

# **CoCoDat: A database system for organizing and selecting quantitative data on single neurons and neuronal microcircuitry**

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## **Abstract**

We present a novel database system for organizing and selecting quantitative experimental data on single neurons and neuronal microcircuitry that has proven useful for reference-keeping, experimental planning and computational modelling. Building on our previous experience with large neuroscientific databases the system takes into account the diversity and method-dependence of single cell and microcircuitry data and provides tools for entering and retrieving published data without a priori interpretation or summarizing. Data representation is based on the framework suggested by biophysical theory and enables flexible combinations of data on membrane conductances, ionic and synaptic currents, morphology, connectivity and firing patterns. Innovative tools have been implemented for data retrieval with optional relaxation of search criteria along the conceptual dimensions of brain region, cortical layer, cell type and subcellular compartment. The relaxation procedures help to overcome the traditional trade-off between exact, non-interpreted data representation in the original nomenclature and convenient data retrieval. We demonstrate the use of these tools for the construction, tuning and validation of a multicompartmental model of a layer V pyramidal cell from the rat barrel cortex. CoCoDat is freely available at [www.cocomac.org/cocodat/](http://www.cocomac.org/cocodat/). Its application is scalable from offline use by individual researchers via local laboratory networks to a federation of distributed web sites in platform-independent XML format using Axiope tools.

## **Keywords**

Relational database, biophysical properties, data sharing, computational modelling, layer V pyramidal neuron

## **Introduction**

Quantitative data on single neurons and neuronal microcircuits are essential for a detailed understanding of information processing in the basic organisational units of the brain. Every individual report, however, provides only a fraction of relevant data on a particular entity like, e.g., an ionic current, so that a complete characterization must be assembled from several sources. Although every neuroscientist has an idea of what publications contain relevant and precise data that can be used for reference comparison and integration, the diversity of experimental approaches and the methodology-dependence of such data effectively hamper their assembly into comprehensive and easy-to-use large-scale databases. At least at present, we cannot dispense of expert knowledge and extensive human labour to choose, collate and evaluate these data from the published literature. Time and energy could be saved if adequate tools for data collation, data storage and for subsequent data browsing and selection were available so that a systematic overview can be gained and informed decisions made. These requirements play a particular role in the planning and evaluation of experiments and are essential to the construction of quantitative experimentally constrained computational models for exploring biophysical mechanisms at the cellular or microcircuitry level.

In recent years, several database systems have been constructed and made publicly available that facilitate the work of the neuroscientist to some extent (for overviews see: Chicurel 2000, Kötter 2001; 2003). However, the problem of inhomogeneous non-standardized and method-dependent data sets makes it difficult to efficiently represent single neuron and neuronal microcircuit data in a database. Existing neuronal databases have dealt with this problem by focusing on a limited and rather homogeneous field of information, such as morphology (Ascoli et al. 2001; Cannon et al. 1998; Gonzalez et al. 2001), single species (Stein et al. 2001), or a qualitative representation of single neuron features (Mirsky et al. 1998), and by customizing their layout accordingly. Thus, the user would have to either consult several different databases to obtain different pieces of

information, or take the database as an initial guide before turning to the individual reports for more detailed or quantitative data. Furthermore, the content of all databases is small compared to the wealth of available data and may not satisfy the specific research needs. Although groups of users might restrict their interest on different subsets of data they are not well served by centrally administered online databases where the users have very little influence on the available content.

We here describe the relational database CoCoDat (*Collation of Cortical Data*), which is designed as an advanced tool for organizing published biophysical, anatomical and electrophysiological data for the needs of the experimental and computational neuroscientist. The database system, including a comprehensive data set of microcircuitry data focused on the rat neocortex, can be downloaded, populated and modified according to the needs of the individual researcher or laboratory. Non-interpreted quantitative descriptions of characteristic features of single neurons and microcircuits, as well as quoted descriptive information, is stored and linked to detailed bibliographical and methodological information adhering strictly to the terminology originally used in the entered publications. Data describing membrane conductances, ionic and synaptic currents, neuronal morphology, connectivity and firing patterns can be stored using pre-defined forms. The design of these forms and the corresponding database tables relies on fundamental biophysical concepts of neuronal properties and has been tested with a representative set of real data. In addition, CoCoDat is equipped with powerful search functions allowing the user to perform combinatorial queries based on flexible specifications of brain site, data category and species.

To demonstrate the functionality and usefulness of CoCoDat we report the successful implementation of a detailed single neuron model of a layer V pyramidal cell from rat barrel cortex. This model was constructed using the tools of the database to find suitable biophysical parameters published by previous studies, and the emergent model behaviour was tested against further

experimental findings extracted from the database. A user-oriented introduction to an early version of CoCoDat has been published previously as a book chapter (D.-Johnsen et al. 2003).

## **Materials and Methods**

### **Design objectives**

The main goal during the design of CoCoDat was to implement a flexible tool for systematically organizing and extracting data sets that would be detailed enough to allow the construction of biophysically realistic quantitative models of single cells and microcircuits. The database design followed four main objectives: (i) Applicability of the methodology to the broad variety of published data, (ii) transparent representation of “raw” (i.e. non-interpreted) data, (iii) flexibility for further development, and (iv) implementation of powerful search and representation tools to aid flexible and informed data extraction. To achieve these objectives, the following was done:

- i. The tables constituting the database were derived from a comprehensive survey of representative electrophysiological and anatomical literature on the rat neocortex from the last ~15 years, ensuring that tables and their fields in CoCoDat reflect the information and values commonly reported in relevant publications.
- ii. Transparency was maintained by the strict 1:1 representation of published data, as well as detailed referencing of the data source (including exact page and figure numbers). By avoiding analysis or interpretation of entered data, the records of CoCoDat are faithful representations of the original descriptions in the published literature. Furthermore, accidental fragmentation and disconnection of the entered data is prevented by the relational database design.
- iii. Using the relational database approach, with linked independent tables containing the actual records, it is easily possible to add or edit single tables if necessary without redesigning the

entire database. As the conceptual structure and the principles of implementation of CoCoDat are informed by our long-standing experiences with the CoCoMac database of interregional connectivity collated from tracing studies ([www.cocomac.org](http://www.cocomac.org); Stephan et al. 2001), the design has been thoroughly worked out and is in principle capable of being integrated to combine microcircuitry details with information on large-scale connectivity.

- iv. We developed comprehensive search functions that allow for user-defined combinatorial searches of the collated data. Crucially, the level of matching between search terms and stored data can be varied through relaxation of search parameters along several conceptual dimensions. Details will be described below.

### **Structure of CoCoDat**

CoCoDat was built using the relational database approach where the collated data are represented in a number of separate tables arranged in hierarchical relationships. Tables are cross-referenced using identifiers that have unique values for each record (primary keys; see Ullman and Widom (1997) for a general introduction to relational database methodology). The database has been implemented using Microsoft Access 2000® and Visual Basic for Applications®, but the data have also been exported in XML format for platform-independent online access (see section on "Distributing CoCoDat").

The data and corresponding database tables contained in the CoCoDat database are organized in four major groups: *Literature*, *Experimental Methodology*, *Mapping of Recording Site* and *Experimental Findings*. These groups are arranged in a hierarchy following two streams that are anchored in bibliographical data, diverge to a group describing the experimental procedures and another describing in detail the recording site(s) before they are re-united in the tables containing the actual experimental findings in question.

Each of the four main groups contains several tables; the most important ones will be discussed in detail below. All data are entered into the database by means of specially designed graphical *forms*. In many cases predefined lists with commonly occurring values (e.g. journal names, recording methods, charge carriers etc.) are used to facilitate and standardize data entry into the database (see Table1). These lists can be flexibly extended by the user.

[Table 1 about here]

All forms are accessed through the CoCoDat *Switchboard* shown in Figure 1. This *Switchboard* is the central user menu in CoCoDat and provides all functions related to data entry and data browsing (left column in Fig. 1), data queries (middle column) and printing of query results in the form of reports (right column).

[Figure 1 about here]

### **Literature data**

Entering literature data into the database is facilitated by the use of a graphical interface *form* giving direct access to the main *Literature* table as well as several sub-tables containing bibliographical details. In addition to a unique ID assigned to each publication in CoCoDat, the *Literature* table contains information on the title, abstract, publication type, type of experimental data, and the data collator for all articles in the database. The sub-tables contain exact bibliographical data according to the type of publication and link to PubMed entry if applicable, as well as the authors' full names and links between the identifying publication ID and the individual author names for search purposes. The field "Web Data" allows users to enter a URL for unpublished data, either as supplementary information for published material or as a separate record in the database.

The literature content of CoCoDat can be searched by selecting "Bibliographic Data" under the heading "Perform Search" on the *SwitchBoard*. Search parameters are typed in individually or can be selected from drop-down menus that show values already entered in the database.

### **Methodological data**

After recording the bibliographical data of a publication, information pertaining to the methodology of the experiments performed is recorded using a graphical form, giving access to all tables containing methodological details.

Data recorded during most electrophysiological experiments are strongly dependent on the specific experimental conditions and procedures utilized. Differences in recording methods, delivery of stimuli, composition of bathing solutions, or even the temperature have large influences, and can give the erroneous impression that results from different publications are contradictory. For the database user to be able to evaluate these methodological influences, we maintain detailed records of the experimental procedures related to each collated dataset.

The main table *Methods\_Electrophysiology* (see Table 1) contains information on experimental preparation, extra- and intracellular solutions, stimulation and recording procedures etc. Further sub-tables contain detailed information on the animals used in the experiments, plane of sectioning for slices and the concentration of every component of the experimental bath solutions that deviate from a standard ACSF (Artificial Cerebro-Spinal Fluid). For each publication in the database, one or more experimental procedures with differing parameters can be entered.

### **Mapping data**

In order to ensure an accurate and flexible attribution of the experimental data to the correct recording site, we use *BrainSite* designators, describing the anatomical position of the recording site

at the levels of *BrainRegion*, *Layer*, *NeuronType*, and *NeuronCompartment*. The designators used at the four levels are not precisely delineated structures such as, e.g., the cytoarchitectonically defined cortical areas in the CoCoMac database. Rather these designators can be seen as provisional entities that are based on generally accepted concepts and nomenclature since precise definitions and techniques for unambiguously determining their properties are often not available. As an example, neuron types and their properties are currently not defined in a principled manner according to unique elementary criteria, but they are described according to heuristic criteria, e.g. IB (intrinsically bursting) vs. RS (regular spiking) pyramidal neurons (Connors and Gutnick 1990). For consistency with the philosophy of the CoCoMac database we regard these heuristic entities as components of a *General Map* (GM). The GM is a non-delineated idealised map conceived to organize these prototypical *BrainSites* according to the general concepts used in descriptive neuroanatomy: in contrast to specific experimental delineations these do not refer to an individual brain, or maybe even species. The user has the option, of course, to extend the mapping data by adding more specific parcellation schemes that identify particular structures of interest in a more precise, but less universal, manner.

Each description of a brain site encountered in the literature is assigned a unique acronym for use in the database. These acronyms with their full textual description are listed in the *BrainMaps\_BrainSiteAcronyms* table. In addition to the *BrainSiteAcronym*, the full name of each *BrainSite* is stored and displayed together with its acronym in forms where *BrainSites* need to be selected (e.g. when entering experimental data or searching the database). Combining the information on brain map (in the examples below, this is only the General Map), *BrainSiteType* (e.g. region, layer, neuron type or subcellular compartment) and the appropriate acronym yields the actual brain site listed in the *BrainMaps\_BrainSites* table with an ID of the form "GM-Ctx\_Vis" (General Map, visual cortex).

While this convention is analogous to the definition of *BrainSites* in the connectivity database CoCoMac (compare Stephan et al. 2001), data representation in CoCoDat rests on additional hierarchical specifications that pave the way for powerful search options. We adopted a way of uniquely identifying a particular site in the brain by combining four such *BrainSite*-IDs at the four levels of description: *BrainRegion*, *Layer*, *NeuronType* and *NeuronCompartment*. These four levels can be seen as a hierarchy of levels of increasing detail. Frequently, however, a coarser, more general level is not specified in the literature so that these levels can also be regarded as independent dimensions of site specification. Combined with the literature-ID of the publication in question, the four *BrainSite*-IDs constitute a *RecordingSite* in the *Neurons* table (compare Table 1) linked to a particular publication. In the case that the publication does not provide information on one or more of the four levels of description, the term "general" is inserted, where e.g. *Comp\_Gen* is the acronym for "general/unspecified compartment" (see figure 2).

On all four levels of description a number of hierarchical parent-child relationships exist between the entered brain sites. As an example, Figure 2 shows the current hierarchy at the level of *NeuronCompartments*.

[Figure 2 about here]

These hierarchical relationships (along with those on the levels of *BrainRegion*, *Layer* and *NeuronType*) are detailed in the table *BrainMaps\_BrainSites\_HC*, designating which *BrainSite* is the *parent* of another at the same level of description. This information is an important part of the implemented powerful search functions that will be described in the Results section.

New *BrainSites*, together with their *BrainSiteAcronyms* and *BrainSiteTypes*, can be added by the user in a dedicated form by clicking the "Mapping Data" button under the heading "Enter/Browse

Data" on the main *SwitchBoard* (Fig. 1). The search routines described below cannot make use of such new *BrainSites* unless their hierarchical relations to existing *BrainSites* are entered as well. This is done via the "Hierarchy Data" button in the same section of the *SwitchBoard* (Fig. 1). Here the user can establish or remove relations for a *BrainSite*. This is aided by an expandable visualization of the hierarchy at the relevant level of description.

## **Experimental data**

To ensure a good balance of standardization and flexibility of CoCoDat for collating and organizing data from the existing literature, we surveyed a comprehensive number of representative articles from the last ~15 years spanning a broad scope of experimental findings as well as different methods and research groups. The main insight from the survey was, not unexpectedly, that the types as well as the formats of the data reported are extremely variable.

Based on the survey, we noted the co-occurrence of reported values from different experiments, which resulted in a division of the experimental data into six categories: *Morphology*, *FiringProperties*, *IonicCurrents*, *IonicConductances*, *SynapticCurrents*, and *Connectivity*. These categories reflect the experimental methodology and the underlying biophysical theory by the division of information into sets of "building blocks" that constitute and define the properties of a neuron. A cell is seen as a basic structure defined by a *Morphology*. Its substructures are furnished with various ion channels with different *IonicConductances*, giving rise to *IonicCurrents* after synaptic (or other) input to the cell (*SynapticCurrents*). These combined properties determine the neuron's measurable "macroscopic" behaviour or *FiringProperties*. When seen as part of a larger network, determining the *Connectivity* also becomes a necessity. An experiment often focuses on data from one of the six categories. However, frequently additional data are also reported in the categories *Morphology* and *FiringProperties* as part of a general characterization or identification of the neuron. This organization of the data precisely corresponds with the division of information

and modelling objects in simulations based on the concepts of compartmental modelling (Koch and Segev 1989; Rall 1964).

Experimental data are entered into CoCoDat in six main tables (some of which contain several sub-tables) whose fields reflect the most commonly reported parameters in the literature. Furthermore, each record for experimental data has a designated field for direct citations from the original publication which provides additional relevant reference and context, as well as the opportunity to include direct reports of data not fitting the pre-defined fields (compare Fig. 8). Similarly, in the field *Comments* the data collator (or subsequent users with additional information) can enter comments or summarized information not fitting in any other fields. Data are entered using custom-designed forms after selecting the appropriate *RecordingSite*. Each record is linked to both the ID of the neuronal recording site and the experimental method in question. In each of the six data categories a different set of standard fields as well as direct references to the text and figures containing the information are filled with the available information. The contents of the six main tables storing experimental data are summarized in Table 1.

The entire process of entering a published article including bibliographic, methodological and experimental data can last from one to several hours, depending on the amount of information in the publication as well as whether or not the publication is structured in a manner that essentially segregates the necessary data into groups compatible with the CoCoDat structure.

### **The relational structure of the database**

As mentioned above, the CoCoDat database has a relational design with the actual data arranged in hierarchically linked independent tables. The tables are linked typically by one-to-many relationships downwards in the hierarchy, meaning that, e.g., a particular article can contain information on several experimental methods or recording sites, which again can be associated with

several experimental findings. The core of the relational structure of CoCoDat is illustrated in Figure 3, showing the main tables and their relations.

[Figure 3 about here]

Here the aforementioned division from the initial literature record into two streams of methodological and mapping data, respectively, that are re-united at the level of the six experimental data categories is easily recognizable.

## **Results**

### **Current status of CoCoDat**

At present most of the collation has been targeted on data necessary for our modelling of local circuitry in the barrel cortex of the rat, with a primary focus on single cell properties of layer 5 pyramidal neurons (see below). Since the necessary data for a given model are not always available (as later illustrated), CoCoDat contains data from a variety of cortical areas and cell types. The current contents stems from 38 publications with 89 records on experimental methodology and 71 neuronal recording sites. Linked to these are a total of 257 records of experimental data distributed as: *Morphology* (42 records), *FiringProperties* (65 records), *IonicCurrents* (68 records), *IonicConductances* (51 records), *SynapticCurrents* (11 records) and *Connectivity* (20 records).

### **Extracting and representing datasets**

Data sets are conveniently extracted from CoCoDat using the *SearchBoard*, which is selected from the main *SwitchBoard* of the database (see Fig. 1). Here the user specifies the constraints on the neuronal structure(s), type of data and animal to be included in the search by selecting the desired *BrainRegion*, *Layer*, *NeuronType* and *NeuronCompartment* along with *DataCategory* and *Species*

(the specification of species is optional). All search terms are combined to a final search string by use of the Boolean AND operator.

Since data are entered in the database according to the originally specified *RecordingSite* in a publication, a simple search for data linked to particular combinations of the four selected *BrainSites* could easily fail to produce all relevant data. For example, without automatic expansion of the query, selecting *GM-Ctx\_SeM* (sensorimotor cortex) as *BrainRegion* would not return data from substructures like e.g. *GM-Ctx\_SS* (primary somatosensory cortex). Therefore, the CoCoDat search routine first expands each selected *BrainSite* into a list that contains all its children, as well as grandchildren etc., according to the hierarchical parent-child relationships recorded in the table *BrainMaps\_BrainSites\_HC*. Since this is done for all four levels of description, the final number of *RecordingSites* to be searched is the all-to-all combination (i.e. the Cartesian product) of the expansions of the four originally selected *BrainSites* (Fig. 4).

[Figure 4 about here]

From this it also follows that by selecting the topmost (i.e. most general) *BrainSite* at each level (general cortical region: *GM-Ctx\_Gen*; general layer: *GM-L\_Gen*; general neuron type: *GM-C\_Gen*; general compartment: *GM-Comp\_Gen*), the user can extract all information in a *DataCategory* for a given *Species* currently contained in CoCoDat.

Since it is often the case that the queried information for a particular *RecordingSite* is not available, either because it has not been entered in CoCoDat yet or because it has never been reported in the literature, we have implemented a feature that allows the user to automatically relax the search-criteria. If the original search does not provide any results, then the search routine (after specification of one of the four levels of description) selects the parent of the initially selected

*BrainSite* and repeats the procedure with a new set of combinatorically generated *RecordingSites*. An example is provided by Figure 5 where an initial query for ionic conductances in the somatosensory barrel cortex (i.e. GM-Ctx\_B as specified *BrainRegion*) did not produce results. After relaxing the precision for *BrainRegion* and repeating the query, two recording sites within the primary somatosensory cortex (GM-Ctx\_SS) with a total of six experimental findings on ionic conductances were found. The relaxation procedure thus allows the user to choose the level of description deemed to be the least critical in terms of data searched for. The relaxed search process is then more likely to produce results from a relevant recording site that are informative and usable for the current question or model.

[Figure 5 about here]

To allow for a direct visual evaluation of the extracted data, a hierarchical representation of the *RecordingSites* based on the hierarchy of each *BrainSite* involved is generated. A branching-tree structure visualizing the hierarchy based on the relationships defined in *BrainMaps\_BrainSites\_HC* is then displayed in the four panels with a number in parentheses giving the number of returned *RecordingSites* that the relevant *BrainSite* is part of (Figures 5 and 6). At the top level of a given hierarchy, the number of *RecordingSites* containing the top level *BrainSite* out of the total number of returned *RecordingSites* is given, providing the user with information about the returned results even without expanding the tree-structures. The user can thus directly determine the distribution of returned information among the selected *BrainSites*. In the case where information is not available on the structure to be modelled and where related *BrainSites* have been included in the search, the user can furthermore visually appraise the "logical" distance between the *RecordingSites* of returned results and, e.g., the modelled structure, which will aid in determining which information is most appropriate for the model in question.

Following a successful query the user can further manually relax the search criteria by selecting the parent *BrainSite* on one or more of the four levels of description. Continuing the example from Fig. 5, Fig. 6 shows a subsequent query where the precision for the *BrainRegion* was further relaxed, i.e. from primary somatosensory cortex (GM-Ctx\_SS) to sensorimotor cortex (GM-Ctx\_SeM). This relaxed query resulted in additional *RecordingSites* with information on the desired data category (i.e. ionic conductances) (see Fig. 6 for details). Overall, the relaxation procedure helps CoCoDat to overcome the trade-off between exact, non-interpreted data representation in the nomenclature of the original report and convenient data retrieval that has been a central problem for previous neuroscientific databases (compare alternative approaches in connectivity databases, e.g. Stephan et al. 2001).

[Figure 6 about here]

Following a successful query, the "Show Details" button under the "Perform Action" heading (Fig. 6) allows the user to summarize the returned search results in a new form (Fig. 7).

[Figure 7 about here]

In this summary form, the four *BrainSites* constituting the *RecordingSite* are displayed, along with the basic qualitative information for the data, i.e. type of ionic current, morphological feature described etc. Quick information on the authors of each datum is obtained by double-clicking the field *ID\_Literature*. For each recording site, a form containing all detailed information on the selected *DataCategory* can be expanded (Fig. 8). The "Display Literature" button displays the bibliographical information with specification of authors of the original publication in a separate window. Similarly, a separate window detailing all experimental procedures used by this study can be opened by clicking "Display Methods". If the study contained information on any other

*DataCategory* than the currently selected one, this information can be directly accessed through up to five buttons on the form (compare Fig. 8).

[Figure 8 about here]

After inspecting the detailed query results for each *RecordingSite*, the user can select the most appropriate information to be printed in *Report* form from the *SummaryForm* (Fig. 7; see tick boxes in the rightmost column). The main *SwitchBoard* (Fig. 1; see heading "Print Reports") then allows to print comprehensive reports of the experimental data, including a description of the *RecordingSite* as well as the associated bibliographic and methodological information. An example of a printed report is shown in Figure 9.

[Figure 9 about here]

### **Distributing CoCoDat**

For maximal flexibility the CoCoDat database can be downloaded as a database (mdb) file in Microsoft Access 2000 format from <http://www.cocomac.org/cocodat/> along with a manual, which details procedures for searching, extracting, and entering data sets. CoCoDat is copy-lefted under the GNU General Public License ([www.gnu.org/licenses/gpl.html](http://www.gnu.org/licenses/gpl.html)) to promote further use and distribution. Since all data extracted from the published literature had been manually entered in the database together with precise references to the original sources, the distribution of the data does not infringe on copyrights. We would appreciate if researchers, who found this database system useful and inserted additional data, made their extensions available again to others either through distribution of the extended mdb file or through merging with our online contents (see below).

We realize that not every user has a Microsoft Access software license to use the mdb file and that coordination of distributed data collations is desirable. As a solution, we also provide the data at a platform-independent web site as XML-formatted catalogues that were created by extraction from our database using the ODBC (Open DataBase Connectivity) interface of the Catalyzer software (<http://www.axiope.com>; Goddard et al. 2003). While this web option cannot provide the routines for data extraction with relaxation of search criteria that were implemented in database-specific Visual Basic for Applications code, it has the virtue of making the database contents fully downloadable and extensible. The further use and adaptation on the user side is facilitated by the Catalyzer software, which can be freely downloaded from <http://www.axiope.com>. Furthermore, integration of additions made by other users with our resource is achieved using the Catalyzer Server extension. Catalyzer Server integrates distributed data resources and provides interfaces for coherent extraction and insertion of data.

Finally, we have set up a mailing list that CoCoDat users can freely subscribe to and that distributes questions and comments to all members of the mailing list. Instructions for using the CoCoDat mailing list are provided at <http://www.cocomac.org/cocodat/>.

### **An experimentally constrained model of a layer 5 intrinsically bursting pyramidal neuron**

As a practical demonstration of the use of CoCoDat we constructed a detailed computer model of an intrinsically bursting (IB) layer V pyramidal neuron from the rat barrel cortex supplementing experimental data (Schubert et al. 2001) with information extracted from the database. The pyramidal neuron morphology (Fig. 10B) was reconstructed from histological sections of a biocytin-stained IB neuron using the NeuroLucida software package (MicroBrightfield, Williston, VT), edited for modelling, corrected for tissue shrinkage, and exported to a file format readable by

the GENESIS 2.2 simulation system (Bower and Beeman 1998) using the CVAPP software package (Cannon et al. 1998).

[Figure 10 about here]

Information retrieved from the CoCoDat database was used to equip the morphology with passive parameters and active conductances using the following search parameters for the *RecordingSite*: *GM-Ctx\_SeM* (sensorimotor cortex), *GM-L\_5* (layer V), *GM-C\_Pyr* (pyramidal cell) and *GM-Comp\_Gen* (general compartment). This query provided directly relevant information from six different papers on channel kinetics and membrane properties for the various compartments of the neuron (summarized in Table 2).

[Table 2 about here]

As information on kinetics and densities of the relevant conductances and currents in layer V pyramidal neurons is currently incomplete in the literature (i.e. no information was provided on time constants accompanying an expression for steady-state activation), a set of conductances used to model bursting properties of layer II/III neocortical neurons (Traub et al. 2003) also contained in the CoCoDat database was used as a basis and modified to fit the model responses to the experimental data, in combination with a detailed kinetic description of hyperpolarization-activated mixed cation conductance  $g_h$  (Williams and Stuart 2000).

Due to the experimental difficulties of recording from basal and distal apical dendrites, most reported data were obtained either in the whole cell configuration or using patches of somatic or apical dendritic membrane. Therefore, we initially assumed that all dendritic domains contain most

of the active conductances (Traub et al. 2003), and adjusted their conductance densities during the fitting procedure. The responses of the IB neuron model to current injections of 200 msec duration were fitted by adjusting kinetic descriptions of the voltage-gated conductances or their densities or the passive membrane parameters. Detailed description of all model parameters can be found in Appendix A, tables A1-A4.

Only one type of high-threshold calcium conductance was included, as the different subtypes have been shown to have very similar biophysical properties (Lorenzon and Foehring 1995). Since the axon was not included in the reconstruction, we located action-potential initiation in the neuron soma. Intracellular calcium ion concentrations were modelled in a thin shell directly under the neuronal membrane following a scheme consistent with the calcium-dependent conductances (Traub et al. 2003). All voltage-gated channels were implemented as *tabchannel* objects within GENESIS and simulations were done in Hines-solver mode using the Crank-Nicholson implicit method of numerical integration with a simulation time-step of 50  $\mu$ sec.

[Figure 11 about here]

As can be seen in Figure 11, the model equipped with conductances based on information extracted from CoCoDat fits the experimentally recorded responses to current injection very well. The only significant discrepancy is a more slowly increasing depolarization before the action potential onset compared to the sharp voltage inflection seen in the experimentally recorded traces. This can be attributed to the simulation of action potential initiation in the large single compartment soma with the slow charging of a relatively large membrane capacitance as opposed to simulations including a reconstructed axon hillock and initial segment as the site of action potential initiation (Mainen et al. 1995).

To further establish the validity of the model, we used CoCodat to search for additional data sets that could be used for further tests of the model under different conditions. Our queries found two suitable data sets: First, Mantegazza et al. (1998) reported an increase in bursting tendencies of IB neurons from rat sensorimotor cortex after treatment with anemone toxin (ATX-II), a selective inhibitor of sodium current inactivation, which leads to an increase of the persistent fraction of the sodium current. This pharmacological manipulation could be mimicked by increasing the  $g_{NaP}$  conductance density in the model by 25%. The model response to a 200 ms 150 pA depolarizing current injection then shows one additional action potential in the initial burst (Figure 12A), which is consistent with the experimental data by Mantegazza et al. (1998).

[Figure 12 about here]

Additionally, we could replicate the experimental findings by Zhu and Connors (1999) on repetitive burst firing for layer V IB pyramidal neurons from rat somatosensory cortex by increasing the amplitude of the simulated somatic current injection from 150 pA to 300 pA.

## **Discussion**

The CoCoDat database provides a convenient and powerful environment for organizing detailed records of quantitative experimental data for scientific reference and biophysically realistic modelling. The grouping of data according to electrophysiological methodology and biophysical theory facilitates the systematic extraction of relevant data. Additional detailed information on experimental methodology simplifies the evaluation or reconciliation of apparent contradictions in the published experimental data, while detailed references to textual and graphical information allow the user to rapidly locate relevant material in the original publications.

As seen in the example model of an intrinsically bursting layer V neuron from the rat barrel cortex, the implementation of a hierarchically organized mapping scheme covering four levels of description (*BrainRegion*, *Layer*, *NeuronType*, *NeuronCompartment*) allows for the extraction of subcompartment-specific information useful for constructing neuron models with differentially distributed membrane conductances and passive parameters. The use of hierarchically arranged *BrainSites* in the mapping scheme furthermore allows for flexible extraction of data from the database using a combinatorial search algorithm to deliver results that best match the user specified criteria. Once a model has been implemented, additional data from the CoCoDat database can be used to test emergent model behaviour. Above, we have described an example for the evaluation of drug effects in the case of a layer V intrinsically bursting pyramidal neuron model.

By invoking the optional automatic relaxation of the initially specified search criteria along the level of description that is deemed to be least critical to a given model, the user can extract the closest possible matching datasets from the database in cases where information on a specifically requested *RecordingSite* is not available. Once a useful dataset has been found, a thorough exploration of the surrounding data space can be performed by manually varying the search criteria. Using the implemented functions to generate printable date-stamped reports of selected data sets, as well as their related data in other data categories and associated methodological and bibliographical information, makes it possible to easily file and track the information available in the database at the time when a particular model was constructed

The survey of comparable data resources presented in Table 3 shows that the CoCoDat database provides resources not previously available from existing databases at the microcircuitry and single neuron level: The particular advantage of CoCoDat is the supply of non-interpreted detailed quantitative morphological and electrophysiological data along with the detailed methodological information important for assessing whether a data set is appropriate for reference or for modelling

in a given study. Other existing databases provide either qualitative electrophysiological data, reconstructed morphologies or specific published models (see Table III). This download is useful if the scientist is looking for a general model of a neuron type or if the model code is sufficiently modular to facilitate easy integration of, for example, a new morphology for modelling of a specific cell. Even so, a significant amount of time will still be devoted to adjusting the distributions and kinetics of voltage-gated conductances to the new morphology and possible differences in experimental conditions.

[Table 3 about here]

The use of CoCoDat is not limited to the amount of information contained in the centrally downloadable version of CoCoDat: Users can incrementally increase their personal data collection using the appropriate forms selectable from the central *SwitchBoard* (Fig. 1). Detailed guidelines for collating and entering data in all categories, as well as instructions for adding *BrainSites* to the already established hierarchies are provided in the CoCoDat manual (available from <http://www.cocomac.org/cocodat>). For laboratories and groups of researchers investigating similar neuronal structures, setting up a central master database with individual database clients for entering new data allows for the rapid accumulation of a large amount of centrally accessible data. In a situation where several collators are entering data into the same database, it is highly advisable that procedures for proofreading records are established to ensure common standards are being adhered to, as has been established for CoCoMac ([www.cocomac.org](http://www.cocomac.org)).

The CoCoDat database shares the principal structure of the connectivity database CoCoMac (Stephan et al. 2001), and because of the compatible mapping schemes it is technically straightforward to integrate the information in the two databases. This would provide the opportunity to link detailed information on large scale anatomical connectivity and local

microcircuitry properties, giving a more complete picture of the organization and processing capabilities of multi-scale networks in the brain. Due to the modular nature of the database it is straightforward to add additional data categories for incorporation of information on e.g. intracellular signaling or distributions of ligand- or voltage-gated ion channels as reported from chemoarchitectural studies. Alternatively, information from other existing databases could be linked to *RecordingSites* in CoCoDat using the XML capabilities of Microsoft Access.

Ultimately, we anticipate that the development of distributed data resources that cater the specific needs of individual researchers or cooperating research groups would also be the best way to serve the community as a whole. No centrally administered resource could provide the required flexibility to respond to the different user needs and priorities, and its continued availability would be always be threatened by the discontinuation of adequate funding. Thus, the most efficient and affordable form of organization would be the distributed use and extension of our database framework and contents with the option to join distributed sources through automated management services. We think that the Catalyzer Server concept, which keeps data in their distributed locations and only centralizes catalogues, upload and retrieval options on one or more servers, could go a long way in this desirable direction.

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### **Table legends:**

**Table 1:** The tables and contents of the CoCoDat database organized in four major data groups.

**Table 2:** Data on different membrane domains in IB layer V pyramidal neuron from the rat barrel cortex, obtained by searching the CoCoDat database.

**Table 3:** Comparison of different databases containing data on the single neuron and microcircuitry level. (<sup>1</sup><http://www.cocomac.org/cocodat>,

<sup>2</sup><http://www.cns.soton.ac.uk/~jchad/cellArchive/cellArchive.html>,

<sup>3</sup><http://www.krasnow.gmu.edu/L-Neuron/database/index.html>,

<sup>4</sup><http://senselab.med.yale.edu/senselab/>, <sup>5</sup><http://cascade.utsa.edu/bjclab/>)

## Figure legends:

**Figure 1:** The central CoCoDat *Switchboard* gives the user access to all forms for data entry, data queries, and generation of printable reports.

**Figure 2:** The current hierarchy defining the logical relationships between *BrainSites* at the *NeuronCompartment* level of description.

**Figure 3:** The relational structure of the main tables in the CoCoDat database. This figure also reflects the division of the data into 4 main groups.

**Figure 4:** The expansion and combination of four *BrainSites* initially submitted to an example query: somatosensory cortex (GM-Ctx\_SS), infragranular layers of isocortex (GM-L\_InfraGr\_IsoCtx), spiny neurons (GM-C\_SpiN) and soma compartment (GM-Soma). Arrows represent the different steps in the expansion and combination of the entered search terms and dotted lines signify compressed entries in the list of queried combinations. A total of  $2 \cdot 3 \cdot 6 \cdot 1 = 30$  potential *RecordingSites* are submitted for the query after the all-to-all combination.

**Figure 5:** Data are extracted from the CoCoDat database using the *SearchBoard* (accessible through the main *SwitchBoard*, see Fig. 1). The illustrated example shows a query for data on *IonicConductances* that combines *GM-Ctx\_B* (barrel cortex), *GM-L5\_IsoCtx* (isocortical layer 5), *GM-C\_Pyr* (pyramidal cell), *GM-Comp\_Gen* (general compartment) with species not specified. Choosing automatic relaxation of the *BrainRegion* returns results from a query that replaces *GM-Ctx\_B* by its parent site, i.e. primary somatosensory cortex (*GM-Ctx\_SS*). Numbers in parentheses following the *BrainSites* in the expanded hierarchies indicate the number of found *RecordingSites* a given *BrainSite* is part of. In the case of *BrainRegion*, *Layer* and *NeuronType*, only the top level of

the hierarchy is part of the two returned *RecordingSites*. No returned *RecordingSite* contains *GM-Comp\_Gen* (general compartment) at the *NeuronCompartment* level, however *GM-Dend\_Ap* (apical dendrite) and *GM-Soma* (soma) each constitute part of one *RecordingSite*. A total of six returned records from the two returned *RecordingSite* contained experimental data in the selected *IonicConductances* data category (see last six entries in Fig. 7).

**Figure 6:** Manually relaxing the *BrainSite* from *GM-Ctx\_SS* (somatosensory cortex) to *GM-Ctx\_SeM* (sensorimotor cortex) following the example shown in Figure 6, increases the number of returned *RecordingSites* from two to four and the total number of returned records in the selected *IonicConductances* data category from six to nine (see entries 2-4 and the last 6 entries in Fig. 7).

**Figure 7:** The summary form gives a brief overview of returned search results and allows for further detailed inspection of the records. Double-clicking the field *ID\_Literature* provides quick information on the authors of the original data as shown in the inset. Further details are obtained by clicking the + sign to the left of each record (see Fig. 8).

**Figure 8:** Detailed view of one expanded record in the summarized list. The insert shows the pop-up window with information on the same *RecordingSite* in the *IonicCurrents* data category. Bibliographic and methodological information on the study in question can be accessed by respectively clicking “Display Literature” and “Display Methods”.

**Figure 9:** The query result shown by Fig. 8 is displayed as a printed report, showing data from the *IonicConductances* category.

**Figure 10:** A. The experimentally recorded I-V characteristics of the IB layer V pyramidal neuron from rat barrel cortex selected for fitting the single-cell model. B. Reconstructed morphology of the

IB neuron. The morphology was scaled and edited, and distinctions between apical subdivisions are indicated. Following the central and leftmost branches of the medial apical dendrite, the distal part is taken to start at the first branch point before the apical tuft (experimental data from Schubert et al. 2001).

**Figure 11:** Comparison of responses of the reconstructed layer V pyramidal neuron morphology equipped with conductances based on information extracted from the CoCoDat database (**red solid line**) and experimentally recorded (grey dashed line) responses to 17 somatic current injections ranging from  $-700$  pA to  $150$  pA in steps of  $50$  pA with stimulus onset at  $t = 0.05$  sec and offset at  $t = 0.250$  sec.

**Figure 12:** A. Replicating the experimental findings by Mantegazza et al. (1998), the model response to  $150$  pA current injection shows one additional action potential in the initial burst when  $g_{NaP}$  is increased by 25%. B. The model also successfully replicates the repeated burst firing reported by Zhu and Connors (1999) during a simulated higher amplitude ( $300$  pA) somatic current injection.

**Table I: Contents of CoCoDat tables.**

<b>Table</b>	<b>Content</b>
<b>Literature</b>	
Literature	<i>ID, title, year of publication, publication type, abstract, keywords, comments and ID of data collator, URL for additional data accessible on the internet</i>
Literature_Abbreviations_Journals	<i>Predefined list of journal name abbreviations</i>
Literature_Authors	<i>Authors initials and last names</i>
Literature_BookChapters	<i>Page numbers, editors, book title, publisher, place of publishing</i>
Literature_Books	<i>Publisher, place of publishing</i>
Literature_JournalArticles	<i>Journal, volume and page numbers, PubMed ID and link to entry</i>
Literature_LinkTable	<i>Links between literature IDs and authors (for search purposes)</i>
<b>Mapping of Recording Site</b>	
BrainMaps	<i>Entered BrainMaps (General Map and other user-specified parcellation schemes)</i>
BrainMaps_BrainSites_BrainSiteTypes	<i>Defined BrainSiteTypes</i>
BrainMaps_BrainSiteAcronyms	<i>BrainsiteAcronyms with their full description</i>
BrainMaps_BrainSites	<i>Brainsites given by a combination of Brainmap, BrainSiteAcronym and BrainSiteType</i>
BrainMaps_BrainSites_HC	<i>Hierarchical relations of BrainSites at each level of organisation</i>
Neurons	<i>RecordingSites given by their LiteratureID, BrainRegion, Layer, NeuronType &amp; Compartment</i>
<b>Experimental Methodology</b>	
Methods_Electrophysiology	<i>Experimental preparation, solution, recording method, stimulation method, species, temperature, text- and figure references, comments</i>
Methods_Electrophysiology_Animals	<i>Animal strain, age, sex and weight</i>
Methods_Electrophysiology_CompConc	<i>Pharmacological components and their concentrations</i>
Methods_Electrophysiology_Preparations	<i>Predefined list of experimental preparations</i>
Methods_Electrophysiology_RecMethod	<i>Predefined list of recording methods</i>
Methods_Electrophysiology_SliceOrient	<i>Slice orientation Predefined list of planes of sectioning</i>
Methods_Electrophysiology_SolutionType	<i>Predefined list of solution types</i>
Methods_Electrophysiology_Species	<i>Predefined list of species</i>
<b>Experimental Findings</b>	
Neurons_Morphology	<i>Morphological feature name, value, reconstruction, citations, text- and figure references, comments</i>
Neurons_Morphology_RecMethod	<i>Morphological reconstruction methods</i>
Neurons_FiringProperties	<i>Firing pattern type, citations, text- and figure references, comments</i>
Neurons_FiringProperties_APduration	<i>Action potential duration</i>
Neurons_FiringProperties_Rinput	<i>Input resistance</i>
Neurons_FiringProperties_Rintra	<i>Intracellular resistance</i>
Neurons_FiringProperties_TauM	<i>Membrane time-constant</i>
Neurons_FiringProperties_Vrest	<i>Membrane resting potential</i>
Neurons_IonicCurrents	<i>Current name, charge-carrier, peak conductance, peak current, reversal potential, voltage threshold, half-activation voltage, peak voltage, citations, text- and figure references, comments</i>
Neurons_IonicConductances	<i>Conductance name, charge-carrier, peak conductance, voltage threshold, half-activation voltage, peak voltage, citations, text- and figure references, comments</i>
Neurons_SynapticCurrents	<i>Synapse type, peak conductance, peak current, peak potential, reversal potential, latency, citations, text- and figure references, comments</i>
Neurons_Connectivity	<i>Target BrainRegion, Layer, NeuronType and Compartment, citations, text- and figure references, comments</i>
Neurons_ChargeCarrier	<i>Predefined list of charge carriers (ions)</i>

**Table II: CoCoDat search results for example model**

Neuronal Compartment	Search results
General compartment	I <sub>K</sub> , I <sub>NaF</sub> , I <sub>NaP</sub> and I <sub>Ca</sub> (Mantegazza et al. 1998), distribution of passive membrane parameters and I <sub>h</sub> (Stuart and Spruston 1998)
Soma	Fast inactivating I <sub>A</sub> /g <sub>A</sub> and slowly or very slowly inactivating I <sub>K</sub> /g <sub>K</sub> (Bekkers 2000), fast inactivating I <sub>K</sub> /g <sub>K</sub> and slowly or very slowly inactivating I <sub>K</sub> /g <sub>K</sub> , calcium-ion dependent BK (Korngreen and Sakmann, 2000) , I <sub>h</sub> (Williams and Stuart, 2000)
Basal dendrites	I <sub>Ca</sub> (Oakley et al. 2001)
Apical dendrite	I <sub>Ca</sub> (Oakley et al. 2001), fast inactivating I <sub>A</sub> /g <sub>A</sub> (Bekkers 2000), fast inactivating g <sub>K</sub> and slowly or very slowly inactivating g <sub>K</sub> , calcium-ion dependent BK (Korngreen and Sakmann 2000), I <sub>h</sub> (Williams and Stuart 2000)
Distal apical dendrite	I <sub>Ca</sub> and I <sub>Na</sub> (Schiller et al. 1997)

**Table III: Database comparison**

Database	Bibliographical Data	Methodological Data	Experimental Data	Model data	Search Functions	Online Accessibility	Additional
CoCoDat <sup>1</sup>	Detailed	Detailed	Quantitative, non-interpreted data on morphology, firing properties, ionic currents and conductances, synaptic currents and connectivity	Quantitative	Advanced combinatorial searches and hierarchical representations	Downloadable	Can be integrated with the CoCoMac database
Duke / Southampton Archive of Neuronal Morphology <sup>2</sup> (Cannon et al., 1998)	References	Some	Complete downloadable experimentally obtained morphologies, few electrophysiological data	None	Selectable from lists	Yes	Software for viewing, editing and converting morphology files. Images of cells.
Virtual Neuromorphology Electronic Database <sup>3</sup> (Ascoli et al., 2001)	References	Some	Complete downloadable experimentally obtained and algorithmically generated morphologies	None	Selectable from lists	Yes	Software for viewing, editing and converting morphology files. Images of cells.
SenseLab Databases (CellPropDB, NeuronDB, ModelDB) <sup>4</sup> (Mirsky et al., 1998)	References	Some	Qualitative	Downloadable implementations of contributed models	Selectable from lists and some combinatorial search functions	Yes	Integrating information on genes and expressed proteins
Hippocampus neuron data files <sup>5</sup> (Gonzalez et al., 2001)	References	Detailed	Complete downloadable experimentally obtained morphologies	None	Selectable from lists	Yes	Images of cells.

## APPENDIX A:

**Table A I: Kinetics of conductances described by steady state (in-)activation**

Conductance	Steady-state activation	Time constant (sec)
$g_H$	$1 / (1 + \exp[(-0.085 - V) / -0.0061])$	$0.0011 \cdot (\exp[25 \cdot V + 6.68])$ [ $V \leq -0.071$ ] $0.0059 \cdot (\exp[-27 \cdot V + 1.69])$ [ $V \geq -0.071$ ]
$g_{NaF}$ activation	$1 / (1 + \exp[(-0.038 - V) / 0.008])$	$0.0125e-3 + (0.007e-3 \cdot \exp[(0.03 + V) / 0.008])$ [ $V \leq -0.032$ ] $0.01e-3 + (0.0725e-3 \cdot \exp[(-0.03 - V) / 0.008])$ [ $V \geq -0.032$ ]
$g_{NaF}$ inactivation	$1 / (1 + \exp[(0.0574 + V) / 0.007])$	$0.75e-3 + (5.75e-3 / (1 + \exp[(0.0335 + V) / 0.01]))$
$g_{NaP}$	$1 / (1 + \exp[(-0.035 - V) / 0.01])$	$0.025e-3 + (0.014e-3 \cdot \exp[(0.027 + V) / 0.01])$ [ $V \leq -0.027$ ] $0.02e-3 + (0.145e-3 \cdot \exp[(-0.027 - V) / 0.01])$ [ $V \geq -0.027$ ]
$g_{KDr}$	$1 / (1 + \exp[(-0.0295 - V) / 0.01])$	$0.75e-3 + (13.05e-3 \cdot \exp[(0.01 + V) / 0.01])$ [ $V \leq -0.01$ ] $0.75e-3 + (13.05e-3 \cdot \exp[(-0.01 - V) / 0.01])$ [ $V \geq -0.01$ ]
$g_{KA}$ activation	$1 / (1 + \exp[(-0.06 - V) / 0.0085])$	$0.185e-3 + (0.5e-3 / ((\exp[(0.0358 + V) / 0.0197]) + (\exp[(-0.0797 - V) / 0.0127])))$ $0.5e-3 / ((\exp[(0.046 + V) / 0.005]) + (\exp[(-0.238 - V) / 0.0375]))$ [ $V \leq -0.063$ ]
$g_{KA}$ inactivation	$1 / (1 + \exp[(0.078 + V) / 0.006])$	$9.5e-3$ [ $V \geq -0.063$ ]
$g_{K2}$ activation	$1 / (1 + \exp[(-0.01 - V) / 0.017])$	$4.95e-3 + (0.5e-3 / ((\exp[(0.081 + V) / 0.0256]) + (\exp[(-0.132 - V) / 0.018])))$
$g_{K2}$ inactivation	$1 / (1 + \exp[(0.058 + V) / 0.0106])$	$60e-3 + (0.5e-3 / ((\exp[(0.00133 + V) / 0.2]) + (\exp[(-0.13 - V) / 0.0071])))$
$g_{CaT}$ activation	$1 / (1 + \exp[(-0.056 - V) / 0.0062])$	$0.204e-3 + (0.333e-3 / ((\exp[(0.0158 + V) / 0.0182]) + (\exp[(-0.131 - V) / 0.0167])))$
$g_{CaT}$ inactivation	$1 / (1 + \exp[(0.085 + V) / 0.004])$	$0.333e-3 \cdot \exp[(0.466 + V) / 0.0666]$ [ $V \leq -0.081$ ] $9.32e-3 + (0.333e-3 \cdot \exp[(-0.021 - V) / 0.0105])$ [ $V \geq -0.081$ ]

Adjusted kinetic descriptions of active conductances using expressions for steady-state (in-) activation and time constants as functions of membrane potential in Volts. [ $g_{NaF}$  = transient inactivating sodium conductance,  $g_{NaP}$  = persistent sodium conductance,  $g_h$  = hyperpolarization-activated mixed cation conductance,  $g_{CaT}$  = low threshold calcium conductance,  $g_{KDr}$  = delayed rectifier potassium conductance, transient inactivating potassium conductance  $g_{KA}$ , slowly activating and inactivating potassium conductance  $g_{K2}$ ].

**Table A II: Kinetics of conductances described by forward and backward rate functions**

Conductance	Forward rate function ( $\alpha$ )	Backward rate function ( $\beta$ )
$g_{KC}$	$53 \cdot (\exp[(0.05 + V) / 0.011]) - \exp[(0.0535 + V) / 0.027]) [V \leq -0.01]$ $2000 \cdot \exp[(-0.0535 - V) / 0.027] [V \geq -0.01]$	$2000 \cdot \exp[(-0.0535 - V) / 0.027] - \alpha [V \leq -0.01]$ $0 [V \geq -0.01]$
Ca <sup>2+</sup> dependence	$\min(0.004 \cdot [Ca^{2+}]_i, 1.0)$	
$g_{KM}$	$26.67 / (1 + \exp[(-0.02 - V) / 0.005])$	$13.33 / (1 + \exp[(-0.043 - V) / 0.018])$
$g_{KAHP}$	$\min(0.1 \cdot [Ca^{2+}]_i, 10.0)$	10.0
$g_{CaL}$	$1600 / (1 + \exp[-72 \cdot (V - 0.005)])$	$(20e3 \cdot (0.0089 + V)) / (\exp[(0.0089 + V) / 0.005] - 1)$

Adjusted kinetic descriptions of active conductances using expressions for forward and backward rate functions as functions of membrane potential in Volts. [ $g_{CaL}$  = high threshold calcium conductance,  $g_{KM}$  = muscarinic receptor-suppressed potassium conductance,  $g_{KC}$  = fast voltage and  $[Ca^{2+}]_i$ -dependent BK-type potassium conductance, and a slow  $[Ca^{2+}]_i$ -dependent potassium conductance responsible for afterhyperpolarization  $g_{KAHP}$ ]

**Table A III: Fitted conductance densities**

	Soma	Basal dendrites	Apical shaft	Proximal apical dendrites	Medial apical dendrites	Distal apical dendrites
$g_H$	$g_h = g_{h,soma} + \frac{g_{h,distal} - g_{h,soma}}{1 + e^{(500\mu m - dist)/50\mu m}}$ ( $g_{h,soma} = 0.15$ , $g_{h,distal} = 6.0$ ; $dist$ = distance to soma)					
$g_{NaF}$	4400	350	350	350	350	62.5
$g_{NaP}$	$0.0032 * g_{NaF}$	$0.0032 * g_{NaF}$	$0.0032 * g_{NaF}$	$0.0032 * g_{NaF}$	$0.0032 * g_{NaF}$	$0.0032 * g_{NaF}$
$g_{KDr}$	1250	350	350	350	350	0
$g_{KA}$	300	20	300	20	20	20
$g_{K2}$	1	1	1	1	1	1
$g_{CaT}$	1	1	1	1	1	1
$g_{KC}$	22.5	22.5	22.5	22.5	22.5	0
$g_{KM}$	29	29	29	29	25	9.25
$g_{KAHP}$	1	1	1	1	1	1
$g_{CaL}$	5	3	3	3	3	15

Fitted densities of active conductances ( $S\text{m}^{-2}$ ). The density of  $g_h$  was calculated for each individual

compartment using  $g_h = g_{h,soma} + \frac{g_{h,distal} - g_{h,soma}}{1 + e^{(500\mu m - dist)/50\mu m}}$  ( $g_{h,soma} = 0.15$ ,  $g_{h,distal} = 6.0$ ;  $dist$  = distance to

soma)

**Table A IV: Fitted passive parameters**

$R_i$ ( $\Omega m^{-1}$ )	$C_m$ ( $Fm^{-2}$ )	$R_m$ ( $\Omega m^2$ )
0.9	0.007	$R_m = R_{m,distal} + \frac{R_{m,soma} - R_{m,distal}}{1 + e^{(500\mu m - dist)/-50\mu m}}$ ( $R_{m,soma} = 4.0$ , $R_{m,distal} = 0.27$ , $dist =$ distance to soma)

Fitted passive parameters. The value of  $R_m$  was calculated for each individual compartment using

$$R_m = R_{m,distal} + \frac{R_{m,soma} - R_{m,distal}}{1 + e^{(500\mu m - dist)/-50\mu m}} \quad (R_{m,soma} = 4.0, R_{m,distal} = 0.27, dist = \text{distance to soma})$$

Figure 1.

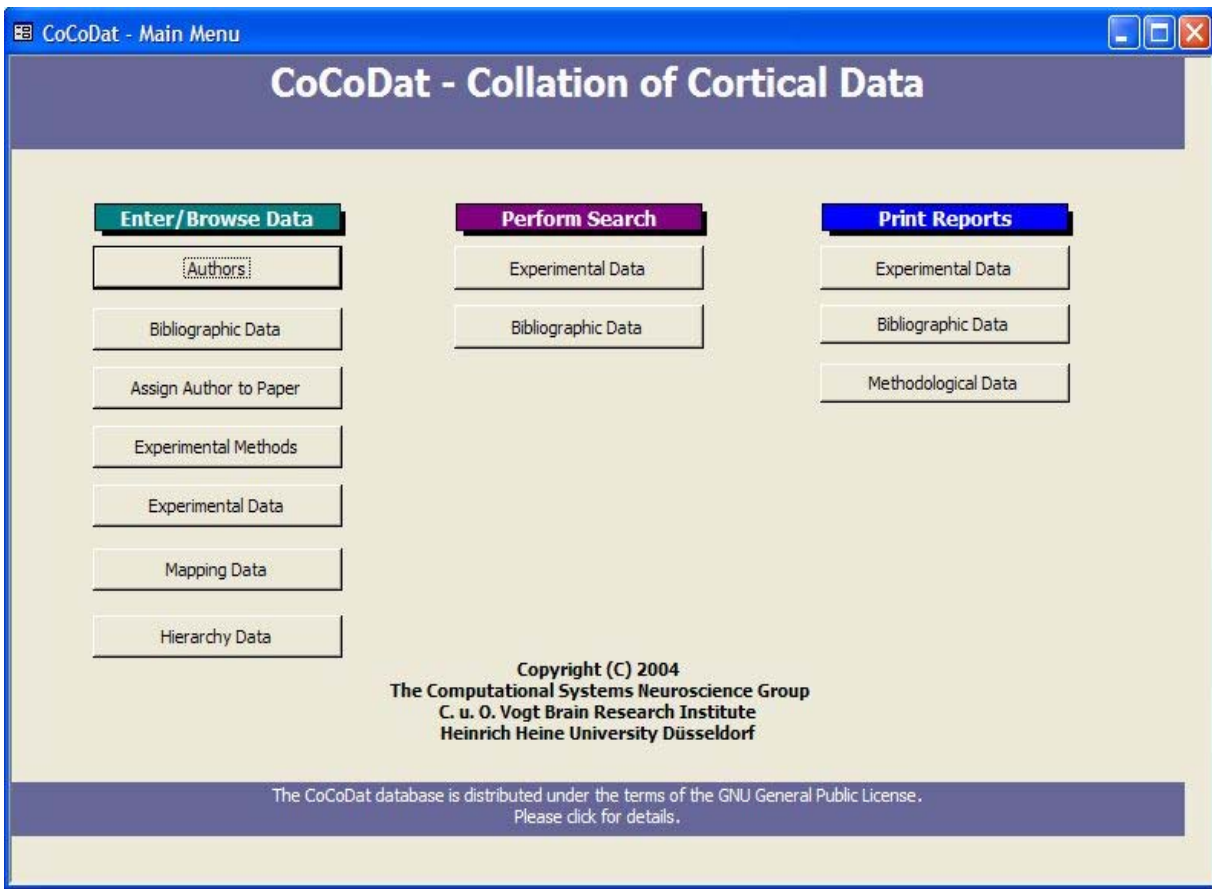


Figure 2.

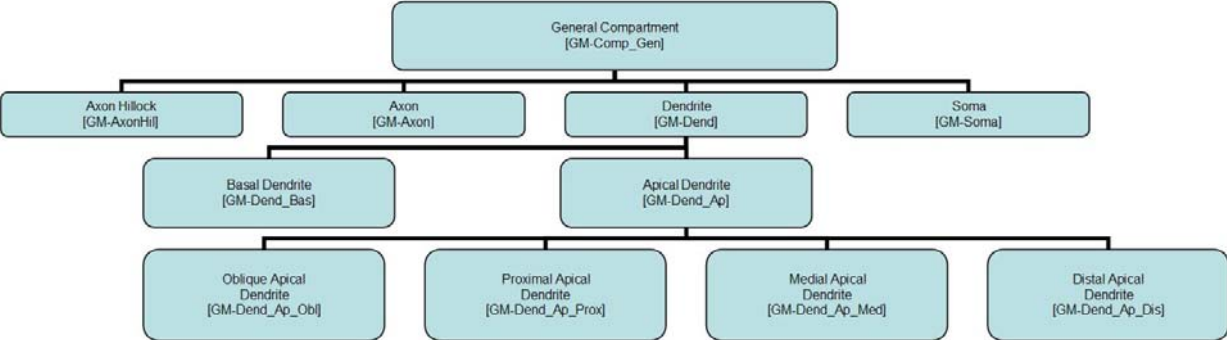


Figure 3.

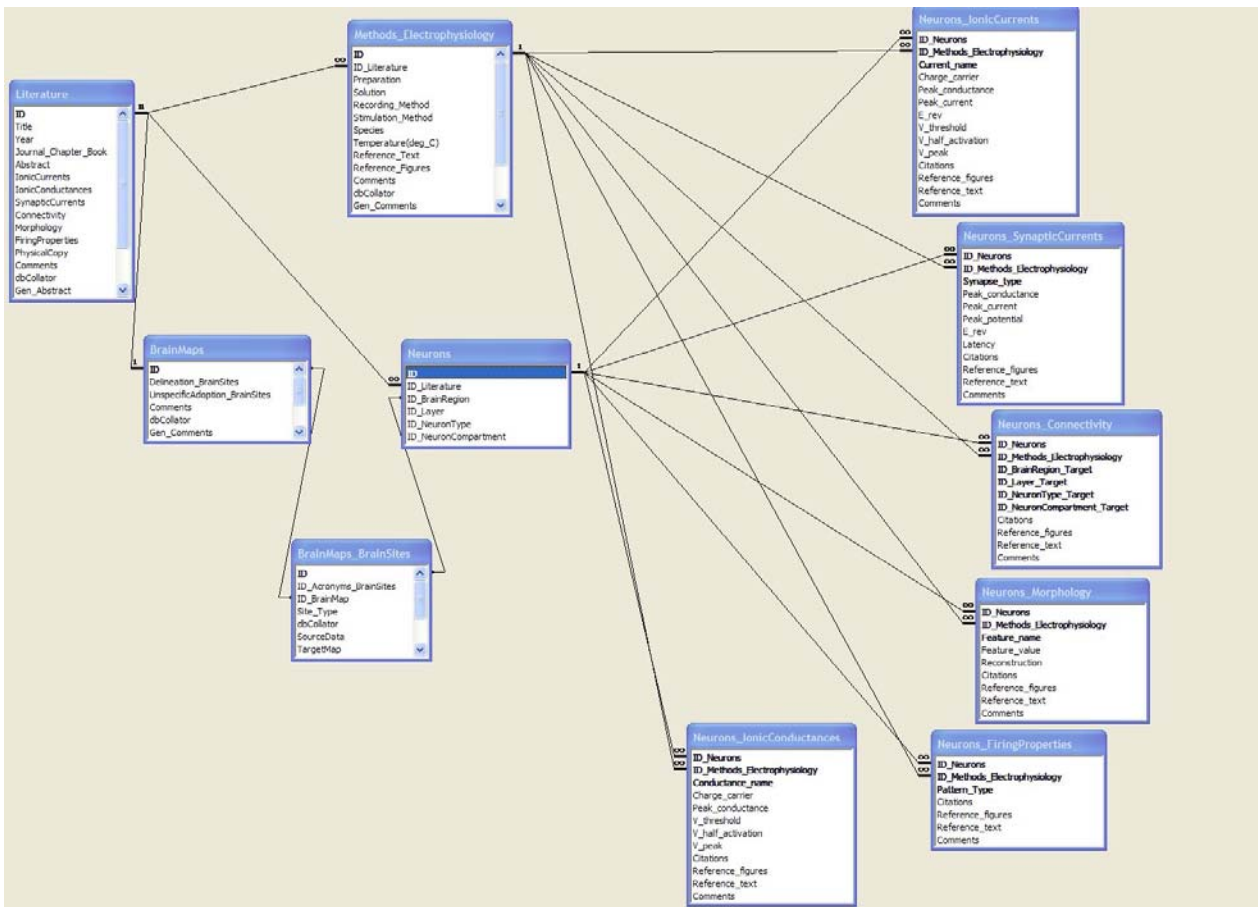


Figure 4.

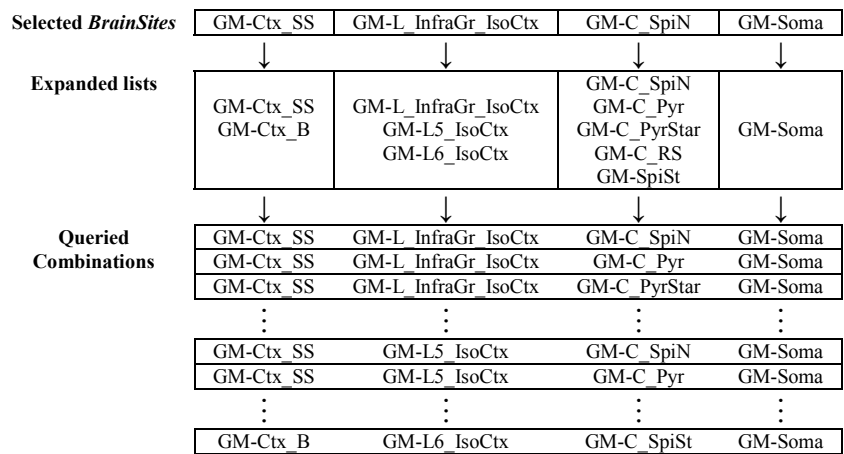


Figure 5.

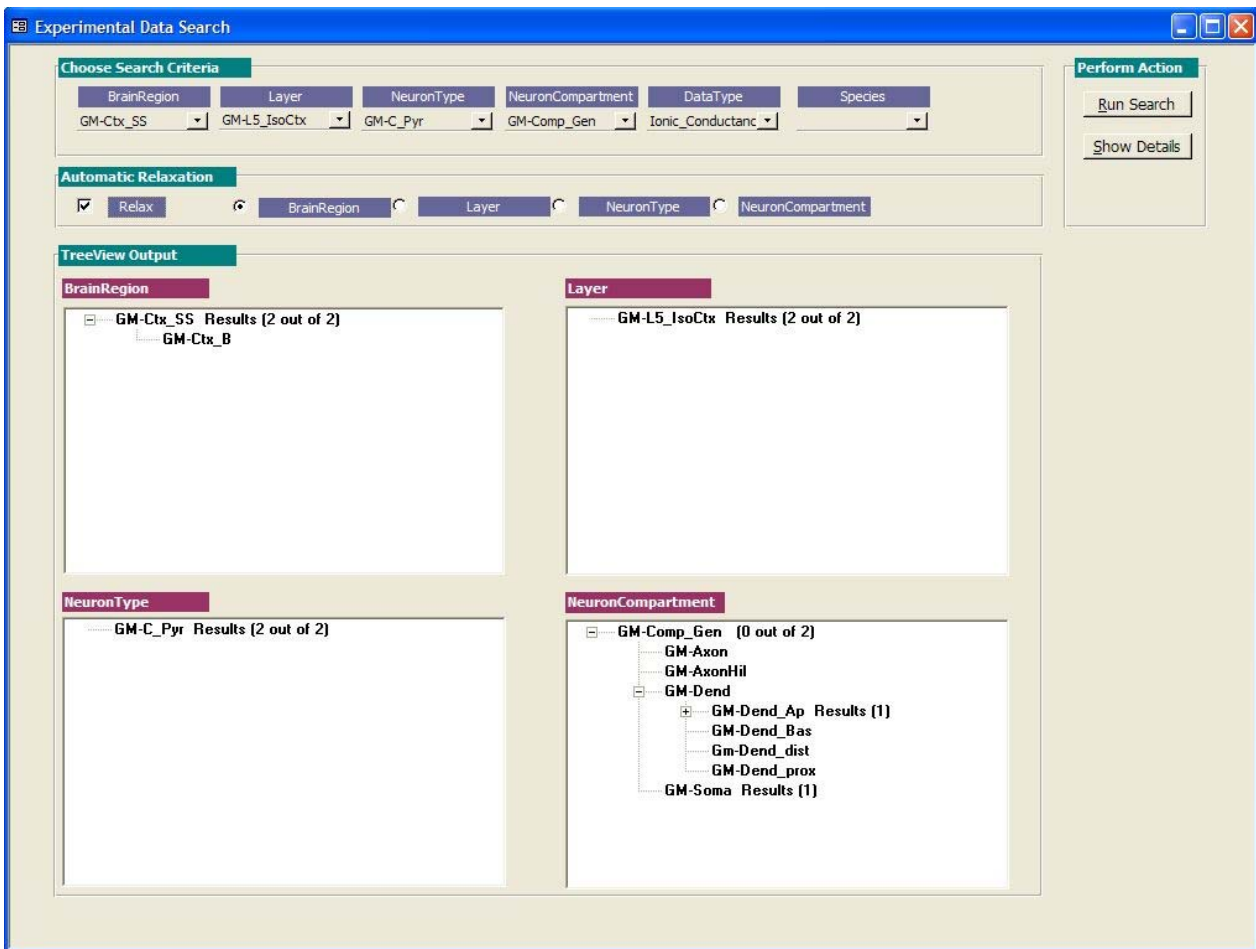


Figure 6.

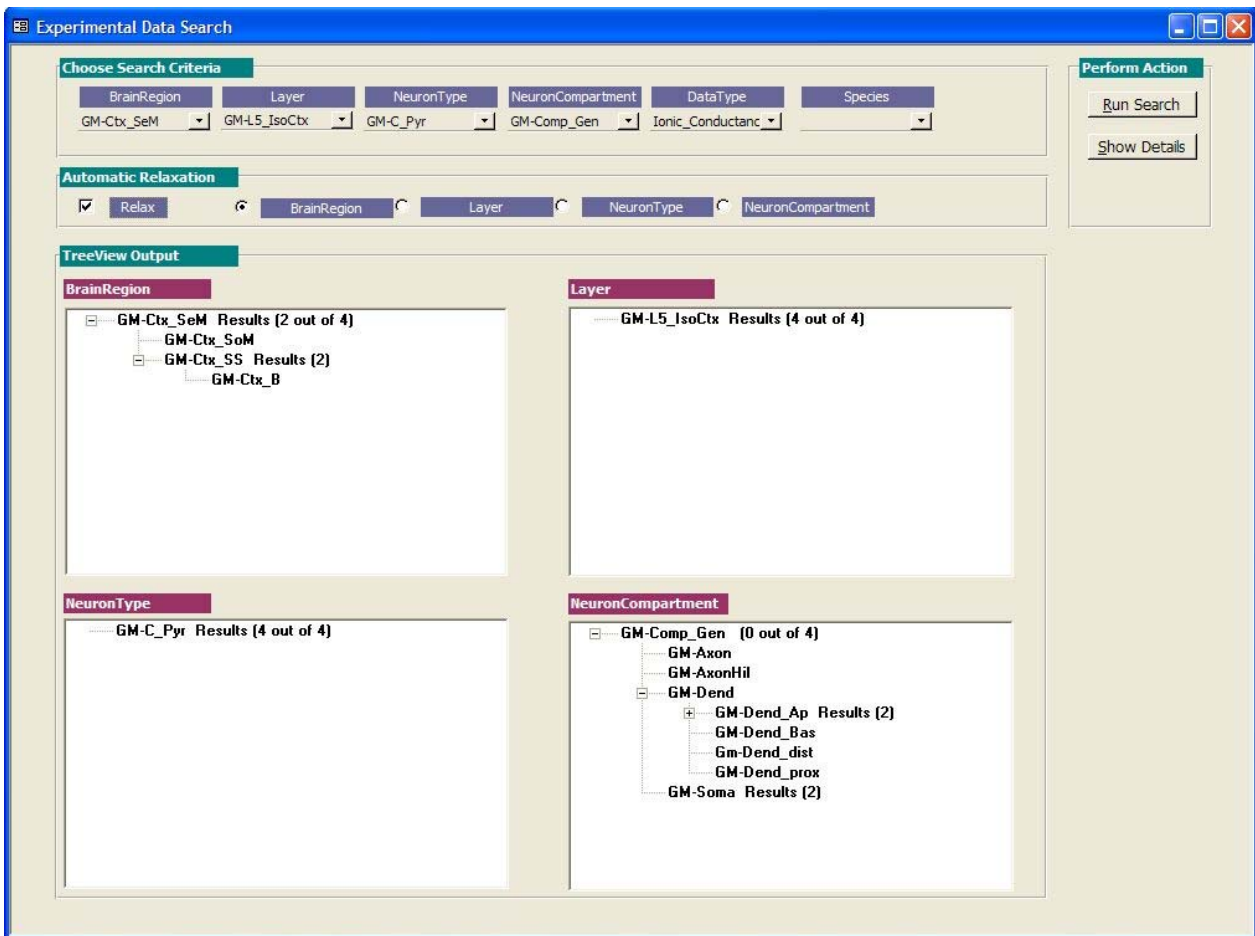


Figure 7.

SearchResults : IonicConductances									
	NeuronID	ID_Literature	ID_BrainRegion	ID_Layer	ID_NeuronType	ID_NeuronCompartment	Conductance_n	Charge_carrier	PrintResult
+	-625879160	B00b	GM-Ctx_SeM	GM-L5_IsoCtx	GM-C_Pyr	GM-Soma	I(A)	K+	<input type="checkbox"/>
+	-625879160	B00b	GM-Ctx_SeM	GM-L5_IsoCtx	GM-C_Pyr	GM-Soma	I(K)	K+	<input type="checkbox"/>
+	1927746281	B00b	GM-Ctx_SeM	GM-L5_IsoCtx	GM-C_Pyr	GM-Dend_Ap	I(A)	K+	<input type="checkbox"/>
+	1006790213	KS00	GM-Ctx_SS	GM-L5_IsoCtx	GM-C_Pyr	GM-Soma	BK	K+	<input type="checkbox"/>
+	1006790213	KS00	GM-Ctx_SS	GM-L5_IsoCtx	GM-C_Pyr	GM-Soma	K(fast inact.)	K+	<input type="checkbox"/>
+	1006790213	KS00	GM-Ctx_SS	GM-L5_IsoCtx	GM-C_Pyr	GM-Soma	K(slow inact.)	K+	<input type="checkbox"/>
+	1006790213	KS00	GM-Ctx_SS	GM-L5_IsoCtx	GM-C_Pyr	GM-Soma	K(very slow inact.)	K+	<input type="checkbox"/>
+	1006932736	KS00	GM-Ctx_SS	GM-L5_IsoCtx	GM-C_Pyr	GM-Dend_Ap	BK	K+	<input type="checkbox"/>
▶	1006932736	KS00	GM-Ctx_SS	GM-L5_IsoCtx	GM-C_Pyr	GM-Dend_Ap	K	K+	<input type="checkbox"/>
*									<input type="checkbox"/>

Literature_ID : Author full names			
ID_Literature	LastName	Initials_FirstName	
▶ KS00	Korngreen	A	
KS00	Sakmann	B	
*			

Record: 1 of 2 (Filtered)

Record: 9 of 9

Figure 8.

The screenshot shows a software interface with a main window titled "SearchResults : IonicConductances" and a pop-up window titled "Neurons : IonicCurrents".

**Main Window: SearchResults : IonicConductances**

NeuronID	ID_BrainRegion	ID_Layer	ID_NeuronType	ID_NeuronCompartment	Conductance_name	Charge_carrier	PrintResult
998919415	GM-Ctx_SeM	GM-L_InfraGr_IsoCt	GM-C_Pyr	GM-Comp_Gen	BK	K+	<input type="checkbox"/>
-625879160	GM-Ctx_SeM	GM-L5_IsoCtx	GM-C_Pyr	GM-Soma	I(A)	K+	<input type="checkbox"/>

**Neuron Details (ID: -625879160):**

- ID\_RecordingSite: -625879160
- ID\_BrainRegion: GM-Ctx\_SeM
- ID\_Layer: GM-L5\_IsoCtx
- ID\_NeuronType: GM-C\_Pyr
- ID\_NeuronCompartment: GM-Soma
- ID\_Methods\_Electrophysiology: 1006622979
- Conductance\_name: I(A)
- Charge\_carrier: K+
- Peak\_conductance: 8.5 + 0.3 pS
- V\_threshold: -
- V\_half\_activation: -24.5 + 3.7 mV
- V\_peak: -
- Citations: "Two distinct types of single-channel were observed in cell-attached and outside-out somatic patches (Figs 2 and 3). One type
- Reference\_figures: Fig. 2
- Reference\_text: pp.613-614
- Comments: More parameters on activation/inactivation and time constants are given.

**Pop-up Window: Neurons : IonicCurrents**

- ID\_RecordingSite: -625879160
- ID\_Methods\_Electrophysiology: 1006622979
- Current\_name: I(A)
- Charge\_carrier: K+
- Peak\_conductance: -
- Peak\_current: -
- E\_rev: about -66 mV
- V\_threshold: -
- V\_half\_activation: -
- V\_peak: -
- Citations: "Two general classes of outward current were seen in cell-attached patches, as in nucleated patches. A fast transient current resembled
- Reference\_figures: Fig. 1
- Reference\_text: pp.612-613
- Comments: -

**Main Window Table (continued):**

-625879160	GM-Ctx_SeM	GM-L5_IsoCtx	GM-C_Pyr	GM-Soma	I(K)	K+	<input type="checkbox"/>
1927746281	GM-Ctx_SeM	GM-L5_IsoCtx	GM-C_Pyr	GM-Dend_Ap	I(A)	K+	<input type="checkbox"/>
-1208544038	GM-Ctx_SS	GM-L_InfraGr_IsoCt	GM-C_Pyr	GM-Comp_Gen	BK	K+	<input type="checkbox"/>
-1208544038	GM-Ctx_SS	GM-L_InfraGr_IsoCt	GM-C_Pyr	GM-Comp_Gen	BK	K+	<input type="checkbox"/>
-1208544038	GM-Ctx_SS	GM-L_InfraGr_IsoCt	GM-C_Pyr	GM-Comp_Gen	BK	K+	<input type="checkbox"/>
-945125805	GM-Ctx_SS	GM-L_InfraGr_IsoCt	GM-C_Pyr	GM-Soma	BK	K+	<input type="checkbox"/>
-2090324328	GM-Ctx_SS	GM-L_InfraGr_IsoCt	GM-C_Pyr	GM-Dend_Ap	BK	K+	<input type="checkbox"/>
1006790213	GM-Ctx_SS	GM-L5_IsoCtx	GM-C_Pyr	GM-Soma	BK	K+	<input type="checkbox"/>
1006790213	GM-Ctx_SS	GM-L5_IsoCtx	GM-C_Pyr	GM-Soma	K(fast inact.)	K+	<input type="checkbox"/>
1006790213	GM-Ctx_SS	GM-L5_IsoCtx	GM-C_Pyr	GM-Soma	K(slow inact.)	K+	<input type="checkbox"/>
1006790213	GM-Ctx_SS	GM-L5_IsoCtx	GM-C_Pyr	GM-Soma	K(very slow inact.)	K+	<input type="checkbox"/>

Figure 9.

<b>NeuronID</b>	-625879160	<b>Conductance_name</b>	I(A)
<b>ID_Literature</b>	B00b	<b>Charge_carrier</b>	K+
<b>ID_Methods_Electrophysiology</b>	1006622979	<b>Peak_conductance</b>	8.5 +/- 0.3 pS
		<b>V_threshold</b>	-
		<b>V_half_activation</b>	-24.5 +/- 3.7 mV
<b>ID_BrainRegion</b>	GM-Ctx_SeM	<b>V_peak</b>	-
<b>ID_Layer</b>	GM-L5_IsoCtx	<b>Reference_text</b>	pp.613-614
<b>ID_NeuronType</b>	GM-C_Pyr	<b>Reference_figures</b>	Fig. 2
<b>ID_NeuronCompartment</b>	GM-Soma		

**Citations**

"Two distinct types of single-channel were observed in cell-attached and outside-out somatic patches (Figs 2 and 3). One type of channel had shorter open times and a mean conductance of 8.5 +/- 0.3 pS (+/- S.E.M., n=3; Fig. 2). Averages of this channel type gave a pure I(A)-like current (Fig. 2A)." p.613

"For convenience, the fast transient and slowly inactivating/non-inactivating currents seen in these patches will henceforth be called I(A) and I(K), respectively." p.614

**Comments**

More parameters on activation/inactivation and time constants are given.

Figure 10.

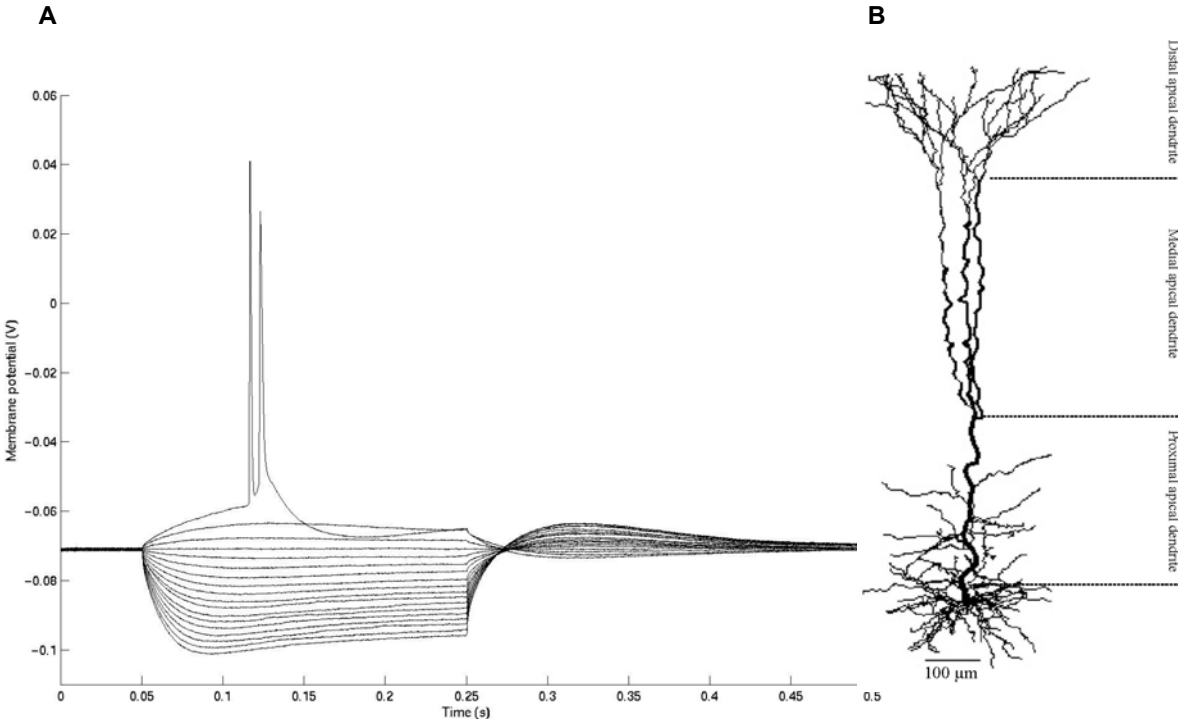


Figure 11.

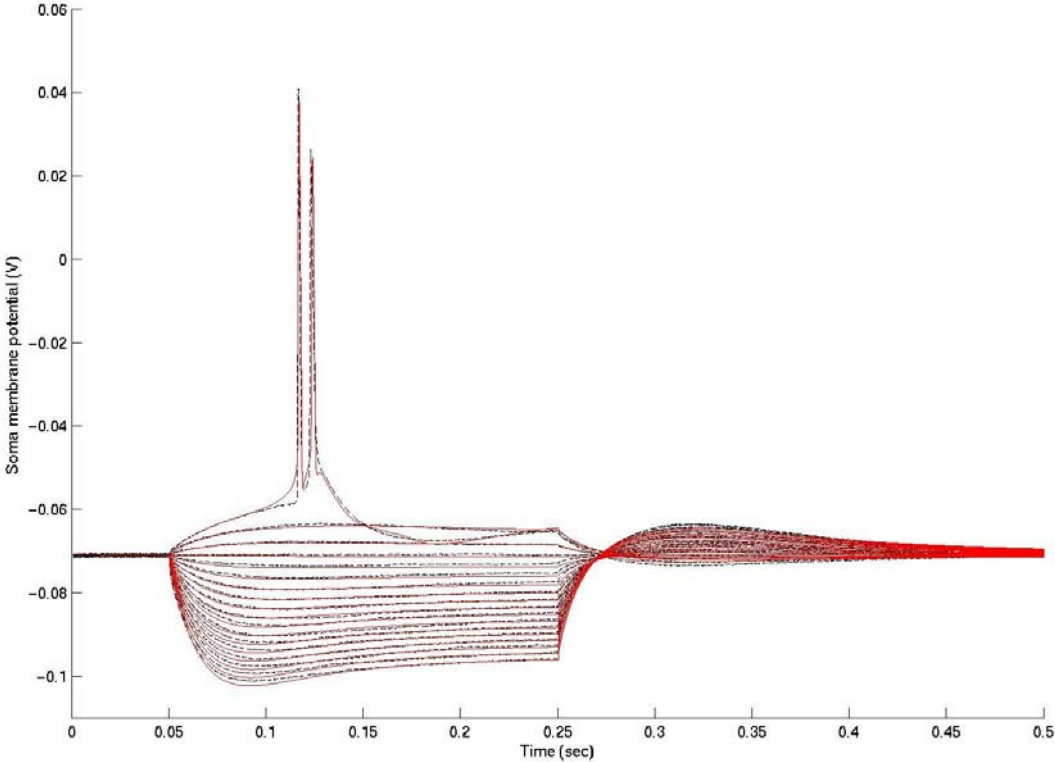


Figure 12.

