualization community until recently. This is

a surprising observation because uncertainty is an inherent property of molecular data [KNL15]. Because atoms are always in a state of thermal mobility, their spatial location is never fixed. As stated by Chung et al. [CBB*16], atomic and molecular calculations should always be accompanied by associated uncertainty measures. Such a positional uncertainty also affects the very common formulation of the SES, because it is directly derived from the atoms' positions, (see Figure 2). In this figure, the surface is colored by the *b-factor*, which describes the thermal vibrations of the individual atoms and is commonly interpreted as a measure of positional uncertainty.

The secondary structure is an abstraction based on atom positions. Atoms that occur in a certain spatial sequence are grouped within a secondary structure element. This group assignment, however, has no ground truth. Different assignment methods may produce different results, but none of them can be described as right or wrong. By deforming the geometry of those structure elements, Schulz et al. [SSK*18] encode the accuracy of the presented group assignment. Uncertainty can also arise from the simulation method. For example, Lindow et al. [LBH18] investigated how the effective atomic radii assumed by a Molecular Dynamics simulation deviate from the VdW radius found in the literature, which can influence the accessibility. Note, that they did not explicitly use UaV in the 3D view, they only showed the radius uncertainty in 2D plots.

These examples show that neither the atom position nor the structural assignment or per-atom accessibility is certain. Thus, molecular visualizations that do not include such uncertainty data are prone to communicate an accuracy of the data that is not actually given. This may lead to situations where the visualization influences the decision-making of the viewer in a wrong way.

As uncertainty is inherent to molecular data, we chose molecular visualization as our scenario for evaluation. We show first that stylized lines open up an untapped information channel to encode scalar data, and second, that such stylized lines can be applied in a domain where additional information channels are needed since most other typical visual channels are usually already occupied.

4. Method

For generating the stylized line drawings, we adapted the Active Strokes method by Bénard et al. [BLC*12]. This method for generating stylized lines consists of three main steps: First, image space lines need to be extracted from the model. The authors recommend the steerable quadrature pair filters by Freeman and Adelson [FA91] and indeed we found that the method is sensitive to the specific line extraction method used. Afterward, samples are extracted from the line drawing. Based on these samples snakes (active contours) [KWT88] are generated to track and vectorize the samples. These snakes rely on a complex set of heuristics to facilitate a faithful approximation of the feature lines for animated sequences. Then, brush paths are created based on the active contours. These brush paths are the base for the final strokes. They provide shape, position, and a temporally coherent parameterization. The last step is to stylize the generated brush strokes. Several stroke attributes such as width, length, and color can be adjusted. Displacement mapping can also be applied to the brush path vertices. Finally, various styles can be achieved by mapping textures to the brush paths. For this purpose, Active Strokes utilize self-similar line artmap (SLAM) textures [BCGF10] as they avoid texture sliding and stroke stretching. This makes styles such as dashed or dotted lines feasible. An overview of the Active Strokes pipeline can be found in Figure 3.

Most of the computations of Active Strokes are executed on the CPU. But as the method is an image space method, data needs to be transferred to the GPU twice. First, the model needs to be rendered as an image space line drawing from which line samples are then extracted to the CPU. Again, at the end of the Active Strokes pipeline, the brush path vertices need to be transferred to the GPU to be rendered. This heavy communication leads to low framerates for more complex models.

We adapted the Active Strokes method to be able to vary the style of the lines according to an underlying scalar field. This is necessary to use them as an additional channel for encoding uncertainty information. First, the uncertainty values are rendered to the surface of the molecule similar to color values. This transforms the scalar values defined on the model's surface from object space to image space. Then, the uncertainty values can be sampled additionally to the other values collected for the line samples by the Active Strokes method. Afterward, the uncertainty values are passed on to the brush path vertices through the Active Strokes pipeline: First from the line samples to the snake vertices and then on to the brush path vertices. Finally, this uncertainty information can be used to alter the stroke attributes. Figure 4 shows several proteins with uncertainty-based line overlays.

5. Line Styles

With the adapted Active Strokes, a wide variety of line styles can be achieved to encode uncertainty. We decided to evaluate the visual variables *sketchiness*, *dashing*, *grayscale*, and *width*.

Sketchiness, *dashing* and *grayscale* or adaptions thereof have been used to display uncertainty in prior works [BBIF12; SMI99; GHL15; GSWD18]. We additionally included *width* in our evaluation. Size as a visual variable for encoding uncertainty in point symbols has already been evaluated by MacEachren et al. [MRO*12]. However, the corresponding variable *width* in line primitives has, to the best of our knowledge, not been investigated yet even though it should be easily achieved in most applications.

Blur, another line variable that has been used for uncertainty visualization was not evaluated in our perceptual study. Applying a blur kernel based on the underlying scalar field to the line drawing is problematic, as neighboring vertices across contours lead to a sudden change in the blurring radius at the center line of the lines. Only blurring directly on the Active strokes leads to an abrupt stop of blurring at the lines' boundaries. In turn, the lines do not appear blurred, but rather like drawn with a grayscale encoding. However, other implementation options should be investigated in the future.

A comparison of the investigated line styles on the same molecule with the same camera perspective can be seen in Figure 1. Figure 5 compares several uncertainty levels encoded with the different line variables on quarter circles.

Sketchiness (Figure 5a): To generate *sketchy* lines, we utilized displacement mapping with the wobbly SLAM textures by Bénard et

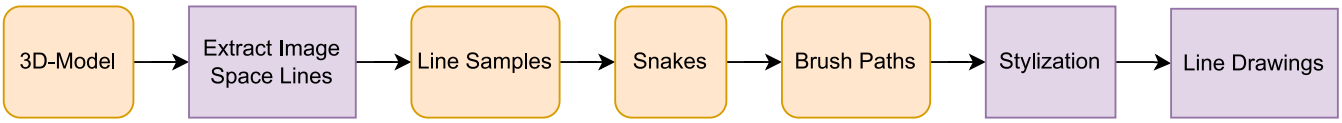
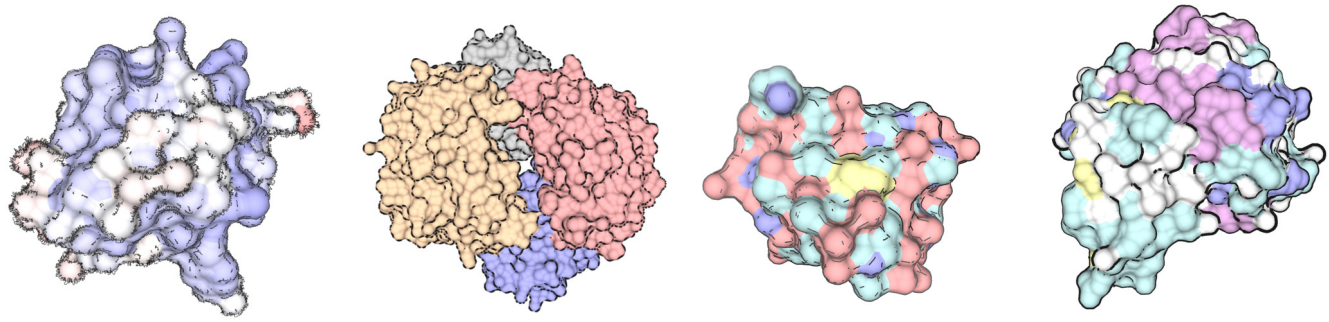


Figure 3: *Active Strokes pipeline. Orange boxes with rounded corners are computed on the CPU while purple boxes with square corners are computed on the GPU. The uncertainty information is passed from the 3D model to the brush paths. It can then be used in the stylization step to create varying line styles depending on the uncertainty at a particular position.*



(a) *Protein 3I40 [TCS*10] colored by b-factor with sketchy lines overlay.*

(b) *Protein 1A3N [TV00] colored by chain with dashed lines overlay.*

(c) *Protein 3I40 [TCS*10] colored by element with grayscale lines overlay.*

(d) *Protein 1I20 [KY98] colored by secondary structure with width lines overlay.*

Figure 4: *Proteins colored by different properties with contours that vary according to the underlying b-factor. The meshes were generated using VMD [HDS96].*

al. [BCGF10]. For higher uncertainty values we scaled the offsets with a factor of up to 20. Higher deviations from the center line encode higher uncertainty. In contrast to Boukhelifa et al. [BBIF12] the frequency of our *sketchy* waves is higher, as lower frequencies can be easily confused for actual geometry (see Figure 6).

Dashing (Figure 5b): The *dashed* lines were generated using SLAM textures with a dot pattern. By stretching the texture along the brush strokes, varying dash lengths can be achieved. It is generally desirable to have long continuous strokes. However, for line styles that depend on stretching textures, the strokes cannot be too long, as every stroke can only have one uncertainty value mapped to the length scaling. Therefore, the length of the brush paths needs to be restricted. For the *dashed* visualizations in this paper, we enforced a maximum brush path length of 10 px. Similar to Boukhelifa et al. [BBIF12], the dashes and gaps of our *dashed* lines grow proportionally. However, their gaps and dashes have the same length while our dashes are longer than the gaps. The reason for this can be seen in Figure 7a. For longer gaps, it gets harder for the viewer to recognize the shape of the object correctly, particularly in three dimensions. The shape is more easily recognizable when utilizing smaller gaps (see Figure 7b). Additionally, we use rounded caps instead of rectangular caps for our dashes. SLAM textures contain small imperfections to ensure temporal coherence [BCGF10]. For SLAM textures with a dot pattern, these imperfections look more organic than for SLAM textures with a rectangular pattern. Therefore, the dot textures, and thus the rounded caps, lead to visually more pleasing results.

Grayscale (Figure 5c): The lines in *grayscale* with varying brightness are black for no uncertainty and white for the highest uncertainty. They have a width of 6 px.

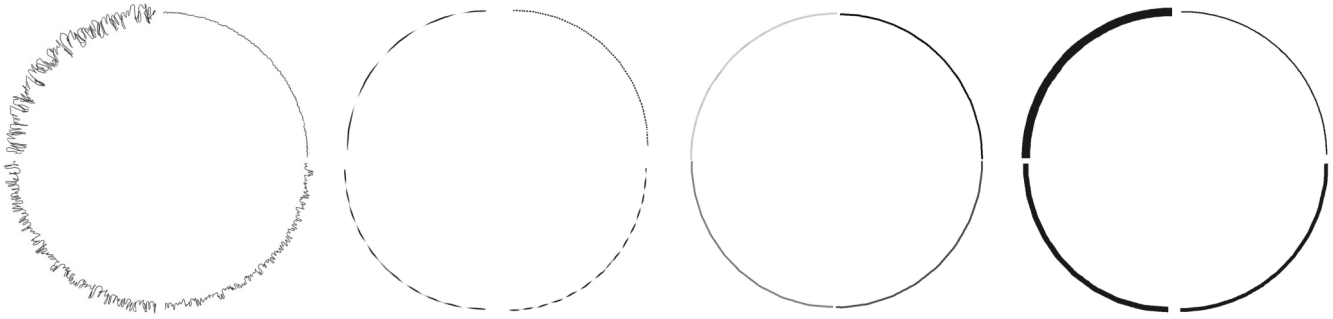
Width (Figure 5d): The *width* can easily be adjusted by scaling the stroke width based on the underlying uncertainty. In our stimuli the line widths range from 3 px to 30 px. We chose to encode higher uncertainty with wider lines as this encoding is probably the least confusing choice for the study participants as there are some similarities to the *sketchiness* variable. There, higher uncertainty is encoded in increased amplitude and thus lines with high uncertainty occupy more space. Additionally, a wider line could indicate more variance in the surface's position. However, one could also argue that certain lines should be drawn wider while uncertain lines should be thinner. Further studies are needed to investigate which encoding is more intuitive or effective.

6. Perceptual Study

To assess the effectiveness of the different line variables, we conducted a perceptual study. We investigated which line variables are best suited for recognizing differences in the underlying scalar field. Below, we describe the experimental setup, the stimuli used, and the recruited participants.

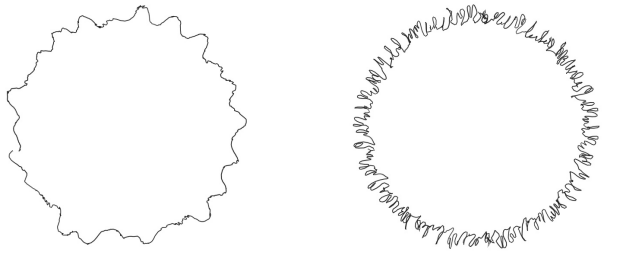
6.1. Experimental Setup

To investigate accuracy and response time, the participants were presented with a set of two-alternative forced choice tasks. Each task consisted of a line rendering with one of the tested variables representing the uncertainty of the underlying model. On the line



(a) *Sketchiness.* **(b)** *Dashing.* **(c)** *Grayscale.* **(d)** *Width.*

Figure 5: *Quarter circles rendered with different uncertainty levels. Starting from the top right in clockwise direction: 5%, 30%, 50%, 80%.*



(a) *Low frequency sketchy waves.* **(b)** *High frequency sketchy waves.*

Figure 6: *Sketchy waves on a sphere. Low frequency waves affect shape perception more than high frequency waves.*

(a) *Gaps and dashes of the same size, rectangular dashes.* **(b)** *Shorter gaps and longer dashes with rounded caps.*

Figure 7: *Longer dashes with shorter gaps facilitate shape recognition.*

rendering, two positions were indicated by arrows. The task of the participants was to point out which position has higher uncertainty. Figure 8 shows an example of one of the stimuli used in the study.

We considered two factors during this study: *Line variable* and *magnitude of the difference* between the uncertainty values at the two tested positions. We chose a within-participant design for both factors. The line variables evaluated were *sketchiness*, *dashing*, *grayscale*, and *width*. For *magnitude*, the differences used ranged from 2% to 80%. We categorized these magnitude values into small (S), medium (M), and large (L) differences. Everything under 10% was considered a small difference S, values between 10% and 40%

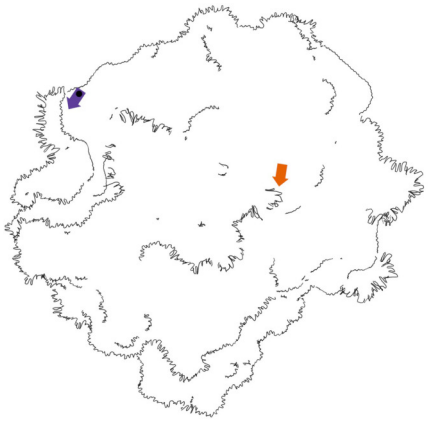


Figure 8: *One of the nine sketchiness stimuli used in the study.*

were considered medium differences M, and everything above 40% was considered a large difference L. Each magnitude class consisted of three instances. In total, we evaluated 36 trials.

6.2. Stimuli Creation

The stimuli were created using three molecular data sets from the protein data bank (PDB): A mutant human lysozym (PDB ID: 1I20 [KY98]), deoxy human hemoglobin (PDB ID: 1A3N [TV00]), and human insulin (PDB ID: 3I40 [TCS*10]). The structures' SES triangle meshes were created with PyMol [Sch] and the lines were rendered using Active Strokes. We used image-space lines generated with steerable filters [FA91] but other feature lines or even lines explicitly placed on the surface could be used.

For each of the three molecules, we selected three camera perspectives and two points on lines on the surface. The camera perspectives and points were chosen such that for every molecule there exists one stimulus for each magnitude category. Each of those scenarios was then rendered with each of the available line variables. The molecules' *b-factors* were used as the positional uncertainty measure on which the variation of the line variables is based.

6.3. Study Procedure

The study was conducted online. The participants were instructed not to use mobile devices for participating and to maximize the study window. First, they were informed about the content and purpose of the study and asked for consent to participate. Next, a questionnaire concerning demographic data had to be answered. Then, the participants were given instructions for the following two-alternative forced choice tasks. Before starting with the main part of the study, the participants were familiarized with the tasks. During the teaching phase, where answers and response time were not recorded, for each line variable one example was given and the corresponding uncertainty encoding was explained. We used a counterbalanced approach for the presentation by pseudo-randomly selecting the stimuli. However, we ensured that two visualizations of the same scenario could not appear consecutively.

6.4. Participants

We recruited a total of 59 participants from various backgrounds. The only condition for participating was to be at least 18 years old. The age of the participants ranged from 18 to 57 years, with a median of 26 years. Two participants reported having the color vision deficiency deuteranopia. However, we designed all the tasks to be colorblind safe. Apart from this, all the participants had normal or corrected to normal vision. Seventeen of the participants were women, 41 men, and one person preferred not to answer. All participants had at least lower secondary education, 85% had a university degree. The majority (36) of participants reported having at least some experience in visualization, with a median of 3.5 years of experience up to a maximum of 16 years. Twenty participants had some experience in molecular biology, with a median of 3 years up to a maximum of 16 years. One might argue that it would have been favorable to only recruit participants that are possible end-users of the visualization method. However, the task did not require specific background knowledge in molecular biology. Therefore, we are convinced that the results are still meaningful, even if only about one-third had this background. Furthermore, there are a variety of possible application scenarios, including but not limited to science communication. We feel that this justifies including a wider range of participants with varying backgrounds. Therefore, even if the visualizations are intended for specific audiences, it is still possible to gain meaningful insights by including participants from the whole population.

7. Results

We evaluated the results of the study using *confidence intervals*, which are supposed to avoid the misinterpretations and dichotomous thinking that are common in *null hypothesis significance testing* techniques [Dra16]. This has been suggested frequently [GA86; Dra16; CC16] and recent publications in visualization and human-computer interaction also use this approach for the evaluation of perceptual studies [HMZ*22]. For both dependent variables—*accuracy* and *response time*—we computed the means and their 95%-confidence intervals. If the 95%-confidence intervals would be repeatedly calculated for different samples from an identical distribution, the population mean would be covered by 95% of those confidence intervals in the long run [GA86]. As recommended by Dragicevic [Dra16], we calculated the confidence intervals by using nonparametric bootstrapping with $10,000$ replicates.

7.1. Accuracy

Figure 9 shows the means and confidence intervals for the accuracy measurements. The graphs show, as expected, that the accuracy increases for larger differences in uncertainty. Interestingly, however, there are only small increases in accuracy between categories M and L. Another interesting finding is that while for M and L, *sketchiness* is among the best performing line variables, it performs the worst in scenario S. Here, the participants seemed to give random answers, as the accuracy is about 0.5. A possible explanation for this is the intrinsic randomness of this line variable. Because of these intrinsic variations, small changes caused by a change in the underlying scalar field might not be noticed anymore. *Grayscale* and *width* seem to lead to better accuracy, while it is unclear if *dashing* does. With a mean accuracy of 0.75 ± 0.06, *width* seems to outperform the other line variables for scenario S. Consequently, this provides good evidence that *width* leads to better results than *sketchiness* and *dashing*. It also seems to outperform *grayscale*, but the effect is likely small.

In scenario M, we were not able to measure a substantial difference in performance between *width* and *sketchiness*. The accuracy of both is about 0.9. There is clear evidence for both techniques to provide better results than *dashing*, which has a mean of 0.78 ± 0.06. They might also work better than *grayscale*, however, here the results are somewhat inconclusive.

For scenario L, the best performing variable seems to be *sketchiness* with a mean of 0.93 ± 0.03. There is only moderate evidence for a difference to *width*, but large evidence for a difference to *grayscale* and *dashing*.

Dashing seems to consistently perform worse than the other methods in scenario L. When comparing the results for the individual stimuli, there is one particularly interesting case (see Figure 10a). This stimuli has a difference in uncertainties of 45% and is, therefore, in the L category. However, when the line variable *dashing* is used for the encoding, the results seem to be just slightly better than guessing (0.58 ± 0.13). All other results have a lot higher accuracies. Possible reasons are imperfections of either the line generating method or the input model. Figure 10c shows fragmentation of the line at the location of one of the test positions (orange arrow). This is an artifact of either the line generating method or the underlying polyhedral model and does probably not overly influence the shape perception nor the line variables *width*, *grayscale* and *sketchiness*. For the *dashing* method, in contrast, it can become a confounding factor, as it interacts with the *dashing* pattern. Consequently, fragmentation can easily be misunderstood as a variation in uncertainty. While this particular example is due to implementation issues in either the Active Strokes method or PyMol's mesh generation, even perfect methods would still generate feature lines that are very short at some points and longer at others. Thus, the accuracy while using the *dashing* variable could probably be improved by using other algorithms, nonetheless, the problem would persist to some extent.

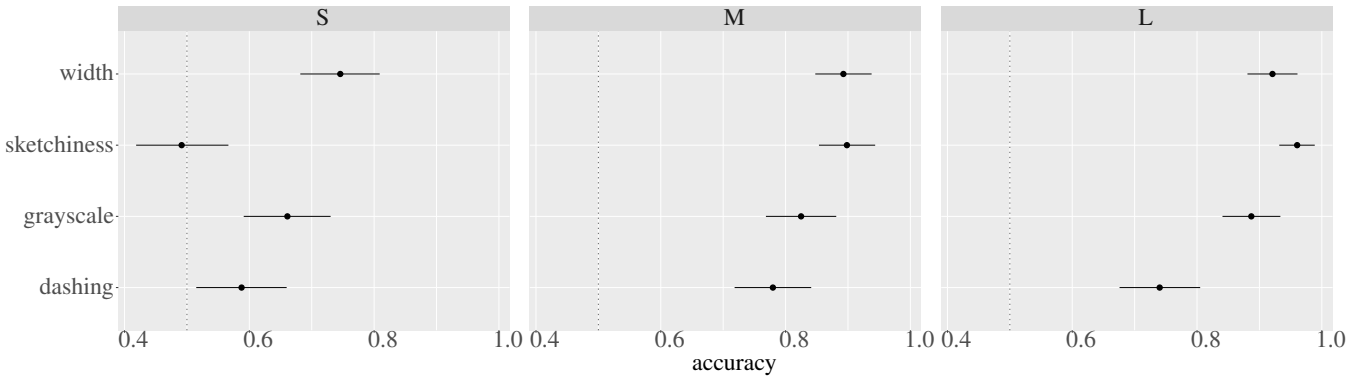
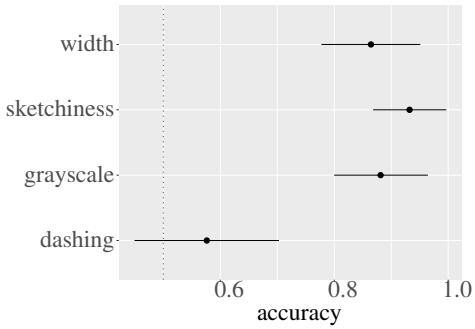
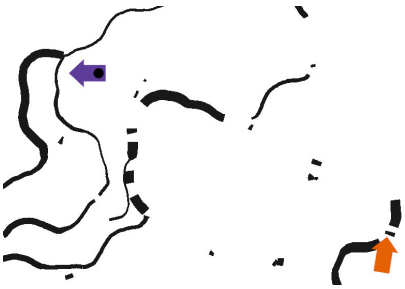


Figure 9: *Means and 95%-confidence intervals for the accuracy measurements. At an accuracy of 0.5 (dotted line) or lower, it can be assumed that the answers have been guessed randomly. From left to right small, medium, and large differences in uncertainty values.*



(a) *Means and 95%-confidence intervals. At an accuracy of 0.5 (dotted line) or lower, it can be assumed that the answers have been guessed randomly.*

(b) *Dashing stimulus.*



(c) *Width stimulus.*

Figure 10: *Accuracy measurements and dashing and width stimuli of scenario L on the molecule 3I40.*

7.2. Response Time

To analyze the recorded response times, we used a log transform on our data to ensure approximate normality. The results presented in Figure 11 have been inverse transformed to the original scale after the calculations. Therefore, the reported means are geometric instead of arithmetic and we report ratios between means instead of differences [GA86]. We removed two extreme outliers from the dataset, where the response time was over five minutes (since we believe that the participants were interrupted by another task in these two cases). All other response times were under 80 seconds.

The response times get shorter for scenarios with bigger differences in uncertainty for all methods except for *dashing*. For the *dashing* method, we were not able to measure an effect of the magnitude of the uncertainty difference on the response time. The reasons for this might be similar to the reasons for the worse accuracy (see Section 7.1).

In class S, the effects of the different line variables on the response time (approx. 8 s) seem to be largely similar. For the medium differences in uncertainty in class M, all techniques except for maybe *dashing* lead to largely similar response times (approx. 6 s). Comparing uncertainties with *dashing* seems to take approx. 7 *s*. Finally, in class L, *width*, *sketchiness*, and *grayscale* can be assessed in about 5 *s*. There is a lot of evidence for *dashing* to lead to slower assessment at around 7.3 *s*.

7.3. Summary and Conclusion

To summarize, our perceptual evaluation gives strong evidence that the line variable *width* seems to be a good choice for facilitating comparisons between several uncertainty values on molecular surfaces. Additionally, *sketchiness* also seems to work very well, as long as the differences in uncertainty do not become too small. According to this evaluation, *grayscale* does also seem suited. However, *dashing* does not seem very suited as it mostly leads to lower accuracy than the other techniques as well as requiring longer response times. Apart from *dashing*, all other tested line variables seem to elicit similar response times. *dashing* is probably most sensitive to the continuity and quality of the input lines, which are also subject to the underlying geometry.

7.4. Limitations

Our results presented in the last sections do have some limitations. Firstly, it is unclear if the results would be similar for models where

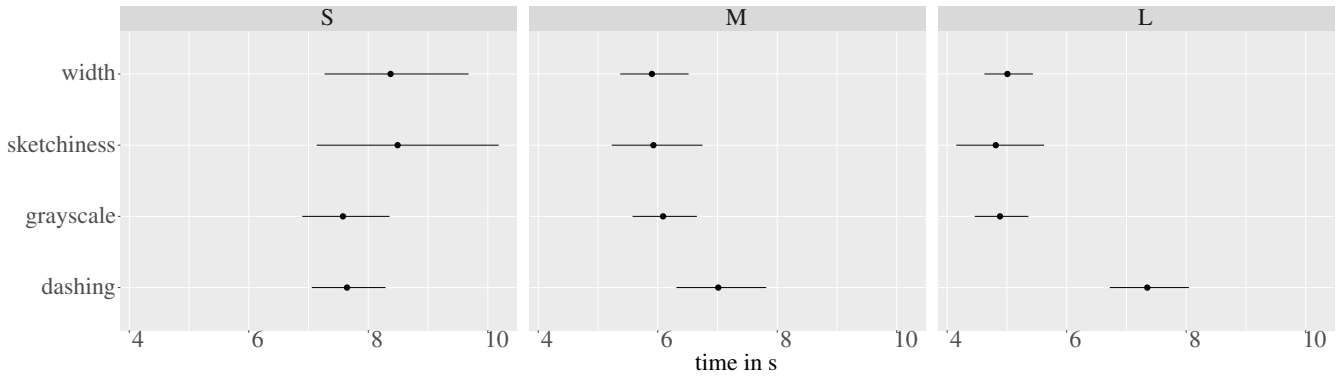


Figure 11: *Geometric means and 95%-confidence intervals for the response time measurements. From left to right small, medium, and large differences in uncertainty values.*

an additional property is encoded in the surface's color. This is very important for most molecular visualizations since properties such as charge or atom type typically need to be displayed as well to allow for a comprehensive analysis. We expect some interference, especially with the *grayscale* technique. Besides, when using the *grayscale* technique over colored surfaces, one would need to further distinguish between varying the value and opacity, which, for white backgrounds, result in the same effect.

A possible limitation for *width* might be, that it is commonly used for encoding the proximity of the viewer to the surface. It would be interesting to investigate if using *width* for encoding uncertainty affects the depth perception or vice versa if higher uncertainty might be confused for higher proximity to the surface.

Although we provided evidence against the use of *dashing*, other varieties of *dashing* might produce more promising results. Moreover, fragmentation in the feature lines, either due to the underlying polyhedral mesh or the Active Strokes method, is harmful to conveying uncertainty values through *dashing*. Feature lines generated with smoother models (e.g. using ray-casting) or an improved line generation algorithm could lead to better accuracies for dashing.

Furthermore, we only evaluated nine scenarios. A follow-up study with more trials could be conducted to represent more of the variance present in different molecular surfaces, camera perspectives, and line positions. We evaluated the line variables for the SES representation of the molecules only. The results might translate to other molecular representations like the popular cartoon model. However, this was beyond the scope of our study and would need to be assessed in further follow-up studies. While feature lines occupy little space and are therefore an interesting visual channel to use, they therefore also tend to be sparse in some regions. Further evaluations should investigate, whether portraying uncertainty information on the lines only is sufficient for the perception of uncertainty in all areas of the molecule.

Finally, other interesting questions could be evaluated in other studies, such as the intuitiveness of the line variables. It would also be interesting to determine how many different levels of uncertainty can be expected to be expressed by varying one line variable.

8. Discussion and Future Work

We presented a new type of Uncertainty-aware Visualization (UaV) for biomolecules. Stylizable lines are used to encode uncertainty into line variables. Therefore, we adapted Active Strokes [BLC*12] to allow a variation based on an underlying scalar field on the surface of a 3D model. More concretely, we applied our method to map uncertainty to the Solvent Excluded Surface (SES), a commonly used smooth molecular surface representation. However, the task did not require a background in molecular biology. We conducted a perceptual study to evaluate accuracy and response time for the four line variables *sketchiness*, *dashing*, *grayscale*, and *width*. We conclude that *width* provides consistently good results. *Sketchiness* seems to also work well if the difference in uncertainty is not too low. *Grayscale* also seems to be suited. The evaluation suggests that while *dashing* does probably lead to worse results than *width*, it still has acceptable accuracy. However, *dashing* does not seem to elicit a high accuracy. Of all the tested line variables it also appears to lead to the slowest response times. For *dashing*, the quality of the input lines—especially the connectivity—appears to be crucial, making it less feasible than the other methods in our scenario.

This is in line with findings by Boukhelifa et al. [BBIF12], who could only find three perceptually distinct levels for dashing, while they found four levels for *grayscale*, *sketchiness*, and *blur*. However, they also reported that the perception of sketchy lines was in general less accurate than for *grayscale*, *dashing*, and *blur* which could not be seen in our results. A possible reason is that we used *sketchiness* with a high frequency to avoid misinterpretations of the geometry in contrast to their low frequency lines.

In future work we would also like to investigate other line styles, especially *blur*. Additionally, combinations of line variables, e.g., dashed sketchy waves or *dashing* as a more uncertain extension to width could be evaluated. It would also be interesting to evaluate other properties of the line variables for uncertainty visualization. The intuitiveness of the line variables could be analyzed or it could be determined how many different levels of the line variables' magnitude can be distinguished. It should also be investigated if a varying line style interferes with the perception of other properties. Furthermore, people's preferences could be evaluated analogously to prior work on feature lines [LBSP14].

Additionally, the generation of stylized lines should be improved. Active Strokes rely on a lot of heuristics and because of their heavy use of communication between GPU and CPU, they are not temporally coherent for medium-sized models. Therefore, a new method would be beneficial for using stylized lines in future biomolecular applications.

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