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Numerical model of the myosin V molecular motor

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Abstract

A variation on a numerical model of the motor protein myosin V presented in a paper by Craig and Linke (2009) is developed. An alternative potential is proposed. All aspects of the model development are derived in detail and tested. Two model tests are created and used to confirm the correctness of the developed model. A simulation demonstrates that the developed model is able to produce a myosin V step.

A didactical transposition is presented in the form of a compendium, in which a numerical model of myosin V by Craig and Linke (2009) is described. The didactical transposition is developed using a methodology of didactical engineering. The didactical study indicated that the content was well recieved by the target group of eight individuals in respect to the scientific complexity and that it evokes motivation for learning. The study also indicated that unsuccessful areas of the didactical transposition existed.

Keywords: Numerical model, myosin V, simulation, biophysics, didactical engineering

Sammanfattning

En variation av en numerisk modell av motorproteinet myosin V presenterad av Craig och Linke (2009) utvecklas. En alternativ potential föreslås. Alla aspekter av modellutvecklingen härleds i detalj och testas. Två modelltester skapas och används för att bekräfta riktigheten i den utvecklade modellen. En simulering demonstrerar att myosin V kan ta ett steg i den utvecklade modellen.

En didaktisk transposition presenteras i form av ett kompendium, där en numerisk modell av myosin V av Craig och Linke (2009) beskrivs. Metodologiskt utvecklas den didaktiska transpositionen med hjälp av didaktisk ingenjörskonst. Den didaktiska studien indikerade att innehållet togs emot väl av målgruppen bestående av åtta personer i hänseende till vetenskaplig komplexitet och att det väckte motivation för lärande. Studien indikerade även att misslyckade områden av den didaktiska transpositionen förekom.

Nyckelord: Numerisk modell, myosin V, simulering, biofysik, didaktisk ingenjörskonst

Acknowledgements

It all begun on a rainy autumn afternoon in Professor Mats Wallin's office at the Department of Physics at the Royal Institute of Technology. 'I have two ideas', he said, 'one is a bit more theoretical and the other one is a bit different but still very interesting. I think that the second would suit you especially well!'. To this day, I still do not know what he insinuated, but I do know that it was a good idea to go with his advice.

Professor Mats Wallin, you have always met my questions with a smile and an open mindset. I am deeply grateful for the enthusiasm you have shown me and for the countless hours that you have spent discussing and guiding me through this process. It has truly been an honour working with you during this project. Thank you.

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A great amount of gratitude is directed towards my fantastic family, my beloved girlfriend Nicole and my friends for all your support during my years at the Royal Institute of Technology. Thank you for all your encouragement, support and positive attitude during these years.

All good things have to come to an end, and this is the end of this chapter. Figuratively and literally.

Contents

Chapter 1

Introduction

The world of molecular motors is truly fascinating. Without them, life would not exist as we know it. Myosin is a family of motor proteins indispensable for the contraction mechanism of muscles, hence being an essential part of the movement of life. In this study, a numerical model of the processive motor protein myosin V is presented. The model is based on a paper by Craig and Linke (2009) where an alternative potential energy has been developed. An elaborate mathematical derivation, model description and two model tests are presented.

Alongside the numerical model, a compendium describing the model in the paper by Craig and Linke (2009) has been developed using a didactical engineering methodology. Didactical properties of this compendium are examined.

Numerical computer models applied on biophysical systems provide useful research tools allowing for cost efficient and safe experiments (Bartocci & Lió, 2016). The models enable experiments to be conducted in a virtual environment where parameters can be adapted to measurement data to replicate a real life environment.

Chapter 2

Study details

In this chapter, the scope and delimitations of the study are described. The aims and research questions of the study are stated.

The study was split into two separate studies but on highly correlated themes. One with a technical focus and one with a didactical focus. For simplicity, these foci have been separated in the report.

2.1 Aims

In this section, the aims of the study are formulated.

Technical Aim

The aim of the technical study is to develop a variation of a numerical model of myosin V presented by Craig and Linke (2009). The aim is to suggest an alternative potential, derive a model mathematically and give a detailed description of the system characteristics. Furthermore, the aim is to develop tests of the model correctness.

Didactical Aim

The aim of the didactical study is the creation of a didactical transposition towards a specific target group. The aim is to transpose the content of a numerical model created by Craig and Linke (2009) and giving perspective on the force term and movement on different length scales.

2.2 Research Questions

In this section, the research questions are formulated.

Technical Research Question

How can the numerical model of myosin V presented in the paper from Craig and Linke (2009) be varied, mathematically derived and described? How can the developed model be tested to assure correctness?

Didactical Research Question

How is the content in a didactical transposition of this topic received by the target group?

- To what extent did the target group acquire an understanding of the difference on movement for micro- and macro length scale?
- To what extent did the target group get perspective on the forces governing movement for micro- and macro length scale?

Chapter 3

Background

"In tranquillo mors, in fluctu vita."
(In stillness death, in movement life.)

In this chapter an overview of the family of myosin proteins is given, together with a more specific description of myosin V. This is followed by a background to the two studies made, in which the current state of research is described for the technical and the didactical areas respectively.

3.1 Myosin

Myosin is a family of proteins with different tasks, operating in eukaryotic cells (Sellers & Weisman, 2008). For instance, myosin II is central in the contraction of cardiac and skeletal muscles in animals, which involves the movement and blood circulation (Reggiani & Bottinelli, 2008). Myosins are therefore central for the existence of life.

Myosin V

Myosin V is a two-headed dimeric motor protein involved in transportation of e.g. cellular information (mRNA) and cell parts (organelles) along actine filaments (Sellers & Weisman, 2008). The movement is made in a stepwise head-over-head motion often directed outwards, towards the cell plasma (Ibid.). An explanation of the stepping mechanism can be found in Appendix B. The step size is about 36 nm (Mehta et al., 1999; Burgess et al., 2002; Walker et al., 2000). The head attachment and deattachment from the actine filament is governed by

chemical transitions. The working range of myosin V is generally in the order of micrometers before dissociating from the actine filaments (Sellers & Weisman, 2008). The water-based solvent in which the myosin V is suspended caters the protein with energy, undergoing an adenosine diphosphate (ADP) - adenosine triphosphate (ATP) cycle.

3.2 Technical Background

In this section, the technical background of the study is described. This involves simulation techniques in a biophysical context and an overview over the current state of research on numerical models for myosin V.

3.2.1 Simulation Techniques in a Biophysical Context

Biophysics and simulation techniques are rapidly growing areas of research (Tibell & Rundgren, 2010). The development of numerical models in a biological context has proven to be very useful. Numerical models are often easier and cheaper to construct in comparison to real experiments. Once a model is constructed, it can be used to make predictions for effective or desirable functions in a biological system and to explore its characteristics. Parameters in the model can be calibrated to real life measurements and adjusted accordingly.

Numerical models can for instance be useful for:

- The study of chemical transitions and its applications.
- The study of biological structures and its applications.
- Medical applications.
- The study of the connection between structure and functionality of a biological and chemical systems.

The movement of micro phenomena such as molecular systems are in some sense different from macro phenomena. Every part of the myosin V protein is so light that the inertial effects are negligible. In a human macro context this behaviour would seem very odd. The fact that inertial effects are negligible is central in the usage of the overdamped Langevin equation for simulations made in this study.

3.2.2 Myosin V Model Research

The motor protein myosin V is a well researched system. Although thoroughly studied, many key properties are still incompletely understood and demand further research. There are speculations about key characteristics in the chemical states, such as the lead head ADP release rate (Vilfan, 2009). The main issue regards the ability to recreate the high processivity efficiency of the protein. That is, the ability of the system to exert a forward motion over a long distance (micrometer) (Vilfan, 2009).

There are different types of theoretical models that describe different aspects of myosin V to model it. Models on an atomic level would be too numerically expensive to be worthwhile, justifying the following type of models incorporating elements of statistichal mechanics. Two different types of models are briefly described below.

Mechanochemical Models

This type of model regards both the mechanical aspects and the chemical transitions regulating the movement of myosin V (Vilfan, 2009). In this study, a mechanochemical model is used.

Discrete Stochastical Models

This type of model uses a set of chemical states to motivate transitions between discrete states (Kolomeisky & Uppulury, 2011). These discrete states correspond to different positions on the track (here the actine filament).

3.3 Didactical Engineering

In order to create a compendium in line with current research, the methodology of didactical engineering was chosen. This choice was based on the design aspect of creating a new learning material, at the same time enabling a didactical transposition in line with an established methodology.

3.3.1 Didactical Transposition

In order to teach knowledge, two things are necessary. First, the knowledge needs to get socially acknowledged (Chevallard, 1988). This is achieved by recontextualization and repersonalization in the meaning of Kang and Kilpatrick (1992). Secondly, the knowledge needs be declared in order to give it legitimacy. Both these factors are considered in the process of making a didactical transposition (Chevallard, 1988).

A didactical transposition can be interpreted as transferring the body of knowledge into a specific context, where the constraints that defines the context are taken into consideration.

3.3.2 Overview

The methodology of didactical engineering is built upon different phases. Artigue (2015) presents these phases in the following chronological order:

Preliminary Analysis

The preliminary analysis is about setting the constraints for the realization (Artigue, 2015). This involves an epistemological analysis of the content to be learned, the context in which it is learned and to whom the content is mediated (Ibid.). The preliminary analysis can be found in Sec. 6.1.

Conception and a Priori Analysis

A central phase in the methodology is the conception and a priori analysis (Artigue, 2015). The conceptualization phase treats the didactical choices regarding the interactions between learner and the knowledge content (Ibid.). The concepts set boundaries for the context in which the knowledge is transferred, involving the determination of so called didactical variables ruling the context (Ibid.). These variables can be interpreted as the conditions governing and making the learning situations possible. The didactical variables are defined in Sec. 6.2.

In order to justify these choices, an a priori analysis is made, describing the relations between the choices, preliminary analysis and

research question (Artigue, 2015). The conception phase and the a priori analysis phase can be found in Sec. 6.2.

Realization, (Observation) and Data collection

In this phase, the material is created - realized - using the earlier phases as a basis (Artigue, 2015). This is followed by a test involving data collection (Ibid.). The observation step is not applicable here, as the nature of this study regards the creation of a study material rather than an observable didactical situation.

The realization phase can be found in Sec. 6.3.1. The data collection is described methodologically in Sec. 4.2.1, specified in Sec. 6.3.2 and the analysis of data can be found in Sec. 7.1.

A Postieriori Analysis and Validation

This phase involves analysing the collected data and validating to which extent the research question was answered (Artigue, 2015). It also involves a discussion about the conformity between the a priori analysis and the a postieriori analysis (Ibid.).

Chapter 4

Methods

"Aut viam inveniam aut faciam tibi."
(I will either find a way or make one.)

In this chapter, the methods of the technical and the didactical studies are described.

4.1 Technical Method

In this section, the technical method is described. The model used as a starting point was made by Craig and Linke (2009). This model was closely followed in this study. A different model for the potential is suggested.

4.1.1 Overview

The technical study was made in the following chronological order:

1. Estimations and corrections to values presented by Craig and Linke (2009) was made. See Section 5.5.
2. The Langevin equation was discretizized using an Euler integrator. See Section 5.3.
3. A test against the equipartition theorem was made to assure the expected movement of the model protein. See Section 5.4.
4. An alternative potential energy was formulated and a mathematical construction of the modified model was made. See Section 5.1.

5. The position Langevin equation was discretizised using an Euler integrator. See Section 5.3.

6. A force versus work test was made to test if the force due to potential energy and the elongation force expressions were correct. See Section 5.4.

7. Data was extracted from the model. See Section 8.1.

4.1.2 Simulation

In order to make a simulation of myosin V, the model was programmed in a Python environment and studied.

Every block of code written was continuously tested either against known values or other means of known available representations, such as mathematical vectors, in order to assure its accuracy. When expanding the system, the system was first tested in the smallest scale possible with three discrete nodes for every new step, until any uncertainties were handled. The system was then rescaled to the expected size of myosin V with nine discrete nodes.

4.2 Didactical Method

In this section, the data collection and analysis method of the didactical study is described.

4.2.1 Data Collection

For the study, a design method for mathematical didactics was used - didactical engineering, described in Sec. 3.3. This was analysed using a qualitative survey in the form of a questionnaire.

Survey

A collection of data was made using a questionnaire. The survey aimed to elucidate the qualitative properties of the compendium. Since the content to be mediated was introducing and giving perspective on the topic, no detailed knowledge was expected to have been transmitted after reading the compendium. A comment was made to clarify

that the aim of the questionnaire was not to test the detailed knowledge of the submitter, but an effort to expose whatever may have been learned and how the learner had experienced the material.

Online Questionnaire

The questionnaire was made using an online tool where the participants could write an answer in empty forms. Screenshots of the questionnaire can be found in Appendix D.

Target Group and the Scope of Research

Cohen, Manion, and Morrison means that "to ensure validity in a test it is essential to ensure that the objectives of the test are fairly addressed in the test items" (Cohen et al., 2011, p. 482). The objectives of this test are related to a target group through the didactical engineering method. The validity in this test is therefore dependent on the questions of the survey being asked to the appropriate group of people. To ensure the validity in the test and the analysis, the survey was conducted with participants having a profile similar to the target group described in the preliminary analysis in Sec. 6.1.

All participants were personally contacted and informed about the terms of participation and were then sent a link to the online questionnaire. The scope of the research was eight individuals.

Discussion on Validity

In a qualitative research, "the aim is somewhat simplified to understand what is analyzed" (Fejes & Thornberg, 2009, p. 19) (author's translation). In this context, this could be interpreted as elucidating the relations between the produced learning material, the intent of the material and the outcome after reading the developed material.

The questions asked in the questionnaire were mainly open. A reason for this was to avoid guiding the participants towards a specific answer and to invite participants to freely express their opinion. In this way, the relations between the learning material and the participants could be exposed without influence. This enhances the validity

of the used research method. A motivation of the intent of each question is specified in Sec. 6.3.2.

4.2.2 Method of Analysis

The analysis was conducted using a content analysis method. Respondents answers are assumed to correspond to their true intention and meaning. An intersubjective interpretation of the data is strived for, although this can be put in perspective in the sense that "what we call our data are really our own constructions of other people's constructions of what they and their compatriots are up to" (Geertz, 1973, p. 9).

Terms of Analysis

The terms of analysis used are recontextualisation, repersonalization, decontextualization and depersonalization in the meaning of Kang and Kilpatrick (1992). In order for the knowledge to be understandable for a specific target group, the content need to be recontextualized and repersonalized in alignment with the target group's characteristics. This means that the content needs to be reformulated personally and contextually in order for a person in the target group to give the knowledge social relevance, hence generating learning possibilities. Once the reader has utilized the content, the knowledge gets decontexualized and depersonalized - coded in the internal coding of the person (Kang & Kilpatrick, 1992).

The didactical transposition and the survey was developed using the same framework, which justifies the alignment of used development method, analysis method and research method.

4.2.3 Justification of Method

The aim of the study was not to create a teaching situation in which the content was to be transmitted. The study consists of the development of a didactic transposition elaborated in accordance with the used theory and methodology.

Relevance of the Used Method in the Context

The relevance of the chosen method in this context can be justified by regarding the mathematical nature of a biophysical model. Biophysics is physics put into a biological context. Mathematics is in turn the language of physics, in the sense that real physical phenomena are translated into a mathematical language in the process of constructing a model. This process enables the real system to be represented and conceptualized by an abstract framework and made understood.

A complexity arises in the mathematical formulation of a biophysical system for a non-experienced reader. This enhances the necessity of a didactical transposition to be made in order to be understood by and made available for the suggested reader. Thus, justifying a method based on mediating the mathematical content of the context. A scientist is driven by an epistemic purpose while making a mathematical model, whereas students do not share this purpose. A key component in the development of a didactic transposition is therefore to motivate the content.

4.3 Ethical Aspects

The data collection has been following the codex of Vetenskapsrådet (2002) (The Swedish Council of Research, author's translation). The four main reqirements were fulfilled. In short, the participants were informed about the terms of participation and that parttaking is voluntary and can be cancelled at any time. The usage of data was clarified and consent was asked from the participants upon submittal of data. No personal information was neither asked for nor stored in order to ensure the anonymity of participants. It seems apparent that no harm can come to the participants or others from participating in this study.

Chapter 5

Numerical Model of Myosin V

"All models are wrong, but some are useful."
George E.P. Box

In this chapter the technical aspects of the study is described. This includes calculations and estimations of parameters, as well as the mathematical model of myosin V that was used for the simulation. The solution to the Langevin equation governing the movement is presented and described. The code tests and the details regarding numerical integration and discretization is described.

5.1 Model

In this section, a detailed description of the model is given. Details regarding the parameters used in the simulation and other constants presented in the model can be found in Appendix A. For a schematic figure of the myosin V model, see Fig. 5.1.

5.1.1 Model Description

The model presented is mainly based on a paper by Craig and Linke (2009).

A mechanochemical model is used in which the myosin V protein is undergoing a series of chemical transitions and having simple mechanical features. The myosin V consists of two heads connecting to the actine filament and seven necks. The necks are linked by six

strongly interacting chains of amino acids, so called IQ motifs. The protein is guided by a coordinated stepping mechanism which e.g. involves intramolecular strain between IQ motifs and tethered diffusion rate. The IQ motifs are coupled in elastic junctions (necks) giving rise to elastic potential energy in the neck domains upon bending. Thermal effects are regarded which gives the system Brownian dynamical properties. Frictional effects due to movement in the surrounding liquid are considered. In the model, the protein is ideally lifted out of its natural environment and only treats minimal aspects of its surroundings. Some further assumptions regarding the system properties are made which are described below.

Semiflexible Segments

The six chains of amino acids can be idealized as six flexible segments as the individual IQ motifs are tightly bound to each other.

Neck Conformation Change

The stepping mechanism involves a conformation change which is present to enhance the processivity of the myosin V protein. An angle to the last segment connecting to the lead head is set in a forward direction in order to create an inner strain in the neck domain. This aims to guide the movement forward. For a more detailed view of the conformation change, see Appendix B. The angle is assumed to change upon phosphate release from ADP.Pi which can be seen in the Appendix.

Free Rotation

A free rotation is assumed about the midpoint neck. Thus, no elastic potential energy is present in this junction. Observations suggest that this is a reasonable assumption (Craig & Linke, 2009).

Actine Filament

The actine filament is regarded as a one-dimensional array with a spacing of L_{filament}. If a detached head diffuses within the range of electrostatical interaction R_{screen} from such a point after ATP hydrolysis, the head attaches to the filament.

5.1.2 Coordinated Stepping

In this section, the coordinated stepping mechanism is explained. An overview over the states can be found in Appendix B.

The six chemical states are central for the stepping mechanism. There is a probability of k_{pq} of a transition from the p:th to the $q = p + 1 (\text{mod } 6)$:th state. Upon head release from the actine filament, the head is searching for a new point of attachment on the actine filament during a free Brownian motion while being leveraged around a neck (Shiroguchi & Kinosita, 2007) (Craig & Linke, 2009).

Telemark State

In order to enhance the processivity, a so called Telemark state is incorporated in the model. The name comes from the leg shape, corresponding to the skiing technique with the same name. The Telemark state is a conformation change, where the angle between segments in the foremost head-neck juncture is set forward from an angle θ_A to θ_B. By setting this angle forward, a strain in the neck region is created, aiming to enhance processivity in the forward direction. Reconfiguration is assumed to occur upon phosphate release from ADP.Pi. See Appendix B for a more detailed view of the conformation change and the stepping process. The evidence of the Telemark state to measurement data is still inconclusive (Vilfan, 2009). In this model it is used in order to enhance processivity.

5.1.3 Mathematical Model

The myosin V parts are modelled as a set of N discrete points (nodes) connected by elastic rods with stiffness C ruled by Hookes law. The configuration can be seen in Fig. 5.1.

Each node corresponds to a junction with an elastic potential energy V_i for bending. The neck-neck junctions have a potential energy V_{NN} and the head-neck junctions have a potential energy V_{HN}.

The total potential energy of the semiflexible segments consist of

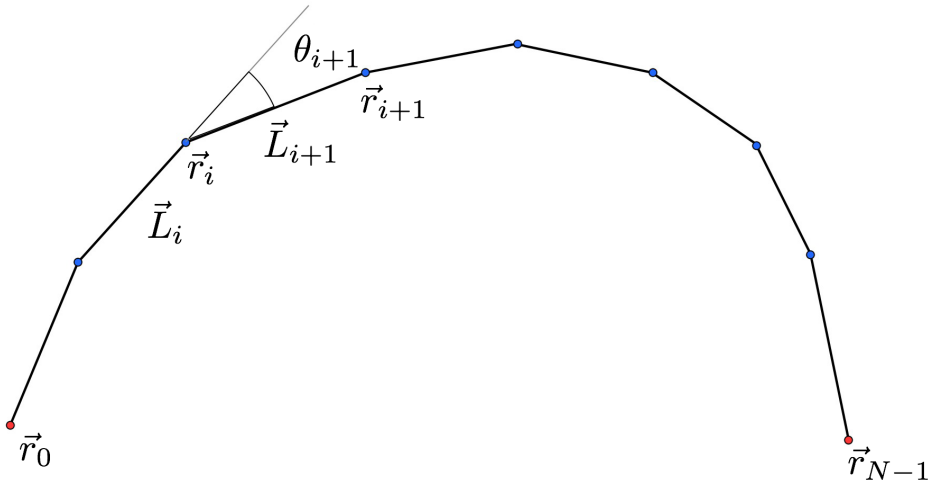

Figure 5.1: Definitions of points, lengths and angles in the myosin V model. Heads are colored in red and necks in blue.

terms U_{el} from elasticity and U_{b} from bending.

$$U = \frac{1}{2}\sum_{i=0}^{N-1} K_i (L_{ij} - l_i)^2 - \sum_{i=1}^{N-2} V_i \cos(\theta_i - \theta_i^0) \tag{5.1}$$

where $j = i + 1$ and $K_i = C/l_i$

$$L_{ij} = \sqrt{(x_i - x_j)^2 + (y_i - y_j)^2 + (z_i - z_j)^2} \tag{5.2}$$

The force contributions of each of these potential energies are treated separately in Secs. 5.1.5 and 5.1.6.

5.1.4 General Definitions

Let $\vec{r}_i = (x_i, y_i, z_i)$ be a position vector for the i:th node. The i:th segment length is given by

$$L_i = \sqrt{(x_i - x_{i-1})^2 + (y_i - y_{i-1})^2 + (z_i - z_{i-1})^2} \tag{5.3}$$

where $i = 1, 2, ..., N-1$. The corresponding unit vector inbetween nodes is given by

$$\vec{e}_i = \frac{\vec{r}_i - \vec{r}_{i-1}}{L_i} \tag{5.4}$$

$i = 1, 2, ..., N-1$. In particular, $|\vec{e}_i| = 1$.

5.1.5 Elastic Forces

The force acting on the i:th part located in $\vec{r}_i$ is dependent on two potential energy terms:

$$U_i^{\text{el}} = \frac{1}{2}K_i(L_i - l_i)^2 + \frac{1}{2}K_{i+1}(L_{i+1} - l_{i+1})^2 \tag{5.5}$$

where l_i is the equilibrium length of the i:th segment.

Force Calculation

Let the elastic force on point i be $\vec{F}_i^{el}$, then

$$\vec{F}_i^{\text{el}} = (F_{xi}^{\text{el}}, F_{yi}^{\text{el}}, F_{zi}^{\text{el}}) = -\left(\frac{\partial U^{\text{el}}}{\partial x_i}, \frac{\partial U^{\text{el}}}{\partial y_i}, \frac{\partial U^{\text{el}}}{\partial z_i}\right) \tag{5.6}$$

In the x-direction for the i:th part:

$$F_{xi}^{\text{el}} = -\frac{\partial U^{\text{el}}}{\partial x_i} = -\frac{\partial U^{\text{el}}}{\partial L_i}\frac{\partial L_i}{\partial x_i} - \frac{\partial U^{\text{el}}}{\partial L_{i+1}}\frac{\partial L_{i+1}}{\partial x_i} \tag{5.7}$$

where

$$\frac{\partial L_i}{\partial x_i} = \frac{x_i - x_{i-1}}{L_i} = \vec{e}_{xi} \tag{5.8}$$

$$\frac{\partial L_{i+1}}{\partial x_i} = -\frac{x_{i+1} - x_i}{L_{i+1}} = -\vec{e}_{x,i+1} \tag{5.9}$$

and similar in all directions. Collecting terms, the elastic force on node i is

$$\vec{F}_i^{\text{el}} = -K_i(L_i - l_i)\vec{e}_i + K_{i+1}(L_{i+1} - l_{i+1})\vec{e}_{i+1} \tag{5.10}$$

for $i = 0, 1, ..., N-1$ using the indexation rule stated in Section 5.1.7.

5.1.6 Bending Forces

A simple variation of Craig and Linkes (2009) bending force is proposed. The bending potential is taken as

$$U_i^{\text{b}} = -\sum_i V_i \cos(\theta_i - \theta_i^0) \tag{5.11}$$

where $i = 1, ..., N-2$. θ_i is the angle between two segments meeting at the i:th point. The i:th equilibrium angle is set to $\theta_i^0 = 0$, similar to

Craig and Linke (2009). This variation of the bending force also implies a 2π-periodicy, which is physically desirable because a segment returns to its initial position if it is rotated 2π radians about one junction.

Using the definition of dot product,

$$\vec{e}_i \cdot \vec{e}_{i+1} = |\vec{e}_i||\vec{e}_{i+1}| \cos(\theta_i) = \cos(\theta_i) \tag{5.12}$$

Eq.(5.11) can be simplified to

$$U_i^{\mathrm{b}} = -\sum_i V_i \vec{e}_i \cdot \vec{e}_{i+1} \tag{5.13}$$

$i = 1, ..., N-2$. In particular

$$\min\{-V_i \vec{e}_i \cdot \vec{e}_{i+1}\} = -V_i \text{ for } \vec{e}_i = \vec{e}_{i+1} \tag{5.14}$$

such that the potential energy is at its minimum for a straight joint.

Preparatory Calculations

For later use, the partial derivatives of $\vec{e}_i$ and $\vec{e}_{i+1}$ with respect to x_i are calculated.

$$\frac{\partial \vec{e}_i}{\partial x_i} = \frac{\partial}{\partial x_i}\frac{(\vec{r}_i - \vec{r}_{i-1})}{L_i} = \frac{(1,0,0)}{L_i} - \frac{(\vec{r}_i - \vec{r}_{i-1})}{{L_i}^2}\frac{\partial L_i}{\partial x_i} =$$

using Eq.(5.8)

$$= \frac{(1,0,0)}{L_i} - \frac{x_i - x_{i-1}}{{L_i}^2}\vec{e}_{xi} \tag{5.15}$$

$$\frac{\partial \vec{e}_{i+1}}{\partial x_i} = \frac{\partial}{\partial x_i}\frac{(\vec{r}_{i+1} - \vec{r}_i)}{L_{i+1}} = -\frac{(1,0,0)}{L_{i+1}} - \frac{(\vec{r}_{i+1} - \vec{r}_i)}{{L_{i+1}}^2}\frac{\partial L_{i+1}}{\partial x_i} =$$

using Eq.(5.9)

$$= -\frac{(1,0,0)}{L_{i+1}} + \frac{x_{i+1} - x_i}{{L_{i+1}}^2}\vec{e}_{x,i+1} \tag{5.16}$$

and similar in all directions.

Force Calculation

The elastic bending force on the i:th part depends on the two adjacent parts. Calculate the force in the x-direction for the i:th part:

$$F_{xi}^{\mathrm{b}} = -\frac{\partial U_{\mathrm{b}}}{\partial x_i} =$$

$$= \frac{\partial}{\partial x_i}\left(\sum_{k=0}^{2} V_{i-1+k}\vec{e}_{i-1+k}\cdot\vec{e}_{i+k}\right) =$$

$$= \frac{\partial \vec{e}_i}{\partial x_i}\cdot(V_{i-1}\vec{e}_{i-1}+V_i\vec{e}_{i+1}) + \frac{\partial \vec{e}_{i+1}}{\partial x_i}\cdot(V_i\vec{e}_i+V_{i+1}\vec{e}_{i+2}) =$$

substituting for Eq.(5.8) and Eq.(5.9)

$$= \left(\frac{(1,0,0)}{L_i} - \frac{x_i - x_{i-1}}{{L_i}^2}\vec{e}_{xi}\right)\cdot(V_{i-1}\vec{e}_{i-1}+V_i\vec{e}_{i+1}) +$$

$$+ \left(-\frac{(1,0,0)}{L_{i+1}} + \frac{x_{i+1}-x_i}{{L_{i+1}}^2}\vec{e}_{x,i+1}\right)\cdot(V_i\vec{e}_i+V_{i+1}\vec{e}_{i+2}) \tag{5.17}$$

and similar in all directions. Multiplicating the parentheses and collecting terms gives the bending force on the i:th part:

$$\vec{F}_i^{\mathrm{b}} = \frac{V_{i-1}\vec{e}_{i-1}+V_i\vec{e}_{i+1}-\vec{e}_i\,(k_{i-1}+k_i)}{L_i}$$

$$-\frac{V_i\vec{e}_i+V_{i+1}\vec{e}_{i+2}-\vec{e}_{i+1}\,(k_i+k_{i+1})}{L_{i+1}} \tag{5.18}$$

where $k_i = V_i\vec{e}_i\cdot\vec{e}_{i+1}$, for $i = 1, ..., N-2$ using the indexation rule stated in Section 5.1.7.

5.1.7 Indexation Rule

If the index of $\vec{e}_i$ is outside of $i = 1, 2, ..., N-2$, the term is absent and therefore omitted from the force evaluation. This rule affects the first and last node (the heads) and applies to both the elastic and the bending force expressions.

5.1.8 Parameters

All parameters and constants used in the model are described and defined under Appendix A.

5.2 The Langevin Equation

In this section, the solution to the equation governing the motion of myosin V is presented.

Each part in the model was integrated with the use of the Langevin equation. To test and simulate the basic motion of myosin V, the underdamped Langevin equation was used under the assumption that every part was free ($F = 0$). After that, the inertial term was neglected and the overdamped Langevin equation was used instead.

5.2.1 The Underdamped Langevin Equation

The Langevin equation is given by

$$m\dot{v}(t) = F(r,t) - \alpha v(t) + \xi(t) \tag{5.19}$$

this can be rewritten to the form

$$\dot{v} = \frac{F}{m} - \gamma v(t) + A\zeta(t) \tag{5.20}$$

where F is an external force. For its use in this study, F was set to zero. $\gamma = \frac{\alpha}{m} > 0$ is a friction coefficient corresponding to the time average over collisions with molecules in the viscous fluid and $\xi = A\zeta$ a Gaussian white noise term to model the thermal fluctuations which time average is zero and variance 1. $A > 0$ is a real scaling factor chosen such as to fulfill the equipartition theorem.

For a more detailed discussion of how A is determined, see Section 5.2.3. For a more detailed discussion about γ, see Section 5.5.2.

Solution to the Underdamped Langevin Equation

Let $F = 0$, such that

$$\dot{v}(t) = \gamma v(t) + \xi(t) \tag{5.21}$$

where $\gamma, \xi \in \mathbb{R}$ and $\dot{v} = \partial v/\partial t$. Set

$$v = e^{at} y(t) \tag{5.22}$$

Differentiation with respect to time gives

$$\dot{v} = \gamma v + e^{at}\dot{y} \tag{5.23}$$

Identify terms and rewrite

$$e^{at}\dot{y} = \xi \tag{5.24}$$

$$\dot{y} = \xi e^{-at} \tag{5.25}$$

Integration with respect to time gives

$$y(t) = v(0) + \int_0^t dt' e^{-\gamma t'} \xi(t') \tag{5.26}$$

Using $v = e^{at}y(t)$, and substiting $\xi(t) = A\zeta(t), A \in \mathbb{R}$ the solution reads

$$v(t) = v(0)e^{-\gamma t} + A \int_0^t dt' e^{\gamma(t-t')} \zeta(t') \tag{5.27}$$

5.2.2 The Overdamped Langevin Equation

The overdamped Langevin equation can be derived from the Langevin equation.

$$m\dot{v}(t) = F - \alpha v(t) + \xi(t) \tag{5.28}$$

where $F = -\nabla U$ and $\alpha > 0$ a friction coefficient.

For macromolecular systems, such as myosin V, the mass for each particle is very small. In this case, the mass is in the order of magnitude $\sim 10^{-22}$ kg. See Section 5.5.1 for an estimation of the mass. Hence, the inertial term $m\dot{v}(t)$ is very small and can be neglected. This gives the overdamped Langevin equation:

$$0 = F - \alpha v + \xi \tag{5.29}$$

Now, let $\xi(t) = AR(t)$. Rearranging terms and using $m\dot{v}(t) = 0$:

$$v(t) = \frac{F}{\alpha} + AR(t) \tag{5.30}$$

where $A^2 = \frac{2k_BT}{\alpha}\Delta t, A > 0$. For a derivation of A^2, see Section 5.2.3. $R(t)$ is a stochastic variable such that $\langle R(t) \rangle = 0$ and $\langle R(t)R(t') \rangle = \delta(t - t')$.

Solution to the Overdamped Langevin Equation

Assume long time steps $\Delta t \gg 1/\gamma$ in order for the initial velocity to get damped out, obtaining an overdamped system. By integration of the solution to the underdamped Langevin equation found in Eq. (5.27) and neglecting the first term, the solution after N time steps is

$$x(t) = x(t_0) + A\sum_{i=1}^{N} R(t_i) \tag{5.31}$$

5.2.3 Adaption of Scaling Factor to the Equipartition Theorem

In this section, the adaption of the scaling factor A to the equipartition theorem is derived for the underdamped and overdamped case of the Langevin equation.

The Underdamped Langevin Equation

In this section the scaling factor for the underdamped case is derived.

By taking the time average of the squared solution to the Langevin equation stated in Eq. (5.27), one obtains

$$\langle v^2\rangle = e^{-2\gamma t}\langle v^2(0)\rangle + 2e^{-\gamma t}\langle v(0)\rangle A\int_0^t dt' e^{-\gamma(t-t')}\langle\zeta(t')\rangle +$$

$$+ A^2\int_0^t dt' e^{-\gamma(t-t')}\int_0^t dt'' e^{-\gamma(t-t'')}\langle\zeta(t')\zeta(t'')\rangle \tag{5.32}$$

where $0 \leq t' < t$ and $0 \leq t'' < t$.

Furthermore, assume that the thermal forces are statistically independent in time to obtain a white noise spectrum. This is a plausible assumption because the myosin V protein is much larger than the molecules in the fluid surrounding it.

During every time step, the force average from many collisions with the myosin V approaches a Gaussian distribution as a result of the central limit theorem (Toda, Kubo, Saitō, & Hashitsume, 1991). The mass of the myosin protein is larger than the mass of individual molecules in the fluid, implying that the time constant of motion

of the particles in the fluid is much shorter than that of the protein (Ibid.). The motion of a myosin part can be idealized as Brownian, because ζ is a Gaussian process with a white noise spectrum (Ibid.). A more detailed elaboration of the validity of this assumpion can be found in Toda et al. (1991, p. 28).

Hence, ζ is Gaussian, thus $\langle\zeta(t')\rangle = 0$. Using $\langle\zeta(t')\zeta(t'')\rangle = \delta(t'-t'')$, where δ is the Dirac delta distribution, one obtains

$$\langle v^2\rangle = e^{-2\gamma t}\langle v^2(0)\rangle + A^2\int_0^t dt' e^{-\gamma(t-t')}\int_0^t dt'' e^{-\gamma(t-t'')}\delta(t'-t'') \tag{5.33}$$

$$= e^{-2\gamma t}\langle v^2(0)\rangle + A^2\int_0^t dt' e^{-2\gamma(t-t')} \tag{5.34}$$

$$= e^{-2\gamma t}\langle v^2(0)\rangle + \frac{A^2}{2\gamma}(1-e^{-2\gamma t}) \tag{5.35}$$

Thus,

$$\langle v^2\rangle \to \frac{A^2}{2\gamma} \text{ for } t \gg 1/\gamma \tag{5.36}$$

Combining Eq. (5.36) with Eq. (5.50) gives

$$A^2 = \frac{2\gamma k_B T}{m} \tag{5.37}$$

where $A > 0$. This solution is applicable for cases with $\Delta t \ll 1/\gamma$ and long integration time $t \gg 1/\gamma$.

The Overdamped Langevin Equation

In this section the scaling factor for the overdamped case is derived.

Assuming a long integration time, for free motion the mean square displacement relation for random walks must be obtained (Kubo, 1966)

$$\langle (x(t) - x(t_0))^2\rangle = 2D(t-t_0) \tag{5.38}$$

where $D = k_B T/\alpha$ is a diffusion coefficient for the fluid, determined by the Einstein relation (Kubo, 1966). N time steps are made in the time $(t-t_0)$, thus

$$t - t_0 = N\Delta t \tag{5.39}$$

Combining Eqs. (5.31) and (5.38) gives the mean squared displacement after N time steps

$$\langle (x(t) - x(t_0))^2 \rangle = A^2 \sum_{i=1}^{N} \left(\sum_{j=1}^{N} \langle R(t_i) R(t_j) \rangle \right) \tag{5.40}$$

Using $\langle R(t_i) R(t_j) \rangle = \delta(t_i - t_j)$ this simplifies to

$$A^2 N = 2D(t - t_0) \tag{5.41}$$

The Einstein relation gives

$$A^2 N = \frac{2k_B T}{\alpha}(t - t_0) \tag{5.42}$$

or equivalently, by using Eq. (5.39)

$$A^2 = \frac{2k_B T}{\alpha}\Delta t \tag{5.43}$$

where $A > 0$. This solution is applicable for long integration times $t \gg 1/\gamma$.

5.3 Numerical Solution

In this section, the numerical solution and discretization is described and the choice of integrator is discussed.

5.3.1 Integrator

For the numerical solution of the Langevin equation an Euler integrator was used. This choice was based on simplicity, as reliable results were obtained for sufficiently small time steps with this integrator.

5.3.2 Discretization

In this section, the discretization of the underdamped and overdamped Langevin equation is described. Details regarding the parameters used in the discretizations can be found in Section 5.2.

Underdamped Langevin Equation

The discretization of the underdamped Langevin equation according to Euler is given by:

$$x(t + \Delta t) = x(t) + v(t)\Delta t \tag{5.44}$$

$$v(t + \Delta t) = v(t) - \gamma v(t)\Delta t + A\zeta(t) \tag{5.45}$$

where

$$A^2 = \frac{2\gamma k_B T}{m} \tag{5.46}$$

and $A > 0$. For more details regarding A, see Section 5.2.3.

Overdamped Langevin Equation

The discretization of the overdamped Langevin equation according to Euler is given by:

$$x(t + \Delta t) = x(t) + \frac{F}{\alpha}\Delta t + AR(t) \tag{5.47}$$

where

$$A^2 = \frac{2k_B T}{\alpha}\Delta t \tag{5.48}$$

and $A > 0$. For more details regarding A, see Section 5.2.3.

5.3.3 Time Step Choice

In order to study different aspects in the integration of the Langevin equation, different time step choices are suitable. Here, this matter is further elaborated.

Underdamped Langevin Equation

If one wants to study relaxation phenomena, a time step choice of $\Delta t \ll 1/\gamma$ must be chosen in order to capture the contributions of the initial term $v(0)e^{-\gamma t}$. For other studies of the Langevin equation, this initial relaxation is not in the area of interest and a time step larger than the relaxation time is suitable. This is because the initial velocity gets damped out within one timestep.

Overdamped Langevin Equation

In the overdamped limit, the upper bound of Δt is only dependent on the consistency of results.

5.4 Model tests

In order to assure the accuracy of the mathematical model and the programming, two tests were developed. The tests will be presented in this section.

5.4.1 Equipartition Theorem Test

In order to assure the accuracy of the programmed model, an equipartition theorem test was developed. For a free particle, the equipartition theorem states that in equilibrium the mean kinetic energy of the system fulfills the following relation in every degree of freedom:

$$\frac{1}{2}m\langle {v_x}^2\rangle = \frac{1}{2}k_B T \tag{5.49}$$

or equally

$$\langle {v_x}^2\rangle = \frac{k_B T}{m} \tag{5.50}$$

where m is mass, k_B is Boltzmann's constant, v velocity and T temperature (K). Equation (5.50) was confirmed with the programmed model results of the underdamped Langevin equation. The theorem was also used to determine the value of A, for more details see Section 5.2.3.

The natural surroundings of the myosin protein is water at $T = 300$ K that acts as a heat bath. This means that the protein undergoes thermal fluctuations at this temperature. Note that the protein is not in equilibrium since it undergoes chemical state transitions that consume energy. The equipartition test applies for the motion if such transitions are neglected.

5.4.2 Force Test

In order to assure the accuracy of the programmed model, a force test was developed. The aim was to compare the work done by the force

and the evaluated force from the simulation when moving a particle over a small distance in order to test energy conservation. Expressions for the force and potential energy can be found in Section 5.1. The test is made in the following steps:

- Randomize the particle positions.
- Calculate the force $\vec{F}_i$.
- Calculate the total potential energy.

$$U_{\text{old}} = \sum_{i=0}^{N-1} U(\vec{r}_i{}^{\,\text{old}}) \tag{5.51}$$

- Move part i a small distance ds in the x-direction.

$$r_{ix}^{\text{new}} = r_{ix}^{\text{old}} + ds. \tag{5.52}$$

- Calculate the total potential energy in the new conformation, given by

$$U_{\text{new}} = \sum_{i=0}^{N-1} U(\vec{r}_i{}^{\,\text{new}}) \tag{5.53}$$

- Using the Taylor approximation to degree one yields

$$U_{\text{new}} = U_{\text{old}} + \nabla U \cdot ds \tag{5.54}$$

  Let $\Delta U = U_{\text{new}} - U_{\text{old}}$ and identify $\vec{F}_i = -\nabla U$, then

$$\Delta U = -\vec{F}_i \cdot ds \tag{5.55}$$

If energy is conserved, the work done by the force should equal the change in potential energy for small ds. Repeat this test for all parts in all directions.

5.5 Estimations and Corrections

In this section, the estimation of the myosin V mass is presented. A correction to- and discussion about the friction coefficients presented by Craig and Linke (2009) is made.

5.5.1 Estimation of Myosin V Mass

The mass of a myosin V part was estimated. The molecular mass of a Myosin V IQ motif chain is approximately 210 000 Da (Sellers & Weisman, 2008, p. 290). Split into 8 identical segments, one segment correspond to approximately 26 250 Da or $m = 4 \cdot 10^{-22}$ kg. This is roughly the mass centered in one of the mathematical nodes in the model.

5.5.2 The Friction Coefficient

The value of γ_H noted by Craig and Linke (2009) implies a very non-physical solution. As can be seen in the first term in the solution to the underdamped Langevin equation (see Section 5.2.1), the relaxation time t_0 is of order $t_0 = 1/\gamma_H$. In this case, a γ_H of this order of magnitude would mean that the relaxation time is hundreds of years, which clearly is not a physical time range for this system.

Instead, the authors have supposedly used another convention for the friction coefficient in the Langevin equation presented in their model. In the studied literature a common substitution is

$$\gamma = \frac{\alpha}{m} \tag{5.56}$$

It is likely that the authors have switched γ_H for α_H when documenting the value in their report.

Assuming this and $m \sim 10^{-22}$ kg (see Section 5.5.1), this implies $t_0 \sim 10^{-11}$ s. A clearly more physical result which also is in line with the numerical value stated in Craig and Linkes' (2009) report. A control calculation is made below to further elaborate and clarify this matter.

Control Calculation

Stokes law gives the drag force on a small sphere moving in a viscous fluid (Laidler, 2003)

$$F_d = 6\pi\eta R v \tag{5.57}$$

where the viscous friction coefficient can be identified as

$$\alpha = 6\pi\eta R \text{ kg/s} \tag{5.58}$$

where η is the dynamical viscosity of water and R the radius of the sphere. The dynamical viscosity of water at 25° is given by (Lv et al., 2016):

$$\eta = 8.90 \cdot 10^{-4} \text{ Pa} \cdot \text{s} \tag{5.59}$$

Experimental data shows that the velocity is approximately (Craig & Linke, 2009)

$$v = 550 \text{ nm/s} \tag{5.60}$$

An estimation of the head length is 5 nm (Craig & Linke, 2009). Assuming a spherical shape, the diameter of a myosin V head is estimated to be in the order of magnitude 10 nm using data from Morel and Merah (1997). Hence, the radius is approximately

$$R \approx 5 \text{ nm} \tag{5.61}$$

The numerical values above gives

$$\alpha = 8.4 \cdot 10^{-11} \text{ kg/s} \tag{5.62}$$

which is in the same order of magnitude as the value from Craig and Linke (2009). This suggests that the value presented is reasonable and that γ_H presented by Craig and Linke is to be thought upon as α_H in this model . The same argument applies for the value of γ_N.

Correction to the Friction Coefficient Dimension

Craig and Linke (2009) has probably made an error in their documentation as the dimensions of their friction coefficient does not match that of a friction coefficient. They have noted the dimension pN/nm which corresponds to 10^{-3} kg/s^2. This should be corrected to units 10^{-3} kg/s.

Chapter 6

Didactical Study

"You are a radar detector."
Darwin Deez

In this chapter, all phases of the didactical study are described. For simplicity, these have been put in chronological order.

6.1 Preliminary Analysis

In the preliminary analysis, the content to be mediated, the context of learning and the target group was identified and set as constraints on the realization phase. Each of these constraints is further described in chronological order below.

Content to be Mediated

The content to be mediated was:

- Giving perspective on movement for different length scales.
- Giving perspective on the forces governing movement on different length scales.
- Giving an introduction to a molecular system put in a simulation context about myosin V. Particulary describing the model made by Craig and Linke (2009).

Context of Learning

The context of learning was chosen a compendium. This choice was based on the format, enabeling an easy way of spreading information. A context can be interpreted as the surrounding contexture of a phenomenon, often in an abstract meaning (Svenska Akademien, 2009) (author's translation). Hence, a learning context can be interpreted as the surrounding contexture that provides learning possibilities or situations for learning. In this meaning, the compendium acts as the surrounding contexture mediating the content, simultaneously providing learning possibilities for the reader. It therefore constitutes the learning context.

Target Group

The target group was set to first year students at university level interested in mathematics and physics. This choice was based on the fact that the students presumably could get interested in the applications of what they were learning or going to learn during their university studies. It also made assumptions regarding their pre-knowledge possible.

6.2 Conception and a Priori Analysis

In this section, the conception and a priori analysis is described.

6.2.1 Conception

In the conception phase, the context constraints for the content to be mediated was made clear in accordance with Artigue (2015) by identifying three key didactical variables: the amount of explanations used, the use of metaphors and the ordering of sections (disposition). These didactical variables are further described below.

Ordering of Sections

The ordering is motivated by asking hypothetical questions in order to motivate the reader to engage further content, and answering them (author's translation):

- Summary - summarizes the content in order for the reader to get an overview of the content and to whom the content is intended.
- Introduction - arouses interest for the content
- How is myosin V modelled? - Awakes the question of what myosin V really is.
- What is myosin V? - Gives an answer to the question.
- How does movement arise? - Gives an idea of and motivates the relation between force and movement.
- How is the movement of myosin V mathematically modelled? - Uses the force-movement-relation.
- What are the applications of molecular models? - Gives an idea of the general applications of molecular models.
- Afterword - Rounds the compendium off and gives information on where more details are available.

The amount of explanations used and the use of metaphors are further explained in Sec. 6.2.2 below.

6.2.2 A Priori Analysis

In this section, the a priori analysis is conducted as described in Sec. 3.3.

Didactical Transposition

In a didactical transposition, many phenomena have to be interpreted and put into available representations (Tibell & Rundgren, 2010, p. 27). Bosch and Gascón describes the process of making a didactical transposition as ”a process of de-construction and rebuilding of the different elements of the knowledge, with the aim of making it ‘teachable’ while keeping its power and functional character” (Bosch & Gascón, 2006, p. 53). Kang and Kilpatricks’ (1992) process of recontextualization and repersonalization can be interpreted as an operationalization of this de-construction and rebuildment of knowledge. These processes aiming to make the knowledge accessible are further discussed below.

Recontextualization

The recontextualization consisted in transferring the knowledge from the biophysical or mathematical context into a more comprehensible context for the target group. This meant developing metaphors with which the target group could envision the complex phenomena and still get an insight into what the model represented. The level of detail presented was altered in order to compensate for more or less accurate presumptions about the target group's pre-knowledge. In this way readers with varying degree of relevant previous knowledge could utilize the material.

Repersonalization

In order to repersonalize the content of the model, assumptions regarding the target group was made, such as presumptions about what could be considered pre-knowledge or not. For example, powers of ten and prefixes could be used without further explanation. Because the target group was first year students on university level, their pre-knowledge is likely that of mid- to well informed upper secondary school students. The target group likely had an insight in and pre-knowledge of the concept of force and its applications from upper secondary school. The assumption was that to see the concept of force in a less familiar context and with a different perspective could arouse interest in the concept of force in the compendium. This was later utilized when regarding the hypothetical reader in the writing process.

Comments on Generalizability

The reader of a text is hypothetical and the didactical transposition is aimed towards a specific target group. Thus, the didactic transposition is not generally applicable. For this reason, Kang and Kilpatrick means that ”the processes of didactic transposition used in a textbook can be termed pseudo-contextual and pseudo-personal" (Kang & Kilpatrick, 1992, p. 6).

The use of Metaphors

One of the challenges for making the scientific content available for the suggested reader is to make the phenomena understandable in terms

of metaphors.

One of the challenges in the area of molecular life science is that the perceivable macro phenomena are explained by sub micro phenomena (Bahar, Johnstone, & Hansell, 1999). In the process of recontextualization, this implies translating sub micro phenomena to perceivable macro phenomena in general. One example of this is the metaphor using a bathing ball and table tennis ball as symbolic representations for collisions between water molecules and a part of myosin V (see Sec. 6.2, p. 12 in Appendix C).

A metaphor is a way of presenting a content with the help of something that the reader already is familiar with, which shares some properties of the content it represents. In the compendium, the representations have been chosen as to strive for independency of the reader's cultural background, enhancing the availability in terms of the reader's cognitive and contextual framework.

Making the Knowledge Relevant

In the created material, the social acknowledgement and legitimation of knowledge was done by declaring the knowledge explicitly and making the purpose of the knowledge explicit. This was made especially in the beginning of sections and in the abstract of the compendium but also continuously in the text.

6.3 Realization and the Collection of Data

In this section, the realization and the collection of data is described.

6.3.1 Realization

The realization phase consisted of writing. During this process, the use of metaphors and the amount of explanations were central. The target group's assumed pre-knowledge could be used as a presumption while writing, as a lower knowledge bound for explanations and metaphors used. Hypothetical questions asked by a person in the target group was continuously considered in order to adjust the level of explanation.

The Level of Detail was Altered

The level of detail may be diminished by re-interpretation and re-contextualization of the real theoretical phenomena. Simultaneously it is being put into terms of more understandable representations for the reader which, at the current level of knowledge, may be necessary for interpreting the phenomena at all. This process can be interpreted as lessening the gap between current knowledge and the knowledge being taught, hence making it more available. This leads to a loss of complexity and detail, but is necessary for the material to be accessible at all.

In the compendium, the level of detail has been varied in the explanation of the same phenomena, making explanations, metaphors and analogies more or less detailed. This enables the reader to get perspective on the phenomena and at the same time varies the level of detail being taught. By varying the level of detail, the content may get more appealing to an audience with different levels of pre-knowledge, increasing the probability of some explanation being suitable in the context of the reader. One example of this is the explanation of chemical transitions in Sec. 3.1 in Appendix C.

Language Choice for the Compendium

The chosen language of the compendium was Swedish. This consideration was a didactical choice based on the target group and was made in order to lessen the barrier between language and knowledge. Since the main target group presumable had Swedish as their language of instruction, the use of English would increase the risk of creating a linguistic barrier between the target reader and the content.

6.3.2 Collection of Data

In this section, the questions used in the survey is presented and the content that the questions aimed to elucidate is described. All questions below are translated by the author. The questions can be found in their original form in Appendix D. The ordering of the questions was made with the intention of inviting the respondent to share her or his impressions before being asked more specific questions about the content of the compendium. For respondents with performance anx-

iety, this may delay any experienced tension which would impact the responses to the earlier questions.

Motivation of Questions

- 1. How interested in the subject were you before and after reading?

  Question 1 aimed to test the correspondance between recontextualizaton and repersonalization against the survey participants.

- 2. Did you find the content of the compendium easy, moderately hard or too hard? Motivate.

  Question 2 aimed to test the agreement between the content presented in the preparatory analysis against the survey participants point of view.

- 3. What did you understand the aim of the compendium to be?

  Question 3 aimed to test the extent to which survey participants' understanding of the purpose of the compendium corresponded to the preliminary analysis.

- 4. What do you think of the compendium addressing the reader with "you"?

  Question 4 aimed to test how the choice of genre agreed with the self-positioning of the target reader.

- 5. Have you developed more understanding for anything after reading? If yes, for what?

  Question 5 aimed to test to what extent the didactical transposition managed to mediate the content in the preparatory analysis to facilitate epistemic access to central concepts.

- 6. Have you learned any new terms? If yes, what or which?

  Question 6 aimed to test to what extent the didactical transposition managed to mediate the content in the preparatory analysis.

- 7. Did the metaphors used help you in understanding the content of the compendium? If yes, in what way? If no, why not?

Question 7 aimed to test the agreement between recontextualizaton and repersonalization and its appropriateness for the survey participants.

- 8. Were any metaphor hard to understand? If yes, which and why?

  Question 8 aimed to test the agreement between recontextualizaton and repersonalization and its appropriateness for the survey participants.

- 9. Describe shortly something that differs between movement on molecular length scale in comparison to movement on everyday length scale.

  Question 9 aimed to test to what extent the participants were able to depersonalize the content and separate it from the metaphors used.

- 10. Was there any information that you missed or wanted to read more about? If yes, what?

  Question 10 aimed to test to what extent the content chosen the preparatory analysis aligned with the target group and how the transposition managed to mediate the content.

- Do you have any other comments regarding the compendium?

  This question was incorporated in order for the participants to be able to express any other opinions or aspects of the compendium not covered by the other questions.

The answers to these questions are analysed in Sec. 7.1.

Chapter 7

Analysis

In this chapter, a summary of the collected data and an analysis of the survey data is made.

7.1 A Postieriori Analysis

Comments made by participants are translated by the author in the analysis. Only answers that were regarded useful for answering the research question were considered. For instance, the last question did not give any answers relatable to the research question. Thus, this question has been omitted from the analysis.

The method of analysis is fully described in Sec. 4.2.2. In short, the analysis was conducted by relating the answers in the survey to the recontextualization, repersonalization and decontextualization, depersonalization process as described by Kang and Kilpatrick (1992).

Question 1

The survey indicated that five of the participants were converted from being uninterested to being interested. This can be interpreted as the recontextualization and repersonalization process being successful in giving the knowledge relevance for the target group. Six of the participants expressed an interest in the subject after reading. Two of the respondents did not express an interest by reading the compendium, of which none were already interested in the topic. As it is unrealistic to expect that a content will be equally appealing to all, even with the

best of presentations, this results points to an at least fairly successful utilization of recontextualisation and repersonalisation concerning motivating the reader.

Question 2

A majority of responses indicated that the degree of scientific complexity was appropriate for the target group. Some constraints were given. For example, a comment expressed that ”it was pretty hard for me because I don’t have that good pre-knowledge regarding the world of math/physics”. Another comment instead expressed that ”it was a good mix of pure physics (formula and similar) and examples that was easier to grasp as a non-physicist”. Two comments expressed a lack of a common thread. There were several comments which expressed a mixed opinion. This points towards a mainly successful agreement between the mediated content and the target reader. However, the result also indicates that the contextual disposition could have been clarified in order to achieve a common thread.

Question 3

The majority of comments directly express one or more of the contents intended to be mediated in the didactical transposition. Only one comment noted ”how force laws work”. Hence, a reasonable agreement exists between the parts of the preliminary analysis and the transposition. This can be interpreted as a fairly successful recontextualization and repersonalization process.

Question 4

All but one participant expressed a positive attitude towards the use of ”you”. Words like ”neat” and ”more personal” was repeatedly used. One person expressed ”offended”. This aspect of the repersonalization is regarded as mainly succesful, but points to the importance of considering positioning when constructing instructional material - something that was not addressed in this study.

Question 5

Half of participants gave an answer related to modelling and myosin V. The other comments had mixed or no topic. The result of the an-

swers was inconclusive. Thus, while the motivational purpose of the text was reasonably achieved, the scientific content was not as clearly conveyed. This is further discussed in Sec. 9.2.

Question 6

Several terms used in the context was submitted but no clear patterns were emergent. The result of the answers was inconclusive.

Question 7

All participants expressed the metaphors as helpful. Several reasons for this was presented: ”it explained in an easier way”, ”you could easily paint a picture in front of youself of how the myosin approximately was built and how it moves”, ”it helped in the text as it gets easier to separate things but I missed a clearer explanation in the pictures of how e.g. the parachuter’s movement differs from the myosin movement”. ”Yes, it was easier to relate the scientific [content] to something in the everyday. [...] It was easier to understand the movement, which was enforced when I watched the video at the end”. ”Yes, so that it was ’touchable’ ”.

This can be interpreted as the metaphors enhancing the relevance of the content, thus giving rise to a sucessful recontextualisation and repersonalization process.

Question 8

One participant expressed that it had a hard time imagining a parachuter in water and also how the parachuter ”moved ” in myosin V’s leg. Five of the participants expressed no troubles understanding the metaphors used. One participant expressed that it did not know. The metaphors were mainly received well by the target group, but possibly with a need to improve the connection between the scientific content and the metaphors.

Question 9

Clearly, some misunderstandings occured. ”Myosin is walking faster than humans”, ”movement on molecular scale can only move in one

direction". Two participants described the "overdamped" characteristic of a molecular system, which is correct.

This clearly indicates that the metaphors gave rise to misunderstandings. While this is always expected, it points to, as mentioned above, a need to utilize the metaphors.

Question 10

Some information was missed by the participants: "Maybe a real picture of what or how the molecule looks like or is similar to", "how the end model looks more in detail". "what the end model looks like in more detail". "I would have liked to see more about what Myosin V is what its purpose is in the body instead of quickly going into how the movement arises", "what the biggest reason is for the difficulty in a more correct simulation of the myosin".

This indicates that some use for a more detailed view of the real model or myosin was expected by the target group. This suggest the content could have been further elaborated in order to meet the expectations of the target group.

Chapter 8

Results

In this chapter, the results of the technical study and the didactical study is presented.

8.1 Technical Results

In this section, the technical results is presented. A numerical model of myosin V, two tests and one simulation result are presented in this section.

8.1.1 Numerical Model of Myosin V

A numerical model of myosin V is presented and derived in detail in Sec. 5.1.

8.1.2 Model Tests

To assure the accuracy of the derived model, two tests were developed and used with a successful result. The equipartition theorem test can be be found in Sec. 5.4.1 and the force test can be found in Sec. 5.4.2.

8.1.3 Simulation Results

Figure 8.1 is showing a simulation of myosin V using the model presented in this study. The parameters used for simulation in order to generate the figures can be found in Appendix A. The sharp edge in Fig. 8.1 indicates that the midpoint juncture potential is zero, because

no energy is needed for bending in this point. The black line represents the actine filament, the blue lines represent the IQ motifs and the circles represent the myosin V heads.

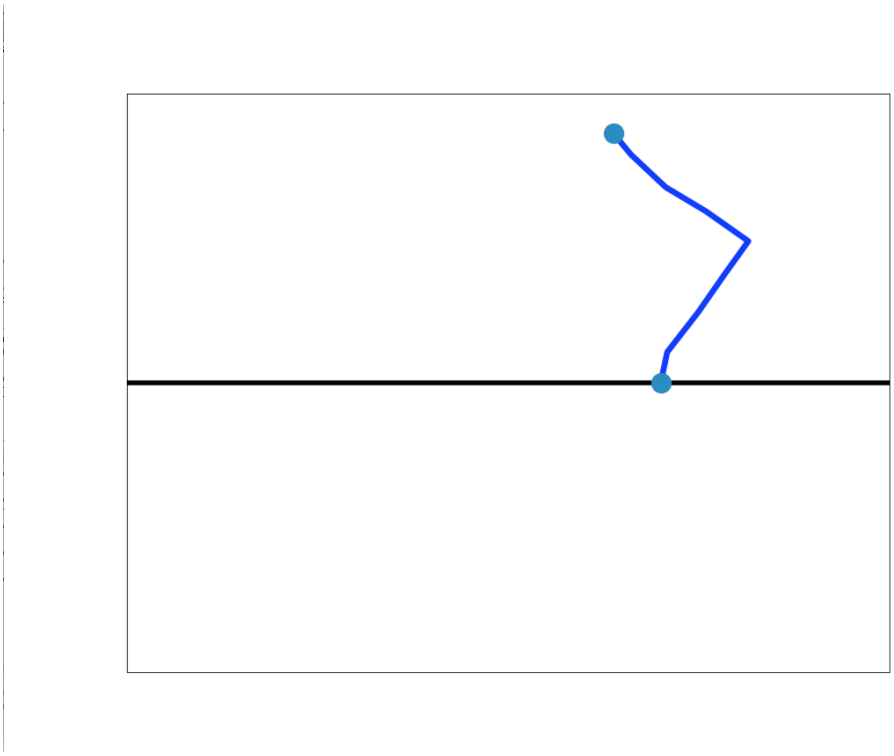

Figure 8.1: A figure showing a simulation of myosin V using the model described in this study.

A simulation was made with a step time of $t \approx 0.000639$ s. This demonstrates the that the developed model is able to produce a step.

8.2 Didactical Results

The survey indicates that the content was well received by the target group in respect to the scientific complexity and that it evokes motivation for learning. The survey indicates that the target group did not fully utilize a correct perspective on the characteristic movement on micro- and macro length scales. Nor did the target group achieve a correct perspective of the force laws governing the motion on micro- and macro length scales.

Chapter 9

Discussion

In this chapter the didactical and technical results are discussed.

9.1 Discussion of Technical Results

In this section, a discussion of the technical results are made.

9.1.1 Areas of Development

The programmed model shows many desirable properties, such as working chemical transitions, a conformation change to a Telemark state and appropriate elastic and bending behaviour. Simulations demonstrate that the myosin V stepping motion is working, see Sec. 8.1.3. Further measurements of the developed model are necessary in order to define its characteristics and further areas of development in respect to experiment data.

Further developments of this model indicates the requirement of simulations with long integration times, aiming to study the myosin V movement in detail. This is outside the time frame of this study.

Future Investigations

A comparison to measurement data regarding e.g. step length. step time, velocities, stall force and efficiency would further define the accuracy of this model. Conducting such experiments was outside the time frame of this study.

9.2 Discussion of Didactical Analysis

In this section, the results are discussed together with a comment on the validity of the result.

9.2.1 Discussion of the a Posteriori Analysis

The results from question 5 and question 7 point towards a need for a more developed agreement between the scientific content and the metaphors used. The survey showed that the metaphors used enhanced the experienced accessibility and relevance of the content, but certain misunderstandings could be avoided by further elaboration of the connections between the scientific content and the metaphors. An area of improvement would therefore be to incorporate a more detailed visualization theory for the development of content- and target group dependent metaphors.

The methodology of didactic transpositions was developed for usage in a mathematical context. An elucidation of the relationships and the dependencies between the mathematics present in a biophysical context may enable a new perspective on the theory of didactical transpositions. In a long term perspective, this may enable the development of new tools for the construction of a biophysical learning material.

Relation to Earlier Research

The connections between the scientific content and the metaphors may be understood in the terms of Bahar et al. (1999). The authors describe the complexity and level of difficulty in a biological phenomena arising by decomposing it into different thought levels, the macro, micro and symbolic level. A phenomena is understood in its full when all levels are covered.

A metaphor may be related to representations of the different thought levels. Novices may find it hard to understand and move inbetween different thought levels (Bahar et al., 1999). If a metaphor is able to either clarify a connection between the thought levels or represent all levels, it may be useful for a person learning the phenomenon. The learner can then be able to use the metaphor to move between thought

levels, giving an ability to fully or partly understand the phenomena. The extent to which the clarifications are necessary are likely target group dependent, as a specific target group can be expected to have specific prerequisites or prior knowledge.

9.2.2 Discussion on the Collection of Data

A questionnaire was likely not the best choice of method in order to explore how the target group experienced the created material. Conducting interviews with the target group may have allowed for a more thorough qualitative analysis. The time frame of this study did not allow for interviews to be planned, conducted, transcribed and analysed due to time restraints.

In order to get analysable answers from participants within the time frame of the study, a questionnaire was regarded as an appropriate choice of method. The questions asked were more specified in order to lessen the amount of text asked for and to provide a more comparable and analysable data in a short time range. Often, closed questions are ''directly to the point and deliberately more focused than open-ended questions. Indeed it would be almost impossible, as well as unnecessary, to try to process vast quantities of word-based data in a short time frame'' (Cohen et al., 2011, p. 382). If interviews would have been conducted, more open questions could have been asked which would allow for other viewpoints of interest to be expressed. This could have allowed for other interesting aspects to emerge from the data.

9.2.3 Validity of Results

The validity of the results could be enhanced by considering a more specific target group. This would enable a more detailed specification of the target group's characteristics and interests. Furthermore, it could enable of a more directed and precise recontextualization and repersonalization process. This could be useful in the preliminary analysis phase of the didactical transposition process.

A larger sample group could give a more detailed indication on the results provided in this study. The sample group was small and the

responses on some questions in the survey were not specific enough to exhibit any patterns. If more responses were regarded, a clearer pattern may have emerged. Another way of enhancing these results would be to ask more directed and precise questions in the survey in order to unify the results or show a clearer discrepancy.

9.2.4 Future Investigations

Question 4 in the survey indicates that considering positioning in the construction of instructional material may have importance for future didactical transpositions.

The survey shows a demand for target group specific metaphors and a theory for the development of such.

9.2.5 Challenges When Writing

One of the challenges when writing was to conduct a didactical transposition into a context outside of school. During my education, only inner didactical transpositions have been studied; transpositions of the bodies of knowledge into a context bounded by a curriculum. An outer didactical transposition is in some sense a broader task with no clear or pre-existing boundaries or framework within which the content must be presented to the learner. One of the main tasks was therefore to identify a potential reader and the key characteristics of this reader in order to distinguish the areas of interest, leading up to a relevant re-contextualisation and re-personalization in the writing process in the preliminary analysis phase.

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Appendix A

Parameters Used in Model

In this chapter, all parameters used in the model is described and numerically defined.

Table A.1: A table showing parameters used in the developed model.

Parameters			
Parameter	Value	Description	Source †
N	9	Number of discrete nodes	
Δt	$1 \cdot 10^{-10}$	Time step. Adjustable, the value stated is the value used for simulations.	
C	$10^{10}kT$	Rod stiffness	Estimation.
$k_B = k$	$1.38064852 \cdot 10^{-23}$ kgm^2/s^2K	Boltzmann constant	
T	300 K	Temperature	Estimation.
L_{spacing}	$36 \cdot 10^{-9}$ m	Spacing on actine filament	(Mehta et al., 1999) (Burgess et al., 2002) (Walker et al., 2000)
α_{H}	$6.2 \cdot 10^{-11}$ kg/s	Friction coefficient	
α_{N}	$4.1 \cdot 10^{-11}$ kg/s	Friction coefficient	
L_{H}	$5 \cdot 10^{-9}$ m	Head length	(Liu, Taylor, Krementsova, Trybus, & Taylor, 2006)
L_{N}	$10 \cdot 10^{-9}$ m	Neck length	(Veigel, Wang, Bartoo, Sellers, & Molloy, 2001) (Moore, Krementsova, Trybus, & Warshaw, 2001)
R_{screen}	$6 \cdot 10^{-10}$ m	Electrostatic screening radius of filament	

† if omitted the source is (Craig & Linke, 2009).

Table A.2: A table showing the potential energies used in the developed model.

Potential energies			
Parameter	Value	Description	Source †
V_{NN}	$50kT$	Potential energy in neck-neck juncture. Adjustable.	
V_{HN}	$50kT$	Potential energy in head-neck juncture. Adjustable.	
V_i	V_{NN} for $i = 2, 3, ..., N-3$ and V_{HN} for $i = 1, N-2$	Potential energy in i:th juncture.	

† if omitted the source is (Craig & Linke, 2009).

Table A.3: A table showing the chemical transition rates used in the developed model.

Chemical transition rates			
Parameter	Value	Description	Source
k_{12}	$1/\Delta t$	Chemical transition rate $*$	(De La Cruz, Wells, Rosenfeld, Ostap, & Sweeney, 1999)
k_{23}	$700s^{-1}$	Chemical transition rate $*$	(De La Cruz et al., 1999)
k_{34}	$-$	Chemical transition rate $*$, diffusion limited.	$-$
k_{45}	$200s^{-1}$	Chemical transition rate $*$	(De La Cruz, Wells, Sweeney, & Ostap, 2000) (Baker et al., 2004)
k_{56}	$15s^{-1}$	Chemical transition rate $*$	(Baker et al., 2004) (Purcell, Sweeney, & Spudich, 2005)
k_{61}	$1.6s^{-1}\mu M^{-1}$	Chemical transition rate $*$. Molar concentration is Q_{ATP}	(De La Cruz et al., 1999)
Q_{ATP}	$1\mathrm{mM}$	ATP concentration	(Yengo, De La Cruz, Safer, Ostap, & Sweeney, 2002)

$*$ The chemical transition rates k_{pq} imply that the probability for a transisition from p to q to occur within one time step is $k_{pq}\Delta t$.

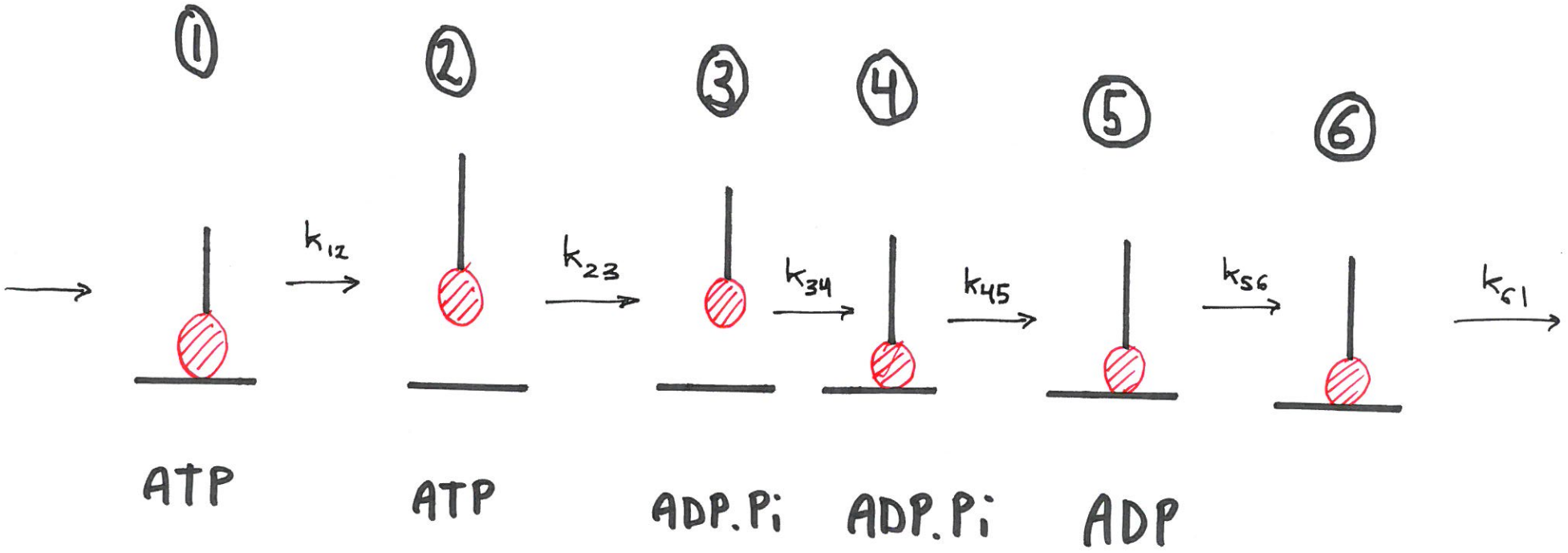
Appendix B

Supplemental Figures

Here, supplemental figures are presented.

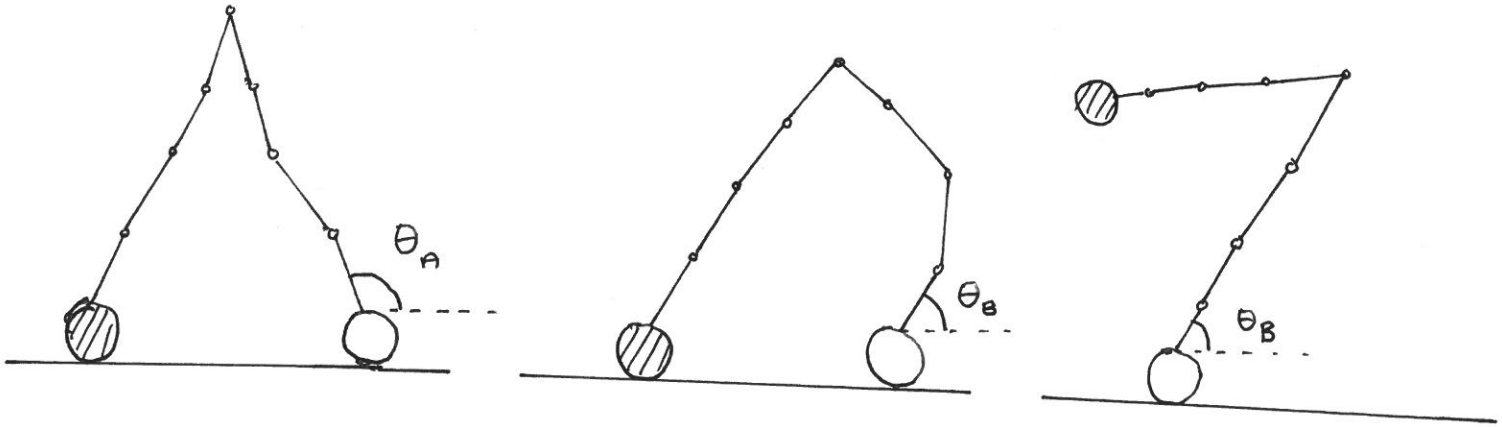
B.1 Chemical Transitions

Here, the chemical transitions are shown.


1
2
3
4
5
6
k_{12}
k_{23}
k_{34}
k_{45}
k_{56}
k_{61}
ATP
ATP
ADP.Pi
ADP.Pi
ADP

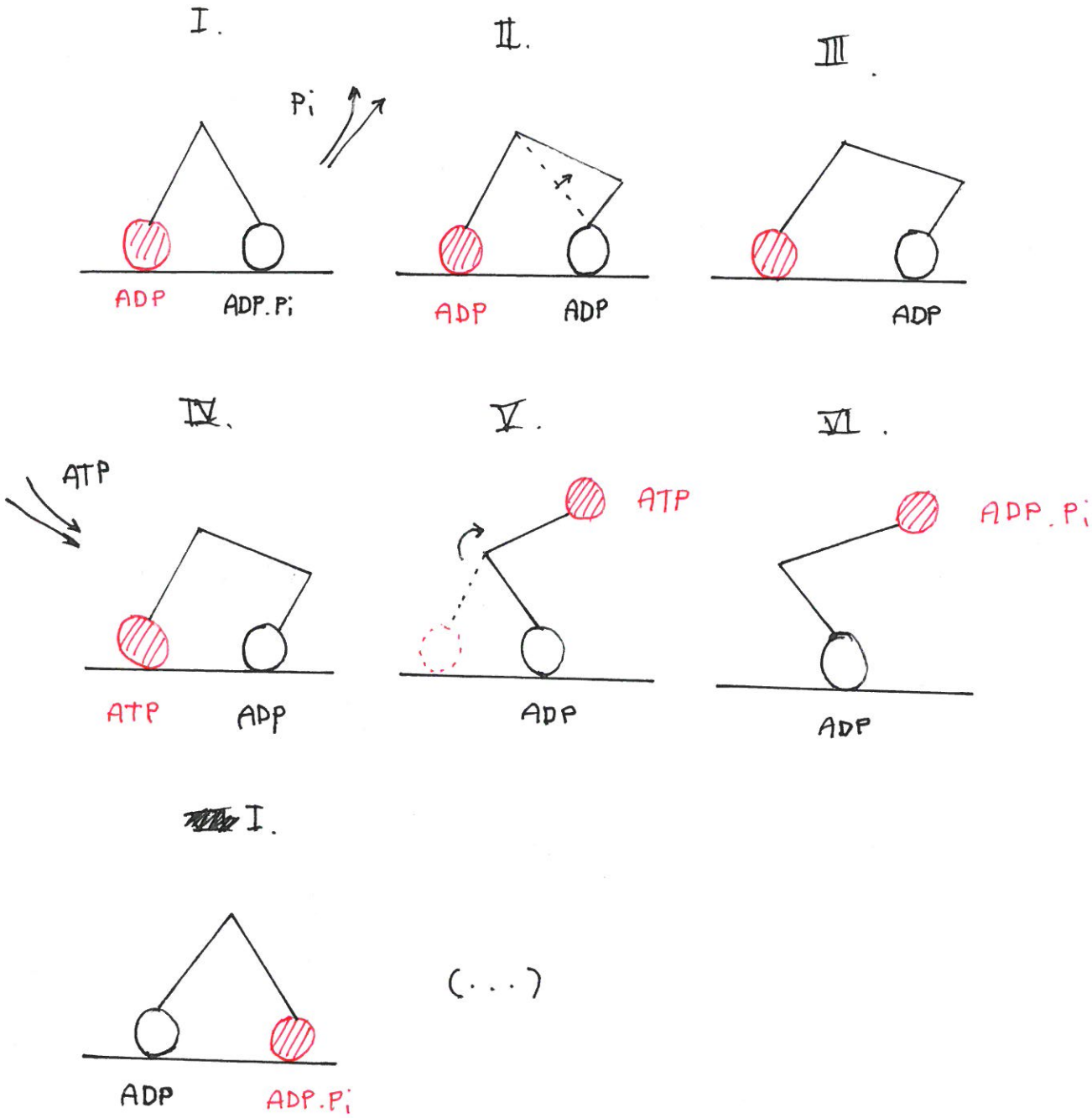
B.2 Conformation Change

Here, the angle change is shown.


θ_A
θ_B
θ_B

B.3 Stepping Mechanism

Here, the stepping mechanism is shown. The myosin V protein undergoes a step by releasing the back head, moving it in front of the other and reattaching to the actine filament.


I.
II.
III.
Pi
ADP
ADP.Pi
ADP
ADP
ADP
IV.
V.
VI.
ATP
ATP
ADP
ATP
ADP
ADP.Pi
ADP
I.
ADP
ADP.Pi
(...)

Appendix C

Compendium

Here, the compendium created in the didactical study is attached.

Motorprotein, fallskärmshoppare och streckgubbar

- perspektiv på rörelse på olika längdskalor

Gustav Sollenberg

Innehåll

1 Sammanfattning

Det här kompendiet riktar sig till nya högskolestudenter som är intresserade av teknik, fysik och matematik. Syftet är att ge en översiktlig och intuitiv inblick i en komplex matematisk modell av ett biofysikaliskt system. I det här fallet en mekanokemisk modell av motorproteinet myosin V. Modellen beskrivs här utan att kräva mer förkunskaper än gymnasiematematik och fysik. Förhoppningen är samtidigt att ge perspektiv på vad rörelse på olika längdskala kan innebära.

Det här kompendiet syftar till att ge en intuitiv beskrivning av en numerisk modell av ett motorprotein som heter myosin V. Att göra en numerisk modell innebär att man gör en matematisk modell av de lagar som styr molekylens rörelse, skriver lagarna i datorkod och simulerar dess rörelse. Kompendiet behandlar ett ämne som sträcker sig lite utanför skolans värld och ger en inblick i hur matematik och fysik kan användas för att avbilda och modellera ett komplext fenomen utan att blanda in för svår terminologi.

2 Inledning

För den som är intresserad av vetenskap, teknik och matematik kan molekylernas värld kännas otillgänglig, men så behöver det inte vara. Nivån i kompendiet är enkel och baseras på bekanta begrepp och exempel.

Du kommer att introduceras till de molekylära motorernas fascinerande värld och ett forskningsområde med en enorm framtidspotential. Det här kompendiet beskriver en modell av motorproteinet myosin V - en molekylär motor som transporterar information eller celldelar inuti celler. Molekyler rör sig dock inte som vardagliga föremål. Hur rörelsen skiljer sig åt kommer du snart att få reda på.

3 Hur modelleras myosin V?

I detta avsnitt beskrivs modellen av myosin V med hjälp av intuitiva resonemang och bilder.

Det finns flera olika sätt att modellera myosin V. En av de modeller som ger bäst resultat mot mätdata är en så kallad mekanokemisk modell där man både tar hänsyn till de kemiska- och mekaniska egenskaper som påverkar myosinets rörelse. Modellen av myosin V är inte helt olik två ben som går framåt. Man kan därför tänka sig myosin V som en person som går på lina och som kan bära någonting med sig.

3.1 Myosin kan ses som en streckgubbe

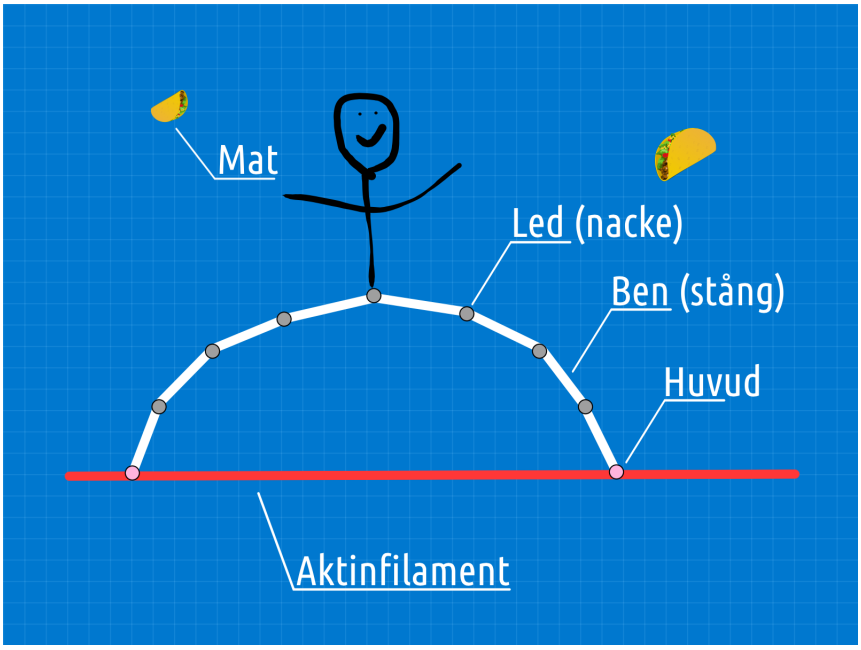
Figur 1 visar en förenklad skiss av myosin V. Motorproteinet kan med lite fantasi ses som en stelbent och darrig streckgubbe utan överkropp och med tre knäleder som går på lina. Linan är ett så kallat aktinfilament som är en vanligt förekommande transportväg i människokroppen. För att orka lyfta på benen måste gubben få energi. Energin kommer från att gubben ständigt bombarderas med molekyler som – om gubben har tur – träffar honom rakt i munnen och omvandlas till energi så att han orkar lyfta på bakbenet och ta ett steg.

I själva verket består ätandet av att streckgubben genomgår en serie kemiska övergångar som är mer eller mindre sannolika. Mer exakt en hydrolys av adinotrifosfat (ATP) som gör att benet släpper, som sedan omvandlas till adinodifosfat med en fri fosfatgrupp (ADP.Pi). Fosfatgruppen frigörs och låter adinodifosfatet (ADP) fästa till aktinfilamentet igen, varefter det omvandlas till ATP och processen kan upprepas. Varje steg i denna komplexa följd av reaktioner inträffar med vissa sannolikheter som beskrivs i modellen.

3.2 Ben

Vardera ben består av tre grupper av tätt sammanbundna aminosyror (eng. IQ motifs) som hänger samman som en kedja. Aminosyregrupperna är så hårt kemiskt bundna att de kan modelleras som elastiska stänger, där stängerna beter sig nästan som en fjäder i en bläckpenna. Den stora skillnaden från den sortens fjäder är att de i modellen bara kan tryckas ihop och sträckas ut men inte böjas i sidled.

Fötterna på benen kallas ironiskt nog för huvuden och är de som fäster på aktinfilamentet tack vare elektriska krafter. Aktinfilament är egentligen



Figur 1: Myosin V kan ses som en streckgubbe som vandrar på ett aktinfilament.

tvinnade precis som ett rep, men modelleras som matematiska punkter på konstant avstånd från varandra. I verkligheten går alltså myosinet runt och runt längs trådarna, medan det i modellen går rakt fram (eller bak). För den mätdata som finns för myosinets rörelse spelar denna typ av rörelse ingen roll. Svårigheten som finns hos modeller idag är att få modellen av proteinet att ta sig framåt lika effektivt som det verkliga myosin V. Det finns därmed behov av att hitta mer detaljerade och verklighetstrogna modeller.

3.3 Knäleder

Stängerna sitter fast i rörliga leder, som kan liknas med ett knä som går att böja i alla olika riktningar eller en kardanaxel på en bil. Knutpunkterna kallas nackar. Vi kan därför tänka på knälederna som kopplingar mellan kedjor av aminosyror.

4 Vad är myosin?

I detta avsnitt beskrivs kortfattat vad myosin V är och vad det gör i cellen.

Myosin är en familj av proteiner som alla har olika uppgifter i cellen. Bland annat är ett av proteinerna i familjen centralt för musklernas kontraktion i kroppen. Med andra ord, möjligheten för dig att röra på dig. Detta kompendium behandlar ett av proteinerna inom familjen - myosin V. Det är ett transportprotein som används för att transportera mRNA och organeller, det vill säga cellulär information och celldelar i cellen. Myosin V väger ungefär 10^{-21} kg och rör sig i 36 nanometer långa steg med en snitthastighet på ungefär 550 nm/s längs så kallade aktinfilament. Det skulle i vår längdskala motsvara en snitthastighet på ungefär 22 km/h, så om myosin V hade varit en person hade den gått ungefär lika fort som en cyklist. Proteinet rör sig omringat av vatten med en temperatur på cirka 37°C. Aktinfilament kan vi tänka på som rep som består av tvinnade trådar.

För att ta reda på hur myosinet rör sig längs aktinfilamenten börjar vi med att titta på hur rörelse uppstår och vad som på verkar hur ett föremål rör sig.

5 Hur uppstår rörelse?

I detta avsnitt beskrivs olika sätt att se på rörelse och hur rörelse på molekylär längdskala skiljer sig från vardagliga fenomen. Det senare görs genom att jämföra med en fallskärmshoppares rörelse.

5.1 Kraft och rörelse

Rörelse kan ses som en konsekvens av att en kraft verkar på ett objekt med massa.

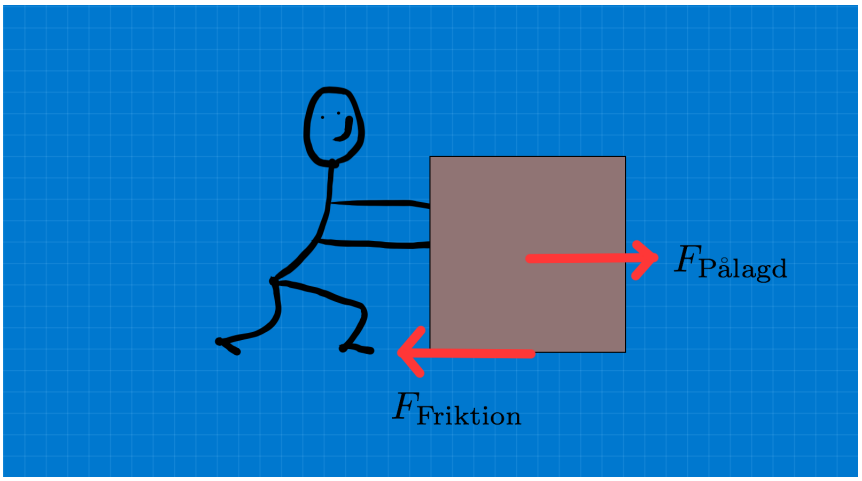
Sätt dig in i situationen att du ska flytta en låda som står på ett golv. Du skjuter runt den på golvet och börjar fundera. Vilket samband verkar finnas mellan den pålagda kraften du skjuter på lådan med och dess hastighet? Fundera och kom ihåg ditt svar medan du läser vidare.

5.1.1 Aristoteles kraftlag

Om vi gör en enkel analys av de krafter som verkar på lådan ser vi att den pålagda kraften motverkas av friktionskraften från golvet. Den totala kraften är summan av kraften som vill putta på lådan, $F_{\text{pålagd}}$ och friktionskraften F_{friktion}

$$F_{\text{total}} = F_{\text{pålagd}} + F_{\text{friktion}} \tag{1}$$

Friktionskraftens storlek är proportionell mot hastigheten, så $F_{\text{friktion}} = -\gamma v$. Minustecknet kommer från att friktionskraften vill bromsa rörelsen och verkar motriktat rörelsen.



Figur 2: Vi tittar på rörelsen av en låda för att illustrera Aristoteles kraftbegrepp.

Nu kan du komma ihåg ditt svar på frågan i början på avsnittet igen. Ett möjligt svar är att ju hårdare du trycker till lådan, desto fortare tycks den åka iväg. En vanlig missuppfattning som följer är att kraften är proportionell mot hastigheten. Det vill säga att ju större pålagd kraft du verkar med på ett föremål, desto högre hastighet får föremålet. Vad skulle det innebära? Matematiskt kan vi skriva detta:

$$F_{\text{pålagd}} = \gamma v \tag{2}$$

där γ är någon friktionskoefficient och v en hastighet. Denna kraftrelation brukar kallas Aristoteles kraftlag. För den totala kraften skulle det innebära att

$$F_{\text{total}} = 0 \tag{3}$$

eftersom den pålagda kraften är lika stor som friktionskraften fast motriktad.

Relationen där kraften är proportionell mot hastigheten kan upplevas intuitivt rätt i vissa sammanhang. Det enda problemet med den intuitionen är att den är felaktig. Vad händer när lådan släpper från dina händer och inte verkar med någon pålagd kraft på den? Jo, $F_{\text{pålagd}} = 0$, vilket måste innebära att hastigheten v är noll om ekvation (2) ovan ska stämma, eftersom γ inte får vara noll. Det skulle alltså innebära att lådan skulle stanna i samma ögonblick den släpper från din hand och så vet vi inte händer eftersom lådan fortsätter att glida en bit innan den stannar.

En annan konsekvens av sambandet skulle vara att tyngre föremål faller snabbare än lätta föremål. Om den pålagda kraften på ett föremål är den av gravitationen $F_g = mg$ och vi tar hänsyn till friktionskraften från luften (luftmotståndet) ger det ur ekvation (2) att:

$$mg = \gamma v \tag{4}$$

Eftersom m och γ är konstanter, måste v vara större om m är större. Galileios experiment där han släpper olika vikter från det lutande tornet i Pisa visar att detta är fel. Om friktionen är försumbar, som när föremålen har samma form och yta, kommer föremålen att falla precis lika fort mot marken oavsett hur mycket de väger. Detta kan testas genom att släppa exempelvis en pingisboll och en golfboll samtidigt från händerna.

5.1.2 Newtons lag

Vad händer i sådana fall med rörelsen när den totala kraften är noll? Enligt Aristoteles kraftlag skulle föremålet stå stilla. Newton ger oss svaret att så inte är fallet. Newtons andra lag ger oss att kraft är kopplat till förändring

av hastighet, acceleration,

$$F = ma \tag{5}$$

Att kraften är noll innebär helt enkelt att objektets hastighet inte förändras - hastigheten är konstant. Det innebär att om objektet stod stilla från början, så kommer det fortsätta att stå stilla. Om objektet förflyttade sig med konstant hastighet från början, så kommer objektet att fortsätta förflytta sig med samma hastighet.

I fallet med lådan innebär en större kraft att hastighetsförändingen hos lådan är större om du trycker till den hårdare. Det är i sin tur denna förändring som ger upphov till en ökad hastighet hos lådan. Iakttagelsen att lådans hastighet blir högre när du trycker med en större kraft är därför korrekt, men kraftbegreppet har ingen direkt koppling till hastigheten. Under hela tiden du har händerna mot lådan förändrar du lådans hastighet, men du upphör att förändra den när lådan släpper från dina händer.

5.2 Hur rör sig en fallskämshoppare?

Det finns en skillnad i hur molekylära, biologiska system rör sig och hur vardagliga objekt rör sig. För att förstå hur det molekylära systemet modelleras ska vi börja med att titta på hur en fallskärmshoppare rör sig och jämföra det med myosinets rörelse.

Utan fallskärm hade den stackars fallskärmshopparen (som nu bara är en hoppare) fallit i fritt fall med konstant acceleration $a = g = 9.82$ [m/s^2] mot marken, oberoende av hopparens storlek, form och massa. g är som bekant tyngdaccelerationen på jorden på grund av gravitationen. Med fallskärm måste friktionen på grund av fallskärmen tas med. Detta ger

$$F_{\text{total}} = F_g + F_{\text{friktion}} \tag{6}$$

Den totala kraften på fallskärmshopparen är summan av tyngdkraften $F_g = mg$ samt luftmotståndet från friktionen i fallskärmen $F_{\text{friktion}} = -\gamma v$. Dessa krafter är motriktade varandra. När fallskärmshopparen lämnat planet accelererar den mot marken och rör sig med allt högre hastighet. När friktionskraften och tyngdkraften till slut blir lika stora blir den totala kraften på fallskärmshopparen noll. Man säger då att fallskärmshopparen har nått sin sluthastighet v_s. Newtons lag ger då att hastigheten är konstant, eftersom krafterna tar ut varandra och den totala kraften är noll.

$$mg - \gamma v_s = 0 \tag{7}$$

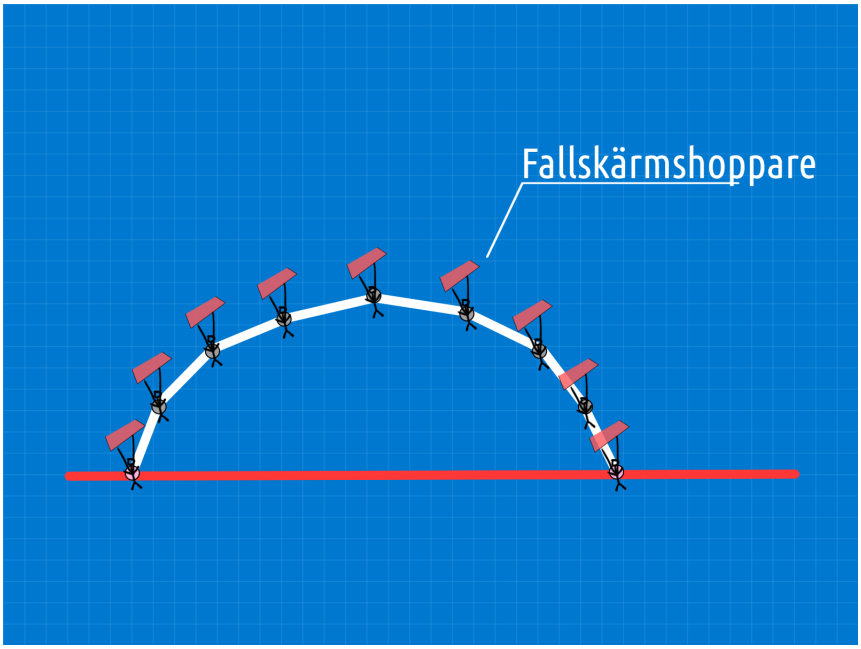
Ett annat sätt att skriva samma sak är:

$$F_g = \gamma v_s \tag{8}$$

Det visar sig att den pålagda kraften (tyngdkraften) är proportionell mot sluthastigheten och Aristoteles kraftlag stämmer för fallskärmshopparen i detta fall! Specialfallet där den totala kraften är försumbar och den pålagda kraften är proportionell mot hastigheten på grund av friktion kallas överdämpat. Det är precis sättet som molekylära objekt rör sig på. Rörelsen kallas överdämpad om friktionen är så stor att rörelsen nästan stannar i samma ögonblick som den pålagda kraften tas bort. Det beror på att dämpningen på grund av friktionen dominerar rörelsens tröghet.

5.3 Myosinets delar är som fallskärmshoppare i vatten

Det är den överdämpade egenskapen som är den stora skillnaden mellan rörelse på molekylär längdskala och vardaglig längdskala.



Figur 3: Myosinets delar kan ses som fallskärmshoppare i vatten som nått sin maximala hastighet.

Ett sätt att se på myosinets rörelse är att tänka sig att jämföra varje del med en fallskärmshoppare som nått sin maximala hastighet. Istället för luftmotstånd består motståndet av att myosinet rör sig i en vätska. Myosin V modelleras därför precis som små fallskärmshoppare i nanoskala, där alla rör sig med sin sluthastighet 550 nm/s i varje tidpunkt. Figur 3 illustrerar detta scenario. Varje fallskärmshoppare skulle vara några enstaka nanometer långa, precis som storleken på segmenten. Man kan tänka sig att fallskärmshopparna håller gummiband mellan varandra som motsvarar de elastiska segmenten i vit färg i Fig. 3.

6 Hur modelleras myosinets rörelse fysikaliskt?

I detta avsnitt beskrivs den matematiska delen av myosinets rörelse intuitivt.

Eftersom kraft och rörelse är tätt förenade begrepp är det naturligt att beskriva myosinets rörelse med hjälp av en kraftekvation. I detta fall används Langevins överdämpade kraftekvation, i varje rörelseriktning ser den ut såhär:

$$F_{\text{total}} = F_{\text{yttre}} + F_{\text{slump}} + F_{\text{friktion}} + F_{\text{elastisk}} = 0 \tag{9}$$

Innebörden av varje term i denna kraftekvation kommer att förklaras nedan.

6.1 Total kraft

F_{total} står för den totala kraft som verkar på en del av myosinet. En del kan vara ett huvud eller en nacke. På grund av friktionen dämpas accelerationen i princip ut, varför ekvationen kallas överdämpad. Värdet på kraften $F_{\text{total}} = ma$ som verkar på varje del blir därför väldigt liten. Så liten att den till god approximation blir noll för att förenkla beräkningarna.

6.2 Yttre kraft på grund av en last

F_{yttre} är den yttre kraft som verkar på en del. Denna term har ett värde om myosindelen exempelvis bär med sig en last eller drar i någonting, annars är den lika med noll. Vi kan tänka oss att det är samma kraft som verkar på våra händer och armar om vi skulle lyfta eller bära någonting. Mätningar visar att myosin V orkar dra en last på $2 - 3$ pN.

6.3 Slumpkraft på grund av värme

F_{slump} är en slumpmässig kraft på varje del som uppstår på grund av värme. I Kap. 3.1 beskrevs myosin som en darrig streckgubbe och det är denna slumpkraft som gör att streckgubben darrar.

Värmen i vattnet som omger myosinet gör att vattenmolekylerna ständigt är i rörelse och kolliderar med myosindelarna. Vi kan jämföra en myosindel med en badboll som vi hela tiden kastar en massa pingisbollar på. Dessa pingisbollar motsvarar vattenmolekyler som krockar med myosinet. Pingisbollarna studsar av, men får badbollen att röra sig litegrann.

6.4 Friktionskraft på grund av kollision med vattenmolekyler

F_{friktion} är en friktionskraft som uppstår på grund av att myosinets delar hela tiden krockar med vattenmolekyler i vätskan som den rör sig i. Precis på samma sätt som en fallskärmshoppare, bil eller ett flygplan hela tiden

krockar med luftmolekyler i luften när det rör sig. Intuitivt är det rimligt att tänka sig att ju snabbare partikeln rör sig, desto fler vattenmolekyler hinner partikeln kollidera med. Därför blir friktionskraften större ju högre fart partikeln har, vilket kan förklara uttrycket för $F_{\text{friktion}} = -\gamma v$. Eftersom friktionen motverkar rörelsen är kraften negativ.

6.5 Kraft på grund av elasticitet och böjning

F_{elastisk} är en kraft som verkar på myosinets delar på grund av motstånd i lederna och elastiska ben. Intuitivt kan vi tänka att det går åt lite extra kraft för streckgubben att använda sina muskler för att böja på knälederna om de är tröga att böja på. Benen modelleras som elastiska stänger, vi kan tänka på dem som fjädrar. Eftersom F_{elastisk} ger ett motstånd är kraften negativ.

6.6 Tolkning

Med streckgubbesmetaforen som tidigare användes kan F_{total} tolkas som den totala kraft som gubbens muskler drar i någon hans knäleder (nackar) eller fötter (huvuden). Som vi vet från Newtons lagar innebär en kraft som är noll att punkterna rör sig med konstant hastighet i varje tidpunkt.

Ett annat sätt att se på myosinets delar är som fallskärmshoppare som alla har nått sin sluthastighet, något som också beskrivs i Kap. 5.3. Vi kan nu bygga på denna analogi genom att tänka oss att alla fallskärmshoppare håller i fjädrar mellan varandra som sträcks eller dras ut mellan dem medan de flyger, fast i det här fallet simmar de i vatten.

7 Vad ska man ha molekylära modeller till?

Nu har du fått läsa lite om hur myosin V modelleras. I detta avsnitt beskrivs några tillämpningsområden för molekylär modellering översiktligt.

Inom medicin- och läkemedelsbranschen kan molekylär modellering vara av intresse för läkemedelsframställning. En möjlig tillämpning för motorprotein kan vara att transportera ämnen inuti eller mellan celler. Dessa transporter kan vara nödvändiga för att läkemedel ska kunna fungera. Motorprotein är även delaktiga vid celldelning, vilket gör dem intressanta inom exempelvis cancerforskning. Att göra numeriska modeller av nya läkemedel möjliggör även att man kan undvika potentiellt skadliga tester på människor och djur. Det medför en etisk aspekt av simulering som kan vara positiv.

I framtiden kan molekylära maskiner utgöra ett helt nytt nanoteknikområde med tillämpningar som vi aldrig tidigare kunnat föreställa oss. Nanoteknik syftar på att tekniken är i storleksordningen nanometer. Att efterlikna naturens molekylära maskiner kan ge inspiration till nya tekniska tillämpningar som grundar sig i miljontals år av utveckling till följd av evolutionen. Inom nanotekniken kan därför biologiska strukturer vara en viktig inspirationskälla.

Tekniken med molekylära maskiner är ett aktivt forskningsområde och det är ständigt under utveckling. Att det är ett aktuellt forskningsområde styrks ytterligare av 2016 års Nobelpris i kemi, tillägnat Sauvage, Stoddart och Feringa för deras molekylära maskin.

8 Avslutande ord

I beskrivningen som har gjorts har många metaforer använts. Trots att de kan ge en inblick i hur myosin ser ut eller hur det rör oss, är det viktigt att nämna att det inte är precis såhär det ser ut i verkligheten. Det finns en skillnad mellan verkligheten, modellen som avbildar verkligheten och de bilder vi gör oss av modellen. Fokus har legat på det sistnämnda i detta kompendium och det kan vara värt att påpeka att myosin V varken är någon streckgubbe, består av badbollar eller fallskärmshoppare. Metaforer är inte tillräckliga för att beskriva myosin V fullständigt i alla sammanhang, men de kan åtminstone ge oss en representation och en uppfattning om vad det handlar om.

8.0.1 Vill du veta mer?

Modellen som beskrivits är gjord av Craig och Linke (2009) och finns att finna i referenslistan nedan om du är intresserad av detaljer. Om du är vill se hur det ser ut när Craig och Linke har simulerat rörelsen av myosin V kan du hitta det under följande länk: `https://www.youtube.com/watch?v=KfEbuHCGIIo`

Referenser

Craig, E. M. & Linke, H. (2009). Mechanochemical model for myosin v. *Proceedings Of The National Academy Of Sciences*, *106*(43), 18261–18266.

Appendix D

Survey

In this chapter, screenshots of the survey is presented.

Undersökning av "Motorproteiner, fallskärmshoppare och streckgubbar"

Undersökningen är frivillig och består av 10 frågor. Tiden för genomförande uppskattas till cirka 10 minuter. Dina svar är anonyma och du kan välja att avbryta din medverkan när som helst utan några personliga konsekvenser. All insamlad data kommer endast att användas i forskningssyfte.

Notera att denna undersökning ej syftar till att testa dina kunskaper inom matematik eller fysik. Undersökningen syftar endast till att synliggöra eventuella lärdomar av kompendiet "Motorprotein, fallskärmshoppare och streckgubbar".

Kompendiet kan du hitta under följande länk:
https://drive.google.com/file/d/19UN0yIY3EO03vvtasNAf1vm6ohaHcz0n/view?usp=sharing

*Required

Frågor

1. Hur intresserad var du av ämnet före och efter läsning? *

- (a) Jag var redan intresserad innan jag började läsningen och jag är fortfarande intresserad.
- (b) Jag var inte så intresserad innan jag började läsningen, men kompendiet gjorde mig intresserad.
- (c) Jag var inte intresserad innan läsningen och jag är fortfarande inte så intresserad.

Frågor

1. Hur intresserad var du av ämnet före och efter läsning? *

- (a) Jag var redan intresserad innan jag började läsningen och jag är fortfarande intresserad.
- (b) Jag var inte så intresserad innan jag började läsningen, men kompendiet gjorde mig intresserad.
- (c) Jag var inte intresserad innan läsningen och jag är fortfarande inte så intresserad.
- (d) Jag var intresserad innan jag började läsningen, men kompendiet gjorde mig ointresserad.

2. Tyckte du att innehållet i kompendiet var lätt, lagom svårt eller för svårt? Motivera. *

Your answer

3. Vad upplevde du var syftet med kompendiet? *

Your answer

4. Vad tycker du om att kompendiet tilltalade läsaren med "du"? *

Your answer

5. Har du fått ny förståelse för någonting efter läsningen? Om ja, för vad? *

Your answer

6. Har du lärt dig något nytt begrepp? Om ja, vilket eller vilka? *

Your answer

Exempel på metaforer som användes i texten: streckgubbe, fallskärmshoppare, badboll.

7. Hjälpte de använda metaforerna dig att förstå innehållet i kompendiet? Om ja, på vilket sätt? Om nej, varför inte? *

Your answer

8. Var det någon metafor som du tyckte var svår att förstå? Om ja, vilken och varför? *

Your answer

9. Beskriv kortfattat någonting som skiljer sig åt mellan rörelse på molekylär längdskala jämfört med rörelse på vardaglig längdskala. *

Your answer

10. Var det någon information du saknade eller som du hade velat läsa mer om? Om ja, vad? *

Your answer

Har du några övriga kommentarer angående kompendiet?

Your answer

9. Beskriv kortfattat någonting som skiljer sig åt mellan rörelse på molekylär längdskala jämfört med rörelse på vardaglig längdskala. *

Your answer

10. Var det någon information du saknade eller som du hade velat läsa mer om? Om ja, vad? *

Your answer

Har du några övriga kommentarer angående kompendiet?

Your answer

Skicka svar

Skicka in dina svar genom att trycka på "Submit" nedan. Genom att trycka på knappen godkänner du ditt deltagande och att svaren får användas i forskningssyfte.

SUBMIT

Never submit passwords through Google Forms.