Illustrative Timelapse: A Technique for Illustrative Visualization of Particle-Based Simulations

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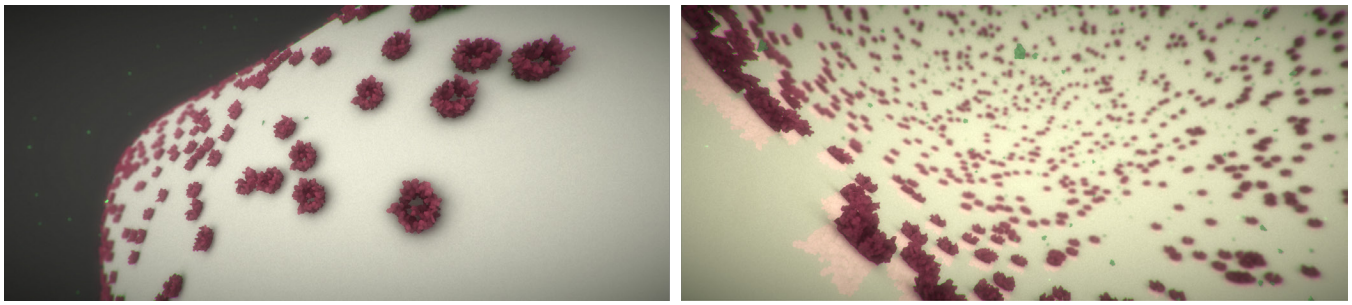


Figure 1: Screen capture of our Illustrative Timelapse method depicting an outer mitochondrial membrane and featuring adenosine triphosphate (ATP) molecules (in green) crossing larger voltage-dependent anion channels (VDAC) proteins (in dark red). Our real-time technique lets us observe results of mesoscale particle simulation in fast-forward while showcasing perceivable moving molecules and a scene full of stochastic motion and interactions

ABSTRACT

Animated movies are a popular way to communicate complex phenomena in cell biology to the broad audience. Animation artists apply sophisticated illustration techniques to communicate a story, while trying to maintain a realistic representation of a complex dynamic environment. Since such hand-crafted animations are time-consuming and cost-intensive to create, our goal is to formalize illustration techniques used by artists to facilitate the automatic creation of visualizations generated from particle-based molecular simulations. Our technique *Illustrative Timelapse* supports visual exploration of complex biochemical processes in dynamic environments by (1) seamless temporal zooming to observe phenomena in different temporal resolutions, (2) visual abstraction of molecular trajectories to ensure that observers are able to visually follow the main actors, (3) increased visual focus on events of interest, and (4) lens effects to preserve a realistic representation of the environment in the context. Results from a first user study indicate that visual abstraction of trajectories improves the ability to follow a story and is also appreciated by users. Lens effects increased the perceived amount of molecular motion in the environment while trading off traceability of individual molecules.

Index Terms: I.3.7 [COMPUTER GRAPHICS]: Three-Dimensional Graphics and Realism—Animation; I.6.3 [SIMULATION AND MODELING]: Applications—

1 INTRODUCTION

In molecular biology, visual explanations such as still images and animated movies are often employed to describe how things work to a lay audience. Empirical studies have also shown that animations are helpful for a better understanding of molecular biology on the academic level [15]. Over the last years, animated movies have become increasingly popular thanks to the introduction of tools such as *ePMV* [16] or *Molecular Maya* [2], easing the import of molecular structures into 3D animation packages. But despite these special-purpose modeling tools, scientific movies are usually still created via hand-crafted key-frame animation, which is tedious, time consuming and therefore can be very expensive, too. The lack of automated techniques clearly hampers the communication of the outcome from biological sciences to the general audience.

In order to improve the way the visual communication is traditionally being made, visualization scientists have experimented with the use of data from computational biology to reproduce dynamic and 3D mesoscale environments. A commonly employed technique is mesoscale particle-based simulation, since it features information about the type and the location of each single molecule over a time-course. This technique was initially developed for systems biologists to study spatial and quantitative properties of biological pathway models.

Direct visualization of the simulation results consist of displaying particle positions on screen, and consecutively for each simulated step. Because particle simulations operate at very small time steps, typically of the order of nanoseconds, the resulting number of steps can often be very large. Observing an entire biochemical process can therefore lead to overly long visualization sequences. Moreover, many processes feature disparities between diffusion rates and reaction rates. Consequently, the interest of viewing such sequences entirely is also arguable, because only a few frames feature events of interest such as molecular interactions.

To shorten the duration of the visualization, it is common to only display simulation frames spaced at a constant given interval. This is usually referred to as *fast-forward* or *timelapse*. However, when using large lapses, the scene may exhibit visual clutter because of the accelerated motion of particles, diffusing in a chaotic and crowded environment. As a result, one can hardly keep track of individual elements throughout consecutive frames, which may be an unpleasant experience and cause a misinterpretation of the scene.

We present *Illustrative Timelapse*, a novel technique to reduce visual clutter caused by dynamic fast-forward visualization of molecular simulation data. Illustrative Timelapse supports seamless temporal zooming and ensures that on any zoom level the motion trajectory of scene elements can be followed by the gaze of human observers. Our technique is inspired by hand-crafted animated illustration techniques that use spatial smoothing of trajec-

tories to guarantee that viewers are able to trace elements of interest. Similarly, Illustrative Timelapse performs trajectory smoothing so that each element is below the maximum velocity that can be followed and tracked by smooth pursuit eye movements. As a result, we obtain a smooth and easily perceivable motion of individual molecules, while remaining in the vicinity of their original motion in accordance to underlying scientific data (Figure 1). We also observed that some artists made the choice of blending abstracted views together with realistic views in order to enhance the viewer's comprehension (see, for instance, work by Drew Berry [5]). Illustrative Timelapse therefore uses a lens system that seamlessly merges the abstracted dynamic visualization with the unmodified fast-forward simulation data to lower the risk of misinterpretation in diffusion speed. We demonstrate Illustrative Timelapse on a real biological model, and assess its effectiveness through a user study.

2 Related Work

We structure the prior work review in two parts. In the first part we relate with research about biology and techniques that employ computational biology to generate illustrative visualizations. In the second part we provide a broader overview of techniques used in different time-dependent visualization and video-based graphics research areas.

2.1 Mesoscale Cellular Visualization

There have been several mesoscale particle-based modeling and simulation tools described in the literature, including *MCell* [24], *Smoldyn* [4] or more recently the *Cellular Dynamic Simulator* [6]. They all feature graphics modules to showcase the results of the simulation. Among those tools, MCell has one of the most advanced visualization modules, *CellBlender* [1], which is a plug-in for *Blender*, a 3D animation package commonly used by 3D artists. The module was introduced to ease the creation of models for MCell by bridging 3D modeling and biological modeling in one single powerful tool. It allows for direct visualization of the particles embedded in their cellular structures represented as 3D meshes (see Figure 2). However, direct visualization of particle-based simulation is mostly intended as a visual support for expert users in their modeling task. The outcome exhibits high visual complexity due to the large number of visualized particles and their diffusion driven chaotic organization, which is impractical for dissemination of biological sciences to a broader audience. Moreover, in case of large temporal simulations it is quite cumbersome to loop over all the frames to locate and understand the events of interest.

Falk et al. [8] presented a tool which reads the results of a particle-based simulation and enables interactive visual exploration of the results. The aim of their visualization is to describe the process of signal transduction on both mesoscopic, and molecular level. The individual molecules are represented in 3D space as spherical glyphs, and their positions are updated over time according to the simulation values. The tool also allows the user to track specific particle inside a cell. The trajectory is represented as a trail in 3D space providing information about directions and reactions. In addition, they employ depth-of-field and depth cues, encoded as a color gradient, to emphasize molecules and their trajectories. This represents a useful focus+context visualization technique, which helps to guide attention in crowded cellular environments. In our work, we employ focus+context techniques not only to filter the visual appearance, but also the level of detail of dynamic properties. In a follow-up work, Falk et al. [9] developed a new technique to improve visualization of large mesoscopic cellular models to observe particle simulations together with real molecular structure data. The entire scene is processed by means of ray casting of spheres, which is efficiently performed on the underlying grid structures holding the molecular positions. Additionally, each molecule has its own supporting grid, which is then traversed based on the given level of detail manner. The authors achieved 3.6 frames per second for scenes containing 25×10^9 atoms.

More recently, Le Muzic et al. [21] proposed a new type of particle systems designed for illustrative visualization of molecular reactions. The main idea behind this work was to show sequences of molecular reactions from a biological model in real-time. This task is challenging with a particle-based approach, due to the stochastic behavior of the particles. They use quantitative simulations instead, to control passive agents and force them to react directly in the viewport. They also use arbitrarily defined diffusion rates in order to perceive moving elements more easily. While the location of elements and reaction is chosen based on illustrative considerations, the quantities and reactions rates remain in accordance with real scientific data. Moreover due to lightweight computation of quantitative models, the simulation is able to run in parallel, where traditional particle approach has to be precomputed. They also proposed a rendering technique capable of rendering fully dynamic molecules without any supporting grid structure, where the reported performance was 10 frames per second for scenes contaitning ca. 3×10^{10} atoms.

The later work adopted a new approach, more oriented towards storytelling rather than strict scientific exploration. However the fact that diffusion rates and thus spatial location of particles are not depicted realistically may lead to misconceptions in audience non familiar with the topic. Only particle-based simulation tools are able to provide this information and yet there is still no elegant solution available that could automatically generate explanatory animated visuals out of this type of data. This work is an attempt to fill the gap left in this domain; with Illustrative Timelapse we aim at providing an interactive and educational tool for spatio-temporal exploration of mesocale particle-based simulations. By adopting illustration techniques from animations and videos, we provide a new way to present complex molecular scenes from particle-based simulations, to achieve a maximum degree of understanding for a broad audience.

2.2 Time-dependent Visualization

In general, time-dependent data can be visualized using either a static or a dynamic representation [3]. While in the information visualization domain static representations are far more common, we explore challenges arising when using dynamic representations in this paper. Wolter et al. [27] presented a model for time-varying visualizations utilizing dynamic representations. In their model, they distinguish between *user time* (the real time we perceive), *simulation time* (time changes in the simulated process), and *visualization time* (a normalized time frame for showing the complete simulation). They demonstrate their model on scientific simulation data that can be visualized with interactively changable temporal resolutions. However, they do not abstract the resulting dynamic visualization in case the processes cannot be followed by human observers any more, due to large velocities in low temporal resolutions.

While there is little related work on visual abstraction techniques for dynamic visualizations, video-based graphics research addresses a conceptually similar challenge to create short video synopses out of long input videos. *Adaptive fast-forward*, for instance, chooses an optimal playback speed based on the estimated information density in the input video to create compact surveillance camera streams [12]. Instead of dropping uninformative frames to create a video synopsis, *Space-Time Video Montage* [17] and *Dynamic Video Synopsis* [23] extract and reassemble informative space-time portions into a smaller video space-time volume. These techniques work well if the input video contains longer temporal sequences or spatial regions of low information density. However, this is not the case in molecular simulations, where the entire environment is filled with constantly moving elements.

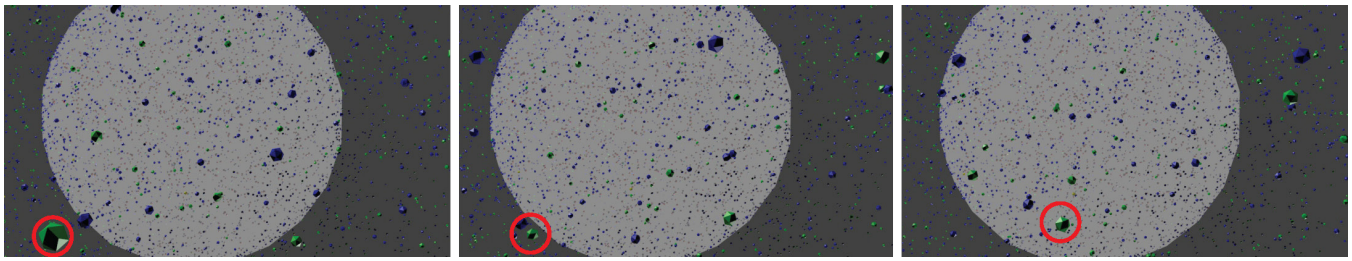


Figure 2: Three consecutive frames of a MCell based simulation visualized using CellBlender. When directly visualizing the molecular positions obtained from the simulation data, it is very challenging to track the molecules in consecutive time steps (cf., red circle).

An extreme case of video synopsis is the compression of a short input video into a single still image. This can be achieved by merging multiple frames with salient content into a static image [25], by visualizing clustered movement trajectories of tracked elments in surveillance streams [13], or a combination of these two approaches [20]. Nevertheless, our goal is to preserve the dynamic representation so users can obtain a deeper understanding of the temporal properties of biochemical processes, as opposed to static representations commonly found in biology text books.

To reduce visual clutter in fast-forward videos, Höferlin et al. [14] investigated different methods to represent elements with high velocities. According to their empirical findings, simple dropping of frames without any visual abstraction led to the best performance when users were asked to detect a specific object in the surveillance video, as well as subjectively rate the motion perception of objects in the video. The videos used in their study were sped-up by a factor of 10 and 20, respectively, and scene elements like pedestrians or cars could still be easily traced without any visual abstraction. In contrast, in molecular simulations, movement speed of individual elements and the duration of a sequence of reactions involved in biochemical processes often differ in a factor of 100 and more. With these speed differences, simple frame dropping, as well as conventional visual abstraction methods like motion blur, fail to preserve traceable object trajectories.

First-person hyper-lapse videos create stabilized fast-forward videos of helmet camera recordings by reconstructing and smoothing the 3D camera trajectory [18]. In our work, we adopt the concept of spatio-temporal trajectory smoothing to create smooth fast-forward visualizations of long input data. However, we smooth the trajectories of the scene elements instead of the camera path. In addition, we ensure that the user is provided with a visual reference to the original speed to prevent extensive misinterpretations of the movement properties of the involved actors.

3 Requirement Analysis

Visualization of particle-based molecular simulations aims at providing a better understanding of cell biology by means of realistic representations [8]. Despite the overall chaos of the output, it reveals important features, such as quantities, spatial distribution, scales, and motion. Most complex biochemical processes also comprise at least two temporal scales: local (e.g., the behavior of a single molecule at a certain time) and global (the entire process that is simulated). While molecules are constantly moving by a constant displacement in every simulation frame, on the other hand, physiologically meaningful interactions may only be happening every 100 step, for instance. So in the case of large simulations ($> 10^5$ frames), it would be quite inefficient and cumbersome to observe the entire sequences of frames. However, speeding up the animation so that more interesting events are happening within a reasonable amount of time would result in a chaotic unwatchable animation. Indeed, individual molecules are moving so quickly between two consecutive frames, that it becomes impossible for a human observer to follow them, as indicated in Figure 2.

Instead of employing molecular simulations, scientific illustrators hand-craft animated visualizations to ensure that the essential information is intuitively presented to the viewer. For instance, in the movie *Apoptosis* made by Drew Berry [5], which is depicted in Figure 3, exemplary reactions in the foreground are slowed down and emphasized, while elements in the background are moving with very high velocity. When watching the video one gets the impression of a very fast overall particle motion, but in reality this impression is a carefully crafted illusion. Assuming the constancy among the shown molecular species, the viewer adopts an impression that the foreground elements are behaving in the same way as the same species in the background, and perceives these as moving similarly fast. We encourage the interested viewer to playback the respective animation for better understanding of this technique.

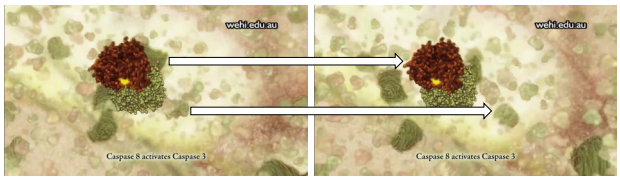


Figure 3: Screenshot of frame m and $m+3$ of a molecular animation [5]. Mind how the main reaction is forced to remain fairly stationary (upper arrow), while molecules in the background move very quickly (lower arrow).

Inspired by such hand-crafted animations, we formulated four requirements for the automatic creation of illustrative visualizations from particle-based molecular simulations:

R1: The visualization should show the simulated process in a reasonable amount of time, irrespective of the number of simulation frames. The duration of the visualization can either be predefined (for instance, to be part of a scientific movie with predefined length) or interactively chosen by the user.

R2: Secondly, it has to be possible to keep track of individual elements in the visualization—especially those with a high degree of interest at a certain time. This means that there should be a maximum velocity of elements in the resulting visualization, so that human observers can visually trace them.

R3: Thirdly, visibility of events with high degree of interest (e.g., molecular reactions or channel protein transfers) should be guaranteed. Reactions are usually represented as punctual events in particle simulations and therefore might be difficult to perceive because they do not last longer than a simulation step.

R4: Fourthly, the visualization should be as realistic and detailed as possible. This requirement is in accordance with the results of a study by Jenkinson et al. [15], which demonstrated that a more realistic depiction of a process can enhance the viewer's understanding compared to a highly abstracted one.

Clearly, these requirements partially contradict each other: A realistic representation of a visualization with a low temporal resolution will lead to large displacements—and, as a consequence, velocities—of individual elements, violating R2. Hand-crafted animations, like the one shown in Figure 3, have demonstrated that there are ways to visually trade fidelity against an appealing representation to create animations that are valuable for a general audience. What is missing is a formalism to apply these artistic principles to visualizations that are automatically generated from scientific simulation data. The goal of Illustrative Timelapse is therefore to find a trade-off to at least partially satisfy all four requirements for the automatic production of illustrative visualizations from particle-based molecular simulations.

4 Illustrative Timelapse

Illustrative Timelapse is an illustrative visualization technique for semantic zooming [22] in the temporal domain. Its concept is based on the the deformation of time exemplified, for instance, in the animation of Drew Berry [5] shown in Figure 3. The motion pattern is selectively simplified in order to convey a particle's trajectory in a clearly understandable motion, rather than representing the entire particle path, which could not be traced by human observers anyway. This selective abstraction can be applied globally to the entire scene, within a dedicated region in the scene, or as a function of eye-space depth.

Illustrative Timelapse performs four operations to fulfill the requirements formulated above:

1. **Temporal zooming** allows users to interactively change the temporal resolution of the visualization at run-time (Section 4.1).
2. **Visual abstraction** smooths the particles' movements according to the temporal resolution (Section 4.2).
3. **Emphasizing** ensures that important reactions are visualized for a minimum duration and visually stand out (Section 4.3).
4. **Lens effects** preserve non-abstracted movements in the context, so that a more realistic impression of molecular motion is depicted (Section 4.4).

With these operations, Illustrative Timelapse supports visual exploration of complex phenonema in a user-defined time frame ($\rightarrow$ R1), trading visualization realism ($\rightarrow$ R4) against good visibility of important events ($\rightarrow$ R3) and easily perceivable velocities ($\rightarrow$ R2).

4.1 Temporal Zooming

As input, our technique uses particle-based simulation data obtained from computational biology. Let us assume that the input particle simulation contains N frames, where each frame represents a discrete step in the simulation of Δt. Each frame contains a set of molecules (particles) given by their type and position. In addition, information about the reactions (type, time, location, and participants) is provided by the simulation tool, which defines the changes in molecular states between frames.

To visualize such a simulation, we map these N simulation frames into a new set of $M \leq N$ visualization frames. The number of visualization frames can be chosen so that $M = d \cdot f$, where d is the desired duration of the output visualization in seconds and f is the number of visualized frames per second. The smaller the desired duration d, the lower the temporal resolution of the visualization and the larger the displacement of elements between consecutive visualization frames. Alternatively, users can directly change the temporal resolution during run-time—for instance when first watching the simulation in a low temporal resolution to get an overview and subsequently zooming in to observe parts of the simulation in more detail. The number of visualization frames would then be $M = \frac{N}{z}$, where $z \geq 1$ is the temporal zoom factor.

For each visualization frame $m \in \{1, \ldots, M\}$, the corresponding simulation frame $n = m\frac{N}{M}$ is obtained from the simulation data. When directly visualizing all the simulation steps so that $M = N$, each visualization element's position $p[m]$ directly corresponds to the position $b[n]$ from the simulation data. Otherwise, we use nearest-neighbor interpolation to determine $p[m]$ from the simulation data.

4.2 Visual Abstraction

From psychology research, it is well known that there is a lower and an upper velocity limit a human observer is able to follow with an uninterrupted, smooth eye movement (*smooth pursuit*). For the upper limit, this threshold lies at 50° to 70° of visual angle per second for predictable trajectories [7], while unpredictable ones need to be slower to be trackable [28]. Since Brownian motion is clearly unpredictable, this means that the amount of displacement per element and frame should be significantly below this $50°/s$ threshold if we want to ensure that viewers are able to follow individual elements with smooth pursuit eye movements. Assuming a visualization frame rate of 60 Hz, a monitor resolution of 110 ppi, and an optimal distance between user and monitor of ~ 60 cm, elements should be displaced significantly less than ~ 40 pixels per frame to stay clearly below this maximum velocity threshold.

We reduce the speed of the particles by smoothing their motion trails, while remaining in the vicinity of their original trajectories. We formulate the smoothing as an Infinite Impulse Response (IIR) low-pass filter in the following form:

$$p[m] = (1-\rho)p[m-1] + \rho b[n], \tag{1}$$

where m refers to the current visualization frame, n to the corresponding simulation frame, $p[m-1]$ is the smoothed 3D position of the particle in the previous visualization frame, and $b[n]$ is the discrete 3D trajectory position obtained from the simulation. The displacement magnitude $\rho \in [\rho_{min}, 1]$ is chosen according to the selected temporal resolution, where ρ_{min} corresponds to an arbitrarily defined minimum value of ρ.

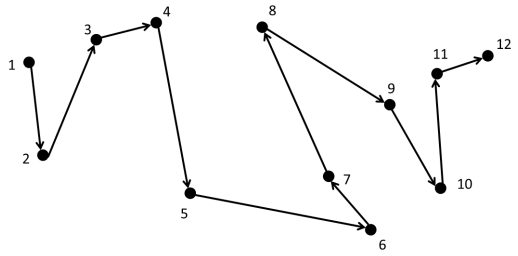
The smooth signal thus is obtained by blending the result of the previous output of the filter (i.e., $p[m-1]$) with the Brownian motion specified by the simulation (i.e., $b[n]$), as illustrated in Figure 4. The IIR-filter coefficients $c_1 = (1-\rho)$ and $c_2 = \rho$ are given by the speed reduction factor ρ. This method is also used in eye tracking research to improve the stability of gaze-controlled cursors [29].

4.3 Reactions Emphasis

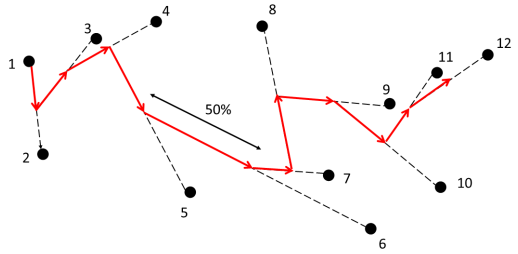
In particle-based simulations, changes in molecular states, e.g., creation, consumption, or membrane crossing, are the results of molecular reactions. As a consequence, such events can greatly enhance the viewer's comprehension of the underlying process. This is why they are often depicted very explicitly in illustrated movies (see, for instance, the connected brown and green macromolecules in Figure 3).

However, in the simulation, reactions are represented as punctual events that only take place in a single simulation step, which is very short and can therefore be hard to perceive. Thus, when creating a visualization in low temporal resolution (fast-forward), reactions will likely be filtered out because they often take place between two visualized lapses. As a result in the visualization, molecules will suddenly change state, without providing any hint about how it occurred or which molecules it reacted with.

We therefore prolong the duration of the reactions, to make them stand out and to inform the viewer about the nature these events. Prior to the visualization, we gather reactions information from the simulation in order to know exactly when a reaction is about to



(a)



(b)

Figure 4: A sample movement trajectory over 12 frames: (a) the original trajectory ($\rho = 1$), and (b) a smoothed version visualized in red ($\rho = 0.5$) which is equivalent to a displacement reduction of 50% of the distance between the current position and the next sampled point on the trajectory.

occur. Reacting elements are then attracted toward the reaction location. Attraction between reaction partners is done by replacing the original trajectory position by the reaction location in the speed reduction formula. Therefore, in the case of an ongoing reaction, the speed reduction factor is also responsible for the reaction duration since it controls how fast molecules are moving. Once reacting elements are located within a minimum distance from their destination, the reaction is signaled by color highlighting. After the reaction, the products again regain a normal behaviour.

4.4 Lens Effects

To preserve a realistic impression of molecular motion despite trajectory smoothing, we introduce a temporal focus+context technique that applies visual abstraction of molecular trajectories solely in the foreground (focus), while showing more realistic—yet often untraceable—motion in the background (context). With a lens effect, parameter ρ (Eq. 1) is dynamically adjusted according to some lens-specific rules. We introduce two lens effects: the **world lens** (Section 4.4.1) adjusts ρ based on the world-space distance to a movable spherical lens, while the **maximum velocity lens** (Section 4.4.2) reduces ρ dynamically, based on an element's displacement in screen space between two consecutive frames.

4.4.1 World Lens

We represent the world lens as a two-layered sphere with an inner radius surrounding the focus region, and an outer radius beyond which we define the context region. The area between the inner and outer radius represents a smooth transition between both regions. We fixed the center of the sphere to the camera position, so that objects with increasing distance from the camera and screen center, respectively, are less abstracted. The world lens concept can be compared with well-known focus+context techniques from the spatial domain, like *fisheye views* [11], which increase the spatial zoom level locally, while preserving an overview in the periphery. Note that the world lens does not affect the temporal zoom level itself, but rather acts as a spatial filter on the amount of visual abstraction applied on the movement trajectories.

The displacement magnitude ρ (Eq. 1) is defined with respect to the element's distance to the world lens as follows:

$$\rho = \begin{cases} \rho_{min}, & \text{if } d \leq r_1 \\ \frac{d-r_1}{r_2-r_1}(1-\rho_{min})+\rho_{min} & \text{if } d > r_1 \text{ and } d \leq r_2 \\ 1, & \text{if } d > r_2, \end{cases} \quad (2)$$

where d is the distance between the particle and the center of the lens and r_1 and r_2 correspond to the inner and outer radius of the 3D lens, respectively. The region between the inner and outer radius is responsible for the soft boundaries of the lens. Coupled with a depth-of-field blur, the world lens mimics an effect often used in animations (compare, for instance, Figure 3). Figure 5 illustrates the effect of the world lens on the visualized particle trajectories.

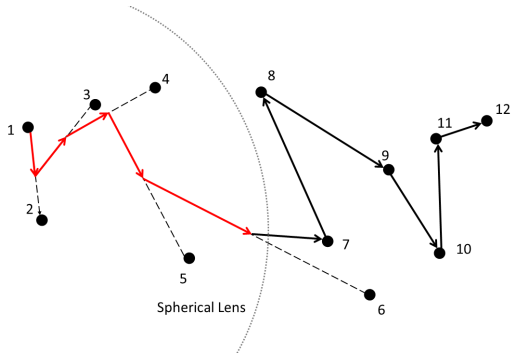


Figure 5: Visual abstraction (red trails) within the world lens (illustrated with outer radius only).

4.4.2 Maximum Velocity Lens

We define the second lens effect by limiting the displacement of molecules between consecutive frames. The user defines a maximum displacement threshold in screen space (d_{max}), which should typically lie clearly below the maximum smooth pursuit velocity threshold (cf., Section 4.2). The displacement magnitude ρ is then defined as follows:

$$\rho = min\{\frac{d_{max}}{\|b^*[n] - p^*[m-1]\|}, 1\}, \quad (3)$$

where $p^*[m-1]$ and $b^*[n]$ are the particle's previous position in the visualization and current position in the simulation, respectively, mapped to 2D screen space. In contrast to the world lens, the amount of visual abstraction is hereby defined solely by the element's trajectory, not its position in world space (see Figure 6).

When using a perspective projection in the visualization, this maximum velocity lens automatically leads to the effect that elements close to the camera appear to move much slower than those further away in z direction. This illusion is due to the differences in size and displacement of particles that are located in the background. Since, in fact, particles move at the same screen velocity, we can achieve a more harmonious effect than with the world lens.

While the world lens requires educated guesses for the maximum amount of visual abstraction (ρ_{min} in Eq. 2), as well as the radii of

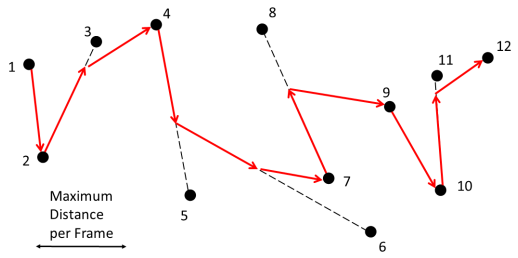


Figure 6: Dynamic displacement reduction based on screen-space distance.

the spherical lens (r_1 and r_2 in Eq. 2) for different temporal resolutions, the maximum velocity lens is defined by the single value of d_{max}, which could be derived empirically from psychophysics experiments. With this approach, it is possible to interactively change the temporal resolution, while ρ is automatically adjusted by the maximum velocity lens. In the simple definition of Eq. 3, visual abstraction is not affected by the element's distance to the screen center on the x-y-plane, as for the world lens. To achieve such an effect, d_{max} can be dynamically increased with increasing distance between $p^*[m-1]$ and the screen center.

5 Implementation

In our work, we employ CellBlender for the modeling of the biochemical process and MCell for the simulation. The simulation tool produces files containing position, type, id, and orientation of each particle, and each file corresponds to a single frame. Since the number of frames can be quite large, we store all the particle data in a compressed format internal to our application. During the compression, we also concatenate all the files in a single file that allows for efficient access via memory mapped technique. Although Blender offers scripting capabilities, we opted for the user friendly Unity3D [10] as a development framework for the proposed visualization. Unity3D enables quick prototyping of graphics applications via scripting in C#, and has became increasingly popular in the biology community [19].

Unity provides its own rendering pipeline for 3D mesh structures, but is rather inefficient when rendering a large number molecular structures. To enable real-time rendering of high quality molecules, we also developed a unity module using tessellation shaders based on the technique proposed by Le Muzic et al. [21]. Another advantage of Unity3D is the set of post-processing effects already available within the solution. Among others, we use a depth-of-field shader to emphasize the function of the lens. The shader code has been modified to behave as a spherical depth-of-field effect so that all molecules inside the lens appear sharp on the screen, even when located out of the focus plane.

6 Use Case

We demonstrate our technique on a very simple model of adenosine triphosphate (ATP) molecules diffusing throughout the mitochondrial outer membrane towards the cytosol. Mitochondrion is a cellular component present in most cells of living species, which is mainly responsible for the energy management of the cell. Its size usually varies between 0.5 and 10 micrometers. On the outer membrane, it features voltage-dependent anion channels (VDAC) proteins, acting as pores and responsible for the passage of molecules across the membrane. Those are around $20-30$ $\AA$ large, which is sufficient to let small molecules, such a ATP, pass through while restraining larger molecules from crossing the membrane. VDAC transport proteins are found in very large quantities across the membrane and are also very densely packed together. In our representation, the amount of molecules (both ATP and VDAC) is voluntarily reduced to a total number of 5000 particles in order to meet with real-time performance and also to reduce both simulation times and simulation output size (which may easily exceed hundreds of Gigabytes for only a few thousands of particles in the case of large time-course simulations).

With Illustrative Timelapse, we temporally zoomed the visualization so that the 10^5 simulation frames (corresponding to a duration of 10μs each) were shown in about one minute. We determined that abstraction levels of $\rho = 0.1$ to $\rho = 0.05$ led to the best visual results with respect of the trade-off between smoothness of trajectories and realism. With these settings, we were able to trace ATP molecules moving through VDAC proteins, while also getting the impression of a scene full of stochastic motion and interactions. During the simulation, a total number of 1183 ATP molecules are crossing the outer mitochondrial membrane through VDAC proteins. ATP and VDAC molecules about to react were highlighted in bright red to guide the user's attention to these events. Although ATP crossing the membrane via VDAC channels is strictly speaking not a biochemical reaction, it is nevertheless an event of interest which is also subject to rates. A similar approach could have also been taken with protein carriers, such as *Lac permease* for instance, where crossing, in this case, is associated with an actual biochemical reaction. Including collision detection between particles and shaders passes involved in the final image synthesis, the simulation was running smoothly at more that 60 frames per seconds on a desktop equipped with an Inter Core i7-3930 3.20 GHz CPU processor coupled with an NVidia GTX Titan GPU processor. Screen captures of our visualization are shown in Figure 7.

7 User Study

We performed a preliminary user study to investigate the effect of an increasing amount of visual abstraction, as well as the lens effect, on the ability to follow individual events, perceived movement speed of the molecules (i.e., the velocity of Brownian motion), and the subjective visual appeal of the resulting visualization. For this purpose, users had to subjectively rate these three aspects after watching videos of the scene described in Section 6. Since our research questions did not involve any interactive exploration of the scene and the desired measurements were solely subjective, the study was performed online.

7.1 Setup

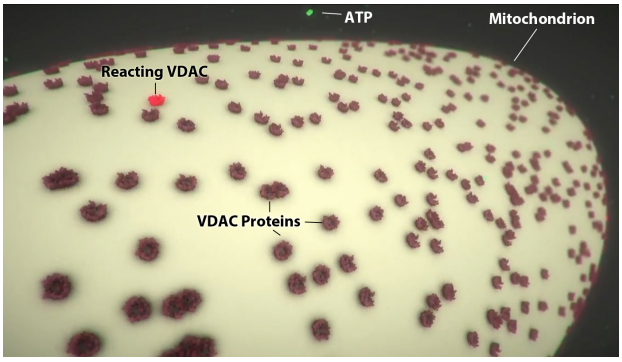
26 users finished the study (aged 24 to 58, four females). Except for two users, all were related to computer sciences and had no extensive knowledge in biology. Two users reported red-green weakness, but produced consistent results and where therefore included in the analysis.

We employed a 3×2 within-subjects design with the following factors:

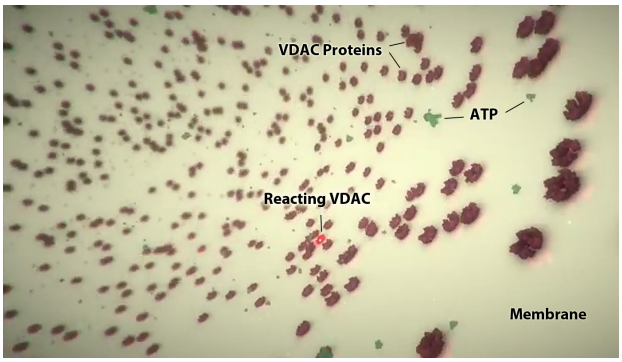
- the amount of **visual abstraction** on three levels: *none* (no trajectory smoothing, but simple fast-forwarding instead), *minimal* (slight trajectory smoothing so individual elements could be partially tracked with a considerable amount of effort), and *smooth* (strong trajectory smoothing so individual elements could be tracked effortlessly), and

- whether or not the visual abstraction was shown only within a spatially limited **lens**.

Since there is no difference between having no visual abstraction with or without a lens, this results in five different visualization



(a)



(b)

Figure 7: Screen capture of our Illustrated Timelapse system which features 5000 particles reacting and diffusing smoothly at more than 60 frames per seconds. (a) View from the outside of the outer membrane (b) View from the inside of the outer membrane.

conditions users had to watch and rate: no abstraction, minimal abstraction with and without lens, as well as smooth visualization with and without lens. The ρ for minimal and smooth visual abstraction were obtained in a small pilot experiment ($\rho_m = 0.1$ and $\rho_s = 0.05$). For the lens effect, we used the world lens with an inner radius of $r_1 = 10$ and an outer radius of $r_2 = 20$, while the mitochondrion shown in the video had a maximum length of $100x10^{-8}nm$.

Since absolute judgment of visual appeal, traceability, and speed is difficult, we used comparative questionnaires to obtain subjective ratings: We showed all pair-wise combinations of the five videos in a side-by-side view, resulting in ten comparisons with two videos each. The videos were presented in embedded *YouTube* players with 720p resolution, and users were free to watch the videos as many times as they wished—synchronously or one after the other. For each comparison, users were asked to select one of the two videos (or "no difference") for the three questions listed in Table 1. In addition, users could leave a comment at the end of the study. The order in which the video pairs were presented was randomized.

Q1	Which video was more visually pleasing to watch?
Q2	In which video was it easier to follow molecules diffusing through the membrane?
Q3	In which video did the molecules move faster?

Table 1: The three questions for each pair-wise comparison.

We expected to observe that visual abstraction would lead to improved traceability, but also reduce the perceived molecular speed dramatically. With the world lens, we expected that users would report that elements move faster compared to global abstraction, but that the capability to trace individual elements is hardly affected.

7.2 Results

For each vote for a particular video, we assigned the value 1 to the respective condition, while we assigned 0.5 for both conditions if the users selected "no difference". We used the *Case V Scaling* model by Thurstone [26] to convert all obtained pair-wise comparison values into interval scale. The values were transformed so that the minimum obtained z-value for each question corresponds to zero.

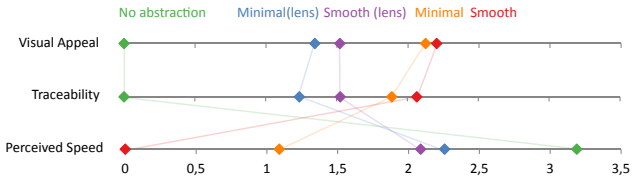


Figure 8: Average z-scores per visualization condition (color-coded) for the three questions listed in Table 1. Higher values are better.

As expected, both global visual abstraction methods (minimal and smooth) led to improved traceability of particles in the visualization (orange and red mark in Figure 8, center), as compared to the non-abstracted version (green mark). Similarly, the perceived speed of particles was much lower in the abstracted visualizations than in the non-abstracted one (see orange, red, and green mark in Figure 8, bottom).

The world lens could not fully preserve the traceability of particles compared to the globally abstracted version (compare blue and purple marks to orange and red marks in Figure 8, center). However, the increased velocity in the context indeed led to a faster perception of overall particle movement (see blue and purple marks in Figure 8, bottom).

In terms of visual appeal ratings, the obtained intervals are very similar to the traceability ratings (compare Figure 8 top and center). In other words, the smoother the overall motion, the more visually appealing the users rated the visualization.

Some users commented that tracing individual elements – especially the small ATP molecules – was generally hard, even in the abstracted versions of the visualization. A few suggested to use stronger visual highlight effects to make reactions more evident. Also, one user criticized the fact that reactions were also highlighted in the *"blurred out-of-focus regions"*, where reactions were *"not at all"* visible—presumably especially in the lens conditions, where the blurred regions were also visualized with non-abstracted motion. One user also reported that *"the different movement speeds for particles nearer and further away in some videos feel weird"*, which was probably caused by the world lens effect.

8 Discussion

Our preliminary user study results indicate that with increased trajectory smoothing, the ability to trace individual elements is better than if observing a non-abstracted visualization. Unsurprisingly, our study also showed that the perceived motion speed was decreased due to the decreased velocity of the elements. Even though this could not be formally evaluated in the course of our experiment, we assume that the implication of a decreased speed perception is most likely an underestimation of Brownian motion speed in comparison to more complex biochemical reactions. The world lens used in our experiment could alleviate this underestimation effect to some extent, but in turn lead to more difficulties keeping track of individual elements, as well as decreased aesthetics ratings.

Due to these observations, together with selected user statements collected during the study, we iterated the lens design and created the maximum velocity lens, described in Section 4.4.2. In addition, the reaction highlighting should clearly be coupled with the lens effect: Only if elements can be easily traced by the observer's gaze, a visual highlight should attract the user's attention to those elements that are about to react. Otherwise, the attention is directed towards contextual scene regions, whose primary purpose is actually to generate a realistic impression of the environment, but not to communicate the story of the visualized process in focus.

Nonetheless, illustrative techniques always compromise realism when providing an explanatory visual description to enhance the viewer's understanding of selected aspects. It is therefore up to the visualization designer to define priorities and choose the level of visual abstraction accordingly—just like visual artists. Our Illustrative Timelapse technique provides full control over the level of visual abstraction, as well as illustrative focus+context parameters, at run-time, and thereby facilitates the creation of illustrative scientific movies that would otherwise take several months.

9 Conclusion and Future Work

With Illustrative Timelapse we introduced a new technique for interactive and educational exploration of particle-based simulation on multiple temporal scales. Our system is capable of showing traceable moving molecules, when viewing processes in fast-forward which is important for an artistic depiction of biological sciences. While abstracting original motion from the simulation we also provide a more faithful representation of the molecular diffusion in the context area, similarly as in famous animated movies. This system also has potential applications to other domains of science that are dealing with complex processes featuring different temporal scales, such a visualization of astronomical phenomena. Whereas this technique has a great potential for dissemination of science it also comprises a few limitations: The first is the fact that simulation has to be computed prior to the visualization which disallows user interaction with the simulation outcome. Another limitation is due to the fact that particle-based simulations do not provide any run-time control over the localization of events of interest. One could solve this issue with an hybrid approach using Brownian dynamics for accurate spatial distribution together with a quantitative approach to trigger reactions of interest on demand directly in the view-port. In the future, we also plan to conduct more empirical research to obtain good candidates for the parameters ρ and the maximum traceable velocity d_{max} in such chaotic systems. In addition, we will explore an improved coupling of reaction emphasizing with lens effects to more reliably guide the user's attention to important reactions in the focus.

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