



Earth and Life Sciences

Centres for Systems Biology Research (CSBR)

**An initiative within the NWO theme Systems Biology
Call for full proposals ('volledige aanvragen')**

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1 Introduction

This document describes the entire application procedure for the establishment or enlargement of centres for systems biology research. Applicants of preliminary proposals have received an invitation to submit a full application, along with feedback from the Evaluation Panel. Only applicants of preliminary proposals are entitled to submit a full application. This version of the brochure emphasises the full application process step, but otherwise only differs in minor details from the versions published previously.

This call for preliminary proposals has been made possible with financial support from the Ministry for Health, Welfare and Sport (VWS), and NWO's research councils for Medical Sciences (ZonMw), Chemical Sciences/ACTS, Exact Sciences, and Earth and Life Sciences, as well as the central NWO organisation. Non-financial support has been obtained from the Netherlands Genomics Initiative, Technology Foundation STW, the Programme Committee Systems Biology and the Task Force Life Sciences.

This brochure is derived from the Strategic Action Plan Systems Biology ('Strategisch Actieplan Systeembioïologie') prepared by the Systems Biology Theme Preparation Committee. This action plan is only available in Dutch. The current level of funding will not allow the entire plan to be realised in full. This brochure, therefore describes a first phase.

2 Aim

In line with the Strategic Action Plan Systems Biology presented in October 2008 by the Systems Biology Theme Preparation Committee, the aims of this programme are as follows:

- To facilitate development of a sustainable systems biology research infrastructure in the Netherlands;
- To promote a coherent, connected and integrated understanding of the different complexity levels that life comprises (molecule, cell, tissue, organ, (information network), organism, population, ecosystem).

This entails:

- Providing the field of systems biology with an excellent starting position and participating in international research initiatives;
- Establishing excellent research bases by building on and connecting with the superb research already being carried out in the Netherlands within the field of systems biology and adjacent disciplines;
- Linking fundamental, technological and applicable knowledge and skills so that innovative new solutions can be realised as a result of the systems biology approach;
- Facilitating an early dissemination and application of knowledge and technology to other sectors like food and health, and industry, by means of early commitment, mutual involvement and dedicated communication;
- Diminishing the gap between data based on single complexity levels and our understanding of other or more complexity levels, or even understanding the system as a whole;
- Supporting the setting up of educational curricula in systems biology.

The current programme enhances the shift from 'describing' life's processes to 'understanding' and 'capturing' them in validated predictive models, and even 'managing' or 'controlling' them. Describing isolated physiological and pathological processes only provides a limited view on causal interactions within and between biological entities, and between such entities and their dynamic environments. The notion that biological entities do not function in isolation, but as (dynamic components of) heterogenic and dynamic systems, has spread rapidly. This fact may be seen as a major achievement of the newly established field of systems biology. This awareness will, no doubt, result in many pressing challenges in 'red', 'blue', 'green' and 'white' biotechnologies being addressed to the benefit of society.

2.1 A definition

Since looking at 'systems' is by no means a recent approach within the life sciences, a description of the innovative nature of systems biology is provided. Throughout their joint report, entitled "Systems biology: a vision for engineering and medicine", the Academy of Medical Sciences and the Royal Academy of Engineering in the UK use a certain definition of systems biology. This definition will serve within the CSBR programme as well:

".. Systems Biology is defined as the quantitative analysis of the dynamic interactions between several components of a biological system and aims to understand the behaviour of the system as a whole, as opposed to the behaviour of its individual constituents. It applies the concepts of systems engineering to the study of complex biological systems through iteration between computational and/or mathematical modelling and experimentation."

Elements of this definition will recur in the evaluation criteria in Section 4.2.

2.2 Scope

The scope of the programme is limited to systems biology initiatives in the life sciences with the following characteristics:

- A scientifically relevant, functional, biological research question, studied in a relevant model system, aiming for results that can be applied to address relevant scientific and/or societal issues, forms the central point of reference for the entire centre;
- The functional behaviour of a group of components, together representing a system, is studied over various biological 'complexity levels' (molecule, cell, tissue, organ, (information network), organism, population, ecosystem). Furthermore, the combination of 'complexity levels', and the intensity by which they each contribute to addressing the research questions, must clearly exceed current practice and, therefore, be novel;
- The integrative, systems biology approach of the centre's proposed activities is exemplified by the 'Modelling cycle' depicted as Figure 1 in Annex 3 (modified after Kitano, *Science* 295, 1662-1664, 2002). A systems biology approach is, further characterised by:
 - taking all the biological complexity levels, required for adequately answering a relevant, functional, biological research question, into full consideration, and that the combination of complexity levels, and the intensity of each level's contribution, are indeed novel;
 - all the scientific disciplines that are relevant as a consequence of the research question, are involved, and this multidisciplinary approach is indeed novel;
- The amount of (molecular, physiological, clinical or other) data requires that quantitative concepts, modelling and mathematics/bioinformatics form core components of the research endeavour, by revealing and identifying functionality relations spanning complexity levels, building numerical models for 'dry' experimenting, and so on. The proposed research should realise the setting up of a model, validated well enough to come to meaningful predictions that can be experimentally verified (predictive biology);
- The central hypotheses are such, that it is essential beyond doubt that a combination of scientific disciplines (medical sciences, biology/life sciences, (bio)chemistry and catalytic science, physics, informatics, mathematics and numerical modelling, technical sciences and engineering), well beyond current multidisciplinary approaches, is required to cover the full complexity of the system of study adequately. Understanding system complexity will require both 'wet' experiments and 'dry' modelling. Training both staff and students to approach questions within the life sciences in a 'systems biology' manner, will probably be necessary. Furthermore, the direct and high level intensity of the multidisciplinary interaction requires that disciplines are sharing a physical location and other facilities as much as possible, and meet, work, and interact face to face on a daily basis whenever possible.

3 Guidelines for applicants

3.1 Who can apply?

Both the (co-)applicants and the host institution (*'instelling'*) must meet stringent requirements.

Requirements for the (co) applicant

Any (co-)applicant should be a senior researcher employed by a research institution (*'instelling'*) eligible for funding by NWO, or by a university in the Netherlands.

Applicants must have a contract with their respective institutions/universities lasting at least until the end of the programme (2015) and there should be no indication of them retiring before the end of the programme.

The applicant should be responsible for all the scientific aspects within the foreseen CSBR and will serve as the contact person on behalf of the foreseen CSBR.

Requirements for the host institution

Both the preliminary proposal and full application must state what entity acts as the CSBR's host institution. A university, faculty, or a combination of faculties within a single university can act as a host institution of one or more proposals. Besides universities, other research organisations eligible to submit proposals to NWO, are acceptable as a host institution. Finally, a combination of one or more faculties and one or more NWO-eligible non-university institutions, can together act as host institution. In all cases listed above, the host institution must meet stringent criteria to be acceptable as a host institution.

(Combinations of) smaller subunits within universities (e.g. research groups), or (combinations of) subunits within NWO-eligible, non-university institutions, are not acceptable as host institution.

A Centre for Systems Biology Research preferably leads to housing groups from various disciplines together 'under a single roof', to form a real, not a virtual, core centre. This ideal situation may not always prove feasible. Including obvious exceptions, like field trial sites, clinical wards, and specialised containment and/or radiation laboratories, up to 25% of the CSBR's research groups, encompassing not more than 25% of the CSBR research staff, may remain or be housed outside the core centre. This is acceptable under the provision that the exception is well-motivated, and intensive interaction between all participating groups is guaranteed (see Section 3.5.3). Not being under a single roof is, to some extent, tolerable. At the same time, selection criterion III (see Section 4.2) clearly indicates the importance of commitment to facilitate intense mutual contacts between all participating groups and researchers. This level of organisational integration, mainly achieved by housing all participants together as much as possible, remains an important indicator for predicting and selecting successful Centres for Systems Biology Research.

Both the systems biology research centre to be established, and the systems biology approach, should form an integral part of the research programme of the applying faculty/faculties or institution(s).

Considerable support is demanded from a host institution. Furthermore, the centre and its activities should continue beyond the period during which granting takes place, has ended.

The 'embedding form', accompanying the preliminary proposal and full application, should clearly demonstrate the host institution's ambitions and commitment with regard to:

- Bringing all relevant disciplines 'under a single roof' as much as possible and encouraging full interaction between all participating groups and disciplines;
- Providing support, including financial support, to ensure the centre will perform optimally;
- Continuing the centre after the CSBR grant comes to an end;
- Endorsing the systems biology approach in the entire institution's research programme.

The goals and ambitions laid down in the 'embedding form' will play an important role in the mid-term evaluation and the subsequent decision on releasing the second half of the granted budget.

3.2 What can be applied for?

Project budget

Just like with the preliminary proposal earlier, the full application, may include a request to provide budgets to cover (over a period of 6 years, 2010-2015):

- Personnel costs of PhD and postdoc researchers and newly to be appointed analytical personnel (costs in accordance with NWO and VSNU agreement);
- Personnel costs for a new chair for a full or associate professor at a Dutch university. The professor will have to be a new appointment, and both the chair and the staff must be specifically focused on systems biology. Continuity of the chair should be ensured until well after the subsidy ceases;
- Part of the cost for dedicated new equipment (see Section 3.5);
- Contribution to communication costs involved with valorisation and delivery of results to stakeholders, to a maximum of 2% of the requested budget.

Besides that, no separate budgets for overhead costs, moving research groups, housing, management and other overhead activities will be provided.

The budget requested per centre lies between € 3 million and € 5 million. The granted budget may be lower than € 3 million, e.g. in the case of partially granted application.

The research budget of the research centres should meet the Budget Guidelines and Specific Conditions (see Sections 3.4 and 3.5 respectively).

Programme budget

The CSBR programme budget amounts to approximately € 13 million, but if a project on the 'special subject' is granted, an extra, earmarked, budget of € 1 million becomes available. 'Special subject' projects (see Section 3.5.2) have to fall within the scope of the ZonMw/VWS research programme "Priority Medicines: Antimicrobial Resistance (AMR)".

Half the granted maximum budget will only become available if a positive assessment is issued at the mid-term evaluation (scheduled to take place during autumn 2012 - spring 2013).

3.3 When can applications be submitted?

Preliminary proposal

Preliminary proposals can not be submitted anymore.

Full application and interview

Only applicants of preliminary proposals are entitled to submit a full application. They may receive an invitation to submit a full application before the deadline of 8 December 2009. In case of delays caused by unforeseeable circumstances, the applicant should contact the programme manager right away. The programme manager will then try to come up with a solution.

Full applications should bear the same title and names of the applicants, unless there is a valid reason (e.g. change in affiliation, strengthening the consortium, Evaluation Panel's feedback) not to do so, and have the same subject and content as the preliminary proposal (unless feedback by the Evaluation Panel indicates otherwise).

Full applications are assessed by the Evaluation Panel without the aid of expert referees. This should be borne in mind when phrasing the application.

A small delegation from an applying consortium may become invited for a short presentation followed by an interview with the Evaluation Panel. These interviews are expected to take place on 14 and 15 January 2010. This interview may take the form of a 'site visit'.

3.4 Drawing up an application

The full application should follow the format provided in the 'CSBR full application form'. This form includes criteria on, for instance, format, font and length of text, size and specification of budgets, signatures, and embedding forms that must be observed.

Contents

With regard to the contents of the application, aspects deserving extra attention are listed here:

- The research activities to be undertaken at the research centre must be described in detail (the full application requires more detail than the preliminary proposal);
- The application (as well as the embedding form accompanying it) should include as many verifiable deliverables as possible: what aims are expected to have been realised at the time of the mid-term evaluation and what aims are expected to be realised before and after the phase subsidised by the CSBR programme ends?
- Although expenses for overheads are not compensated, how the host institution will support, organise, staff, and manage the centre should be specified.

Another important aspect, part of the application as well as of the embedding form, is the continuity of the research centre. Consequently, host institutions have to meet certain requirements (see Section 3.1).

Budget guidelines

The requested contribution to the budget for a Centre for Systems Biology Research may not exceed € 5,000,000 for the entire 2010–2015 period. Assuming that some of the applications will only be granted in part, the programme budget mentioned under Section 3.2 will allow for the setting up of 3 to 4 centres in this first call.

3.5 Specific conditions

As the CSBR programme grants centres rather than projects, some 'specific CSBR conditions' apply, in addition to the NWO general subsidy regulations ('*NWO algemene subsidievoorwaarden*'). A copy of the most recent version will be included with the granting letter. Specific conditions for CSBR are listed below:

1. Staff are not employed by ZonMw, NWO or VWS, but by the research institution(s) involved. The employer has to send Personnel Information Forms (PIF) to the programme secretariat as soon as any new staff member starts his or her contract. The centre officially starts as soon as the first signed and completed PIF has been received by the programme secretariat and the employment of the employee has officially started. The host institution then receives the first payment and a document from the programme secretariat indicating when the next (conditional) payments are scheduled to take place;
2. A progress report must be submitted annually in December. It comprises all the centre's activities. The report describes the centre's:
 - a. personnel developments and scientific progress,
 - b. progress (research, education and otherwise) in relation to planning (and any deviations from previous plans and the motivation behind the changes),
 - c. publications, patents and other products.

The obligation to submit progress reports annually forms one of the responsibilities of the main applicant who acts as scientific coordinator.

If the centre performs poorly, the Steering Group may decide to discontinue the subsidy;

3. Halfway through the programme, the centre will be subjected to a mid-term evaluation. Only if the outcome of this evaluation is positive shall the second half of the subsidy be released;
4. Equipment exceeding € 25,000 is refunded to a maximum of 75%;
5. The centre's subsidised period ends as soon as employees are no longer paid through CSBR but no later than 2015, when the CSBR programme as a whole ends. Personnel cost for individual staff may be reimbursed until after that date in accordance with an accepted PIF;
6. Within 3 months of the subsidised period of the centre coming to an end a final scientific report must be sent in by the scientific coordinator;
7. Within 3 months of the subsidised period of the centre coming to an end a final financial report must be submitted to the CSBR programme secretariat. After both the final scientific report and the final financial report have been accepted, the final level of the subsidy will be calculated and agreed upon and the final payment shall subsequently be made;
8. In all publications, press releases and dissertations that (in part) rely on CSBR financial support, the financial support of NWO, ZonMW and/or the Ministry for Health, Welfare and Sport (VWS) must be acknowledged properly;
9. Several years after 2015 a questionnaire and/or report may be required from the core host centre and/or scientific coordinator to report the centre's progress and research intensity after the subsidised period ended;
10. Since Centres for Systems Biology Research dedicated to 'special subjects' (see Section 3.5.2 and annexe 1) will be financed by CSBR as well as AMR, such centres must observe the conditions of both CSBR and AMR.

3.5.1 Programme considerations

To optimise the positive impact of the Centres for Systems Biology Research on the Dutch research infrastructure, a limited number of centres may be founded which, preferably, cover different aspects of the broad field of systems biology. The Evaluation Panel advises the Steering Group on the basis of a set of criteria (see Section 4.2). The quality of full applications, together with financial considerations regarding the budget, will normally determine which proposals are granted. The Steering Group may, however, take 'Programme Considerations' into account:

- Upon advice of the Evaluation Panel;
- Upon advice of the Programme Committee;

- On its own initiative.

These programme considerations, regarding both preliminary proposals and full applications, are limited to: 'The distribution over research subject categories (e.g. plants, animals, (industrial, pathogenic) micro-organisms, man), and optimal utilisation of existing and new facilities within the Netherlands, with the expressed aim of optimising the impact and influence of the systems biology approach, through the CSBR programme, on the field of life sciences as a whole.'

3.5.2 Special subject

The subject of 'infectious disease', in the sense of the ZonMw programme "Priority Medicines: Antimicrobial Resistance (AMR)", enjoys a 'special status'. It refers to the interest and financial contribution of VWS. Granted 'special subject' applications are in part financed through the AMR-earmarked part of the CSBR programme budget. The chances of 'special subject' full applications becoming granted within CSBR doesn't differ from that of regular projects. Items like:

- Which proposals qualify as 'special subject proposals';
- What are the aims of the AMR programme which will, in part, be realised through this CSBR programme;
- What is the role of the AMR Programme Committee and what are the criteria for its 'eligibility check' and 'evaluation of relevance (*i.s.* AMR)' for preliminary proposals and full applications;
- What happens to a proposal/application that fails to meet the AMR's criteria;
- How do the criteria for proposals to be in part financed through the AMR-earmarked part of the budget differ from those of regular proposals, can be found in Annex 1.

3.5.3 Location

A Centre for Systems Biology Research is a non-virtual centre. This means each centre is organised and (mainly) localised at one specific site, preferably even in a single building, on adjacent floors. The host centre, and applying faculties and/or institutions should be committed to achieving an optimal physical concentration of contributing groups, staff and facilities (See Section 4.2, evaluation criterion III). Two types of situations that will, under the conditions mentioned, not impair Criterion III, are listed below:

- '*Force majeure*' may prevent a group, activity or facility from moving to the core CSBR. Examples (from Section 3.1) include: a trial field, a medical ward, a radioisotope laboratory, a research group located at, and integrated with, another university;
- 'Proportionality' may prevent the moving of a group, activity, or facility to the core CSBR because the cost or damage to research activities incurred by moving the group may outweigh the benefit of easier information exchange and cooperation within CSBR.

These exceptions, however, are only acceptable if full interaction and cooperation between all participating groups and researchers is fully warranted and at least three quarters of the participants, and participating groups, are, or will indeed be, housed together in a core centre (e.g. one building or neighbouring buildings on a campus).

The location and housing for the research centre must reflect its permanent status.

3.5.4 Duration

Although the CSBR programme will draw to a close in 2015, the established centres should last much longer. The full application, and embedding form, must therefore

provide detailed information about how the continuation of the centre after 2015 is safeguarded. Section 3.1 contains requirements host institutions have to meet in advance to facilitate successful embedding.

3.6 Submitting an application

Applications must be submitted via the Iris electronic submission system. See the NWO website (www.nwo.nl) and use the 'subsidy guide' ('*subsidiewijzer*): www.nwo.nl/nwohome.nsf/pages/SPPD_7AK3L2_Eng.

Applications should use the prescribed forms for CSBR full applications. When filling out the forms, the maximum permissible number of words to be used must not be exceeded.

A hard copy version of the CSBR embedding form for full proposals should be completed and signed by a representative of the host organisation, who is authorised to sign and take on obligations on behalf of that organisation and any other organisations involved. It should be sent to the programme's secretariat by post preferably within 2 weeks of the full application being electronically submitted, but no later than 31 December 2010. If this requirement is not met on time, the evaluation process may be discontinued. If a unforeseeable problem occurs, and the programme manager is informed on time, he will try to work out a solution.

4 Assessment procedure

4.1 Procedure

The procedure started earlier this year by the Programme Committee announcing a call for preliminary proposals (*'vooraanmeldingen'*), to be submitted electronically before a set deadline. These preproposals were individually evaluated by the Evaluation Panel (see Section 4.3). The criteria used are described in Section 4.2. The marking took place using the standard NWO 9-point scale ('1' meaning 'excellent', '3' standing for 'very good', '5' meaning 'good', etc.). Through teleconferencing and via e-mail, the Evaluation Panel reached an advice. Based on the findings of the Evaluation Panel and the programme considerations described under Section 3.5.1, the Steering Group invited applicants to submit a full application.

Full applications, submitted before the deadline of 8 December 2009 shall again be evaluated individually by Evaluation Panel members. During this phase, the Evaluation Panel may ask applicants to hold a short presentation and/or to be interviewed by the Evaluation Panel (probably on 14 or 15 of January 2010, or to permit a 'site visit' by a delegation specifically appointed for this purpose by the Steering Group. After that, the Evaluation Panel shall discuss the full applications submitted, interview and/or 'site visit' impressions, and 'Programme Considerations'. It will agree upon the final marks and a ranking list to be issued as an advice to the Steering Group, and will inform the Programme Committee.

Once the Steering Committee has reached a decision, the applicants shall be informed of this and granting and rejection letters shall be sent out as soon as possible.

The CSBR granted will be subject to a mid-term evaluation in 2012, initiated by the Steering Group. Besides the mid-term milestones included in the application, other general and specific (output) mid-term evaluation criteria, derived from the granted application, may be included in the granting letter. Findings from (mid-term) site visits, which have been laid down in a report, together with a rebuttal on behalf of the centre's management, will be included in the mid-term evaluation. If the evaluation results in a (conditional) positive assessment, the second part of the grant can be made available according to the conditions laid down in the granting letter.

The procedure also consists of periodic reports on general progress, communication efforts, implementation/application, embedding efforts and/or other aspects, in accordance with the conditions mentioned in the granting letter.

4.2 Criteria

A preliminary proposal form and a preliminary embedding form, do not provide the same level of detail as the full application and embedding form. The criteria are therefore applied in accordance with the level of detail required for preliminary proposals and full applications respectively.

Please note that for the 'special subject' (see Section 3.5.2 and Annex 1) additional criteria are in place.

The four evaluation criteria have equal weighting and are:

Criterion I: 'Scientific Quality'

'Scientific quality' refers to many aspects, including:

- The quality, and track record of the research groups involved, and the new and established constituents of the centre, as well as the quality of existing facilities;
- Is the project coherently focused on a common, relevant, functional, scientific issue, representing a scientific breakthrough, in a relevant model system, using new (combinations of) methods, ideas and approaches? Are milestones specific, relevant and realistic?

Apart from the systems biology content and approach (criterion II): does the centre have input from different disciplines consistent with the research question addressed?

Criterion II: 'Systems Biology Content'

Systems biology content will be measured through two key aspects that are of special interest for systems biology and are listed below:

- The 'appropriateness' to addressing the centre's research question by applying systems biology according to the characteristics listed in Section 2.2/Figure 1, and its extra scientific and/or practical value;
- The level of commitment to an integrative approach, as a consequence of the research question addressed, connecting several subsystems and/or complexity levels (molecule, cell, tissue, organ, (information network), organism, population, ecosystem) in line with programme aim 2 (see Section 2), and as shown in Figure 1, included as Annex 3 to this document.

Criterion III: 'Governance and Organisation'

Four of the aspects that are particularly relevant for CSBR are:

- Apart from setting up a centre, to what extent does the host institution show a clear commitment to the systems biology approach (in research, in education) and how well will the centre fit in with other relevant activities?
- Is there, apart from specific exceptions, a full and clear commitment to having all relevant scientific expertises located 'under a single roof', and to ensuring an optimal mixing and interaction of disciplines?
- Is the 'line of command' clear and in accordance with the centre's tasks and responsibilities?
- How committed are the participants to continuing the centre and its research and educational activities after the CSBR subsidies have come to an end? Will the centre include and continue a new chair for a full or assistant professor?

Criterion IV: "Applicability"

Criterion IV encompasses:

- How important will the potential contribution of knowledge and insights to be generated by the centre be to solving/attenuating a relevant (life sciences) problem in society, technology and/or the economy?
- What are the chances of the generated insights being implemented and used immediately or in the medium or long term?
- How well-developed is the centre's plan for aspects like 'intellectual property', 'stakeholders as co-developers', 'networking', and 'specific dissemination efforts'. To what extent does the plan demonstrate that these aspects have been incorporated and integrated in the centre's activities.

4.3 Composition of committee

This section details the 'Programme Governance and Management'.

The NWO Centres for Systems Biology Research (CSBR) programme makes use of five administrative bodies:

- Steering Group;

- Programme Committee;
- Evaluation Panel;
- AMR programme committee (responsible for ZonMw's 'Priority Medicines: Antimicrobial Resistance (AMR)' research programme) which evaluates 'relevance' in the sense of AMR of CSBR proposals which (in part) fall within the scope of AMR;
- Programme secretariat and administrative programme support office.

4.3.1 The Steering Group

The Centres for Systems Biology Research programme is supervised by a Steering Group. It was set up on 1 April 2009 and consists of representatives, mainly board members, of the bodies that contribute financially to the programme (see Section 1, Introduction). The Steering Group is mandated by the boards of the financing organisations to take decisions regarding CSBR on their behalf.

The Steering Group:

- Will ensure the implementation of the scientific components of the Programme Document CSBR, and safeguard its compliance with the Strategic Action Plan Systems Biology, within the framework of the NWO theme "Systems Biology" ('*Systeembio*logie');
- Will foster new activities within the theme 'Systems Biology' and search for additional resources in order to realise a larger part of the Strategic Action Plan Systems Biology;
- Will install a CSBR Programme Committee, a CSBR Evaluation Panel and may install one or more 'site visit delegations';
- Will, after having issued a Call for Preliminary Proposals, subsequently issue a Call for Full Applications;
- Will consult and advise with regards to associated (national) programmes, within or outside the NWO Theme 'Systems Biology', and may undertake efforts to enhance cooperation;
- Will be responsible (in as far as the level of the NWO theme 'Systems Biology' as a whole is involved) for reporting, monitoring, impact, assessment, valorisation/implementation/application and communication to both stakeholders and the public at large;
- Will ensure, and/or supervise, embedding activities aiming at integrating the centres' activities by 2015, when this programme ends;
- Will take the initiative in having the programme evaluated, when it draws to a close in 2015;
- Is mandated to take granting decisions on the basis of advice provided by the Evaluation Panel, and determine the research budgets and grants for approved applications within the prevailing budget;
- Will decide on requests for major changes within granted projects. Minor adjustments, and financial adjustments not exceeding € 25,000, will be the responsibility of the programme support office;
- Will be responsible for approving the budget for NWO's Theme 'Systems Biology'. Currently the programme's budget amounts to about € 13 million. The aim is to find additional funding, in order to realise a larger part of the Strategic Action Plan Systems Biology;
- Will initiate a mid-term (autumn 2012-spring 2013) review, which may include 'site visits'. It will decide on releasing the second half of the subsidies for each individual Centre for Systems Biology Research funded.

4.3.2 The CSBR Programme committee

The CSBR Programme Committee is established and supported by, the Netherlands Organisation for Scientific Research (NWO). It is appointed by the Steering Group.

Day to day progress and finance are managed by staff of ALW, in conjunction with ZonMw and NGI, coordinated by a Programme Manager of ALW.

The CSBR Programme Committee:

- Is involved in preparing calls for proposals, and may provide advice regarding calls for proposals to the Steering Group or other bodies;
- Is responsible for issuing advice on budget and programme considerations. It may propose to merge (parts of) applications or to grant only a certain part of an application, either for financial reasons or because of programme considerations (see Section 3.5.1);
- Will monitor general progress and cooperation, bottlenecks, valorisation/implementation and the state of the centres' embedding activities. The Programme Committee will keep the Steering Group informed about the programme's progress and shall implement the Steering Group's decisions and suggestions;
- Will supervise the execution of the programme, and advise other bodies accordingly;
- Will harmonise the mutual processes (like communication about the programme, monitoring of its progress, (interim) evaluations, valorisation efforts and embedding activities) and establish and maintain contacts with each centre's scientific coordinator, main applicant, Principal Investigator, director and manager.

4.3.3 The CSBR Evaluation Panel

The CSBR Evaluation Panel, like the Programme Committee, is appointed by the Steering Group. It consists of foreign experts that work abroad and, together, cover most of the broad field of systems biology. Panel members meet the NWO requirements regarding involvement with either applicants or applications. Evaluation Panel members are preferably included in the Committee that will perform the final evaluation at the end of 2015 or early 2016.

The CSBR Evaluation Panel:

- Assesses the preliminary proposals individually via email, in accordance with NWO's general rules and guidelines and the CSBR Programme Brochure. The individual assessment will, if necessary, be followed by a teleconference meeting, during which views will be exchanged, proposals and programme considerations will be discussed, and the final advice regarding the preliminary proposals will be agreed upon;
- Assesses the full applications. Preliminary marks and elaborations are sent in by individual panel members. Subsequently, the Evaluation Panel meets for interviews with applicants and/or to discuss the applications. It then confirms its final marks, final elaborations, final ranking list and final granting advice to the Steering Group.

Although it is not primarily responsible for Programme Considerations and budgetary consequences, the Evaluation Panel, may advise on such aspects whenever appropriate.

4.3.4 Other committees involved

In addition to the programme committees directly involved, the ZonMw programme committee on "Priority Medicines, Antimicrobial Resistance (AMR)" also plays a role. Details about this committee can be found on the ZonMw website.

Furthermore, the Steering Group can install *ad hoc* committees, like 'site visit delegations', and '(mid-term) evaluation committees', to perform certain tasks on its behalf and report the findings to the Steering Group.

5 Other information

5.1 Programme secretariat

- Theo Saat, NWO-ALW, programme manager
- telephone: +31 70 344 07 91
- e-mail: t.saat@nwo.nl

- Rob Diemel, ZonMw, co-programme manager

- Luc Rietveld, NGI, observer

- Priscilla Bruinsma-Smiet, NWO-ALW, secretary
- Nel Roos-Kornet, NWO-ALW, secretary

5.2 Further reading, related documents

- Subsidy guide NWO
(http://www.nwo.nl/nwohome.nsf/pages/SPPD_7AK3L2_Eng);
- Programming study on antimicrobial resistance,
Programmeringsstudie AMR (available through ZonMw website)
<http://www.zonmw.nl/nl/onderwerpen/alle-programmas/infectieziektebestrijding/actueel/antimicrobiele-resistentie/>);
- *Strategisch Actieplan Systeembioologie* (available through the NWO website)
http://www.nwo.nl/nwohome.nsf/pages/NWOA_7KVH57;
- CSBR full application form;
- Full Embedding Form “CSBR inbeddingsformulier” accompanying the full application.

6 Annexes

6.1 Detailed information regarding the CSBR 'special subject': "Priority Medicines: Antimicrobial Resistance (AMR)"

(partly copied/modified from the respective AMR programme documentation)

As mentioned earlier in this brochure, preliminary proposals and full applications on the subject of 'infectious disease' in the sense of the ZonMw programme "Priority Medicines: Antimicrobial Resistance (AMR)" enjoy a special status. In order to qualify for this special status, preliminary proposals or full applications must meet the following requirements and description:

- Applications fall within the scope for Systems Biology research plans as elaborated under Section 2;
- Applications, or at least a part of the applications, meet the requirements of the programme "Priority Medicines: Antimicrobial Resistance (AMR)" as elaborated in this sub-Section ('eligibility check');
- Largely copied from the brochure of the AMR programme:
The aim of the ZonMw programme 'Priority Medicines: Antimicrobial Resistance (AMR)' is to contribute to controlling the problem of antimicrobial resistance. This can be done by stimulating scientific research aimed at the sound use of available antibiotics and by contributing to the development of new methods and medicines and interventions. Relevant AMR themes for this CSBR programme are:
 - The role of antimicrobial use in inducing and transmitting resistance;
 - Mechanisms and targets for new antimicrobial drugs and vaccines.
- Both preliminary proposals and full applications must pass an 'eligibility check' by the AMR Programme Office. It checks whether the project, or at least part of the project, addresses one or both relevant AMR themes listed under the previous bullet. The AMR Programme Committee evaluates the 'relevance *in sensu* AMR', of preliminary proposals and full applications according to the criteria listed later in this annex;
- Besides investigating the specific infectious disease, the research activities must focus on generating general scientific concepts, theories, models which can be applied in fundamental research and/or to other (infectious) diseases.

Preliminary proposals or full applications that fail to meet the AMR requirements will automatically continue the evaluation process as an ordinary preliminary proposal or full application.

(Parts of) some of the full applications that might be granted by the CSBR Steering Group, may satisfy the AMR conditions. If during its 'eligibility check' and 'relevance evaluation' the AMR Programme Committee establishes this then such a granted project may be partly or fully financed through AMR. The conditional part of the CSBR programme budget, earmarked for AMR by VWS, will be released for this purpose.

The general criteria for the evaluation of 'relevance' as used by the ZonMw programme "Priority Medicines: Antimicrobial Resistance (AMR)" are: (see Section 5.1 for a ZonMw-contact and/or visit the ZonMw website '*Programma Infectieziektebestrijding*': <http://www.zonmw.nl/nl/onderwerpen/alle-programmas/infectieziektebestrijding/publicaties/de-programmatekst/> (in Dutch):

- Does the project fall within the generic and specific scope of the AMR programme, and does it contribute to its aims (eligibility check)?
- Is the project innovative and/or will it generate new insights?

- Does the project meet societal needs and/or does it fill gaps in scientific knowledge?
- Are effort, input and invested financial resources proportionate to the expected results and impact?
- Has sufficient attention been paid to aspects such as gender, culture, age, the patient's perspective and specific risk groups? Specific risk groups with regards to antimicrobial resistance are:
 - Sufferers form acute and chronic infectious disease;
 - Infectious disease in relation to a specific age;
 - Infectious disease in relation to a specific socio-economic situation;
 - Infectious disease in relation to aspects of a person's lifestyle;
 - Infectious disease in relation to environmental influences;
 - Infectious disease in relation to risk-enhancing circumstances, either within a professional or leisure setting;
 - Infectious disease in relation to a suboptimal physical condition.If target groups are selected, please elaborate on why certain groups are or are not included.
- For projects aimed at research and development: Efforts to disseminate and implement results. Depending on the character of the full application, aspects which may be considered are:
 - Is the strategy for the dissemination and implementation of results adequate?
 - Are stakeholder groups and groups of users well defined?
 - Are such groups actively involved?
 - What specific dissemination and implementation activities are scheduled to take place?
 - Are the right people/groups involved in these activities?

Please note that full applications which no longer qualify as 'special subject' applications and/or do not obtain a rating of at least 'good' under the criterion 'relevance' (in the sense of AMR) in the AMR committee's evaluation, automatically continue the evaluation procedure as 'non-special subject' full applications, under the normal conditions for full applications.

6.2 Preliminary Time Schedule (non-binding)

8 September 2009	Preliminary proposals submitted electronically. Eligibility check by AMR and/or CSBR.
Mid-October 2009	Preliminary proposals evaluated by the AMR committee and/or CSBR Evaluation Panel. (Some) applicants receive feedback (regarding AMR and/or CSBR aspects) and an invitation from the Steering Group to submit a full application.
8 December 2009	Full applications submitted electronically. Eligibility check by AMR and/or CSBR.
Early-January 2009	Evaluation Panel provides preliminary evaluation of full applications via e-mail; ZonMw's AMR committee evaluates 'relevance' <i>in sensu</i> AMR. Invitations for interviews go out.
14 & 15 January 2010	Meeting of the Evaluation Panel, interviews, final marks, elaborations, ranking and advice
Early February 2010	ALW staff check budgetary consequences of advice
February 2010	Steering Group decision
February 2010	NWO informs the main applicants about the decision. Official letters follow abt. 2 weeks later.
Early 2010	Setting up organisation, hiring new staff
Early 2011	Fully staffed, operational centre
Autumn 2012-Spring 2013	Mid-term review: go / no go decision
2013	Mid-term Symposium and/or other theme communication activities organised by CSBR, ZonMw and/or ALW
2015	Embedding the centresis completed
End of 2015 / Early 2016	Final evaluation of programme and/or theme

6.3 Figure 1: Modelling cycle in Systems biology

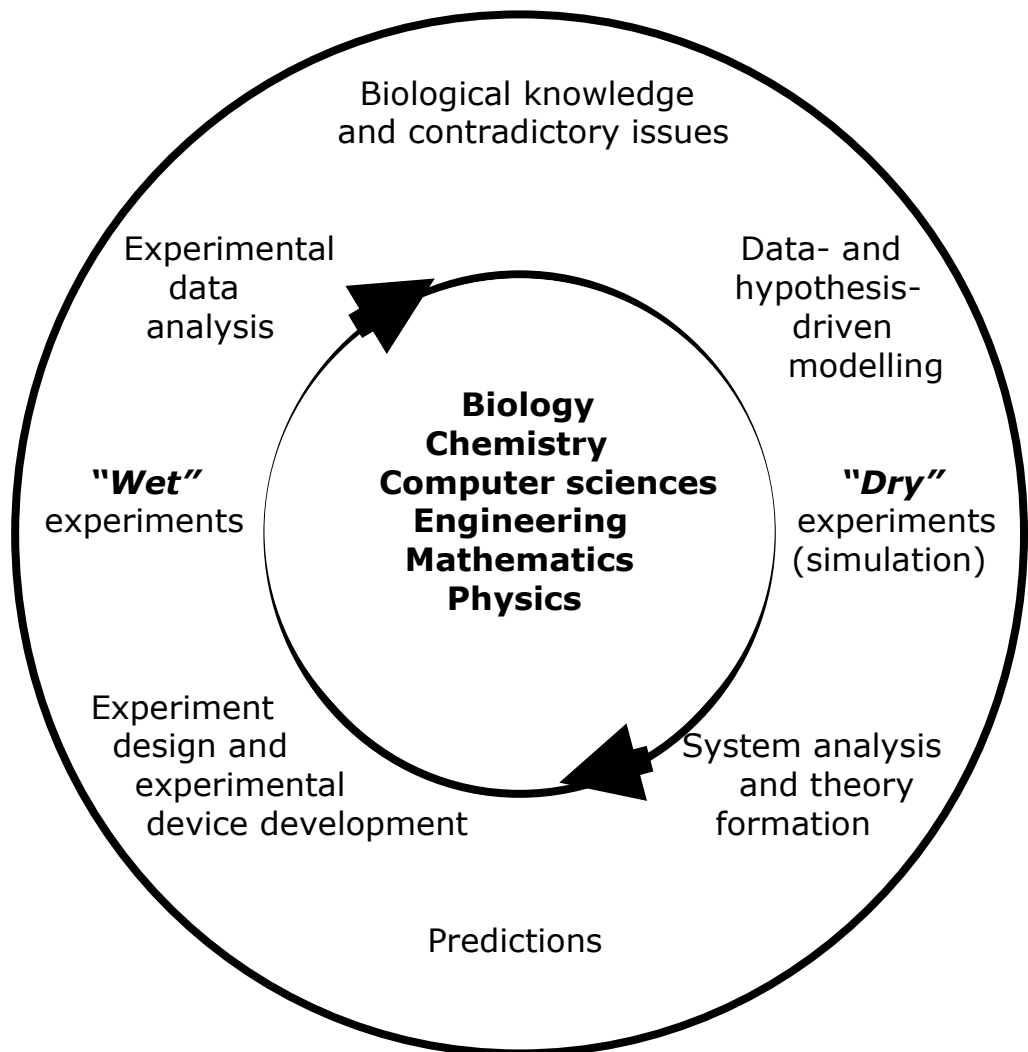


Figure 1

The modelling cycle in systems biology and the involvement of different scientific disciplines. (modified after Kitano, *Science* 295, 1662-1664, 2002; Reproduced and modified from: '*Strategisch Actieplan Systeembioologie*', October 2008)