At the end of the thesis it is appropriate to consider the results from the previous chapters in the light of the questions and hypotheses put forward in the Introduction. Recapitulating, we posed two questions:

1. Does our model have an explanatory value with respect to the processes and mechanisms during early neural development?
2. Can our model be of value for the comprehension of motor disorders caused by neurological damage, ultimately leading to a better diagnosis or treatment of these disorders?

We will summarize in this chapter why both questions can be answered positively. Consequently, we will speculate how computer simulated models of neural development might be used further to study neural development.

We have shown how patterned neural activity, which is generated endogenously in circuits of spinal neurons, may shape basic neural circuits in the spinal cord during its earliest stages of development. Crucial to our research are the two closely related building blocks of self-organization and Hebbian learning. We have shown how, at least in our model, the application of these two concepts leads to a demonstration and verification of the - more to the biological reality molded - ‘selective stabilization’ hypothesis (Changeux and Danchin, 1976). This demonstration is not conclusive, but is, in the terms of Amit (1998), an attempt to schematize the underlying biological system. As a schematization it provides an experimental platform which can be used to identify relevant parameters and their mutual correlation.

The ‘selective stabilization’ theory may be part of the answer to a modern formulation of the pivotal problem in development: how can a complex, three-dimensional organism be specified in, essentially, a one-dimensional string of amino-acids? Our research is an example of how complex behaviour, in this case patterned motor behaviour, may develop from only a small set of rather simple assumptions. This small set can be compared to a small part of the genetic code. We have provided an example of a process in which the genes specify the path along which in a self-organizing fashion the observed complexity of form arises, of which (motor) behaviour is a special case (Thelen and Smith, 1994).

In setting up a modelling study the amount of (biological) realism that is put into the model is one of the major considerations. Have the relevant parameters been taken into account sufficiently? On the other hand, the opportunity to select and choose the amount of realism is also one of the main advantages of the modelling approach: only the supposedly important features have to be taken into account. Simulations can later prove or refute the initial assumptions. For the model pre-
resented in this thesis we have made a number of modelling choices. These choices involve the single neuron model, the mathematical formulation of the Hebb-rule, the introduction of the S.A.C.s, the choice of the types and numbers of neurons in the neural model, the stylized flexion and extension movement of the mechanical model, the muscle model for the two muscles and the transfer-function of the sensors in the muscles. Despite the existence of more complex models for all of these model components, the assembly of sub-models forming the full model appeared to be sufficient to meet the objectives of our study. This is a sufficient justification for the choices.

In the experimental chapters we have demonstrated what effects patterned neural activity may have on the functional development of spinal circuits. Obviously, we can not prove that the processes we described actually occur during the development of an organism. However, given the generally accepted ideas and dogmas in developmental neuroscience, our results can be considered to be a firm indication for the presence of a developmental process in which patterned neural activity results in self-organization. It provides a possible explanation for fetal motility. Following Prechtl’s suggestion that species of which the fetus is motile have been favoured during evolution (Prechtl, 1984), this might emphasize the primacy of the development of intricate neural activity patterns.

The motor behaviour that our model spinal circuits generate is a stylized motor pattern. Certainly in the healthy fetus or infant this simplistic and stereotyped movement is not the most likely movement pattern. It has been shown extensively that the complexity of the movements of an infant is an excellent sign of the neurological condition of the infant. Stereotyped movements are characteristic of infants with a motor disorder, in contrast to healthy infants, who show variable motor behaviour. This is an indication that a healthy CNS already from early on generates much more complex commands. Variability in motor behaviour is the default manner of operation of the CNS and motor system.

In order to establish a more formal way of thinking about motor development in terms of patterned motor behaviour, we want to forward an analogy between the development of motor behaviour and mathematics. The prologue to the analogy is that, although in mechanical terms any movement can be built up from solely two basic motor patterns, i.e. flexion /extension and endorotation /exorotation, the movement is generated by a complex neural command (note that although some consider abduction /adduction the third basic motor pattern, it is only a special case of flexion /extension). The actual analogy is that the complex neural command leading to any movement is built up from a set of basic neural commands. These basic neural commands can be seen as the neural base vectors constituting the complex neural command, in the same manner as a point in Euclidian space can be specified using three coordinates. In normal circumstances the ‘neural base vectors’
are disguised in the complex motor behaviour; they can only be investigated in experimental, or pathological, situations. We suggest that the neural command generated in the circuits in our model, leading to the stylized flexion/extension, constitutes such a ‘neural base vector’, i.e. it is a ‘basic neural command’. Another example of a ‘neural base vector’ is the manner in which our model circuit reacts to a mechanical perturbation. In chapter four we have shown how ‘neural base vectors’ can be combined into a complex neural command, leading to complex motor behaviour.

The analogy can be extended to include variability. **Primary** variability is the process in which the basic neural commands and their resulting motor patterns are discovered and mapped, but also encompasses the process of combining these basic commands into complex motor behaviour to explore the entire space of possible movement patterns. **Secondary** variability is the process in which the infant learns to select which combinations of basic patterns are the most plausible to generate specific movements.

The latter enables us to make the transition from the study of developmental neurobiology to the study of motor disorders caused by damage of the developing brain. Using the terminology from the analogy, the capacity to acquire and combine all base vectors into a complete map seems limited in infants with motor disorders like cerebral palsy. It is as if the ‘neural explorative expedition’ to create the full map of neural commands and resulting motor patterns is not carried out completely. Using a computer model like the one introduced in this thesis the development of the ‘neural base vectors’ should be further investigated. A computer model can be used to find ways in which the coverage of the map could be maximized. New therapeutical techniques could either be based on new insights from modelling research, or, after having been conceived in another fashion, be first investigated and tested using a model.

Suggestions how our model could be adapted to study spastic cerebral palsy have been provided in chapter five. To study cerebral palsy meaningfully, it is necessary to increase the complexity of the model and, foremost, to include more realistic supra-spinal commands. We hypothesize that the neural circuits that we investigated in this thesis are not severely affected in infants with CP. In CP other systems are not able to control, i.e. properly sequence, the neural circuits generating the basic flexion / extension movement: the motorneurons innervating the anti-gravity muscles are hyper-excited through disturbed supra-spinal signals.

Another example is the motor behaviour in some anencephalic fetuses, in whom cortico-subcortical control of the spinal circuits is lacking. Their movement pattern is characterized by stereotyped flexion and extension movements of the extremities. We suggest that their ‘neural explorative expedition’ has been severely restricted so that their motor map only contains the basic motor patterns, which
develop first, before cortical and subcortical influences come in. Actually, our model, without variable supra-spinal signals impinging on it, can be considered to reflect an extremely damaged CNS. In the normal developing brain variable commands coming from supra-spinal pathways are conveyed to the spinal circuits as reflected by the various existing neurons in the model, or to new types of neurons that can be added to the model network.

In conclusion, we are convinced that computer models provide an experimental paradigm which is well-suited to study neurobiological development and therefore also, as one of its possible consequences, to study the pathophysiology of motor disorders caused by brain damage. Is the application of models to study development new? Certainly not; on the contrary, it is a very old idea. More than 2000 years ago, Aristotle was one of the first to recognize the scientific implications of models for studying development. The same book we mentioned in the Introduction, “On the generation of animals”, contains a passage in which he introduces “automatic machines” which were shown as curiosities, probably on fairs. About these machines he states: “As, then, in these automatic machines the external force moves the parts in a certain sense (not by touching any part at the moment, but by having touched one previously), in like manner also that from which the semen comes, or in other words that which made the semen, sets up the movement in the embryo and makes the parts of it by having first touched something though not continuing to touch it. In a way it is the innate motion that does this, as the act of building builds the house. Plainly, then, while there is something which makes the parts, this does not exist as a definite object, nor does it exist in the semen at the first as a complete part.” (Aristotle, translated in Platt, 1912).