A preliminary study of local research fronts: the case of neuro-science

Statement of purpose

The overall objective of this study was to test the applicability of a set of bibliometric techniques aiming at the identification and bibliometric mapping of strength areas of the University of Gothenburg (GU). For this purpose, papers classified as neuro-science and authored by at least one GU-researcher were applied as test bed. The objective in particular was to identify outstanding neuroscience-papers in terms of relative citation frequency, their cognitive context and to map collaboration associated with these papers.

Data and methods

The bibliographic publication database of Gothenburg University (GUP) was applied as the primary data source. Thomson Reuter's Web of Science complemented GUP with citation data. Finally, field-average citation scores based on Web of Science data were compiled and assembled during May 2012 by CWTS, Leiden University. Citations to papers were compiled without self-citations.

Common bibliometric mapping techniques are cluster analysis and multidimensional scaling (MDS) which were applied in this study in order to complement the descriptive data analysis.

With regard to the data collection process, a number of selection requirements were decided on so that papers of concern should:

- have a field-normalized citation frequency[1] four times the average field citation score;
- have a citation window of at least two full calendar years (24 months);
- belong to one of the document types article, review or proceedings paper; and
- be published during the period of 2006-2010.

The set of papers fulfilling these requirements we denote **Set *A***. This set consisted of 21 papers.

In order to create a set of papers suitable for cluster analysis the following steps were taken:

- All papers citing at least one of the papers in set *A* were downloaded from *Web of Science* during April 2012 (updated 2012-04-27). We denote this **Set *B***.
- Papers in **Set *A*** that belonged to the document type article or proceedings papers were added to **Set *B***, constituting a temporary set.
- The temporary set was searched for duplicate papers which were removed; this final set we denote ***C***.

[1] The field-normalized citation frequency for a paper is computed on basis of the field-normalized citation score, that is, the (weighted) citation average based on all (WoS) papers from the corresponding field(s) to which a specific paper is classified.

Set *A* and ***B*** provided information about which papers stand out in terms of citedness during the period of observation, as well as which later papers, and by extension, which universities, countries and fields, that have built their research on these papers by referencing them.

Set *C* was applied for the mapping of weighted citation links between papers and was constituted by papers published during the period of 2006-2012 (April), exclusively belonging to the document types article or proceedings paper. The reason for delimiting document types in this case was that items like book-reviews, editorial materials and letters are seldom cited. Furthermore, review articles, although often highly cited, have a tendency to unduly influence the citation network due to both the tendency of being highly cited as well as carrying long reference lists. This set was also applied for the mapping of cognitive structures (research themes) on basis of key-words.

A particular problem should be accounted for: as we operate with classifications on the journal level (not the document level) papers published in journals of the multidisciplinary type (e.g. Nature) or in journals with a more general scope (e.g. Lancet) may be missed as they are not assigned to neuroscience. Basically, this problem was dealt with by scanning plausible journal titles for neuroscience papers item by item. However, this method is unsatisfactory as a lay-man level of judgment may be insufficient. With regard to similar, future studies it is recommended that a "top down" approach is applied where all papers of interest, regardless of journal classification, are partitioned in one go.

Citation relations and weighted direct citations

Weighted direct citation links between papers was preferred before the more traditional co-citation analysis as more pertinent information is made available. However, conclusions can only be drawn on basis of a quite limited set of papers; namely those papers that are related to each other by direct citations during the publication period of 2006-2012 (April), as opposed to the traditional cocitation analytical method where a large number of cited references in the source papers is used for the generation of clustered co-cited pairs. However, it is traditionally (and for technical reasons) *citing* papers that are applied for the labeling of cocitation-clusters on basis of title-words or key-words, which means that an *indirect* and less reliable method for the labeling of clusters is applied when using the cocitation-cluster method.

A reference to a paper from another paper constitutes a direct citation link. In the current context, we consider a direct citation an indication of subject-similarity. Next, the simultaneous occurrence of two references in the bibliography of a third paper constitutes a co-citation of the two referenced papers. We consider this an indication of subject-similarity between the co-cited papers. Comparing the list of cited references (bibliographies) in two papers by computing the intersection of common references constitutes a third measure of similarity – bibliographic coupling. In this study, all three citation relations have been combined in a single measure – weighted direct citations (WDC).

The principle of WDC is that the direct citation of a paper may be strengthened by the two other citation associations (Persson, 2010). In the figure below, a graph depicting citation relations between five papers (A-E) over time (*t*), illustrates the summing up of citation relations between pairs of papers, assigning equal weight (one score) to all three types of relations. For example, the pair B-D is assigned one score for the direct citation link (B→D), one score for the common referencing of E and finally, one score for being co-cited by A. Thus, this pair is assumed to be the most similar pair of all in the graph. As illustrated by the graph, papers separated by longer distance in time, are less likely to share common references or being co-cited or cited.

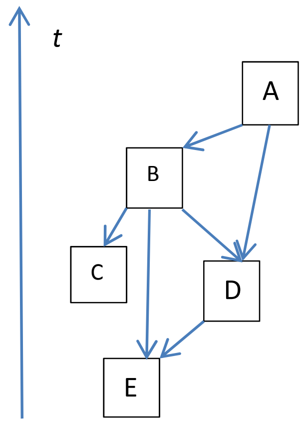

Figure 1. Graph illustrating a hypothetical citation network.

Results

The presentation of results starts with the set of identified high-impact papers, **Set *A***. Next, collaboration patterns on both the institutional and the author-level are elaborated. A cluster analytical approach is presented next with the aim of mapping the cognitive context of papers in **Set *A***. Finnally, a mapping based on key-words from papers in **Set *C*** was performed.

Papers with an outstanding citation record

In total 21 papers meeting set criteria and classified as neuroscience[2] were identified (Table 1). A total of four papers were review articles, one was a proceeding paper and the remaining papers were all genuine research articles. As can be concluded from Table 1, there was great variation with regard to the *field-normalized citation frequency*, which was computed as the ratio between the *observed citations* and the *expected citations* (the field-average citation scores) for one or more fields to which a paper is assigned. When computing the relative citation frequency, one also takes into account the variation of the citation interval, that is, the period where a paper has been available.

As can be concluded from Table 2, there was also great variation with regard to the journal impact factors (JIF)[3] of the journals in which these papers were published. Rank ordering the papers according to corresponding JIF, we can see that there is a cut-off point at the 5th rank position, above which high impact journals classified as *Multidisciplinary Sciences* or *General & Internal Medicine* hold the top positions (rank 1-3), followed by *Nature Reviews Neuroscience*. We can appreciate that several more specialized journals are included in the list and that 11 journals out of 21 occur only once.

All papers but one were authored by at least one researcher affiliated with *Institute of Neuroscience and Physiology* at University of Gothenburg. Two papers were co-authored with researchers from *Institute of Biomedicine* and three papers with researchers from *Institute of Clinical Sciences*. We also count two instances where an author was affiliated with two institutions at GU.

Finally, In Table 3 we list all authors and mark those affiliated with GU as well as first author positions. We note that in nine out of 21 papers, the first author position is taken by an author from University of Gothenburg.

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[2] Or otherwise identified as neuroscience papers, see the method section.
[3] The JIF is computed as the average citation of papers published year t or t+1 during year t+2 in a journal *A*.

Table 1. Source-papers meeting selection criteria (Set *A*): Relative citation frequency computed as the ratio between observed citations (minus self-citations on author level) and the average field citation (considering publication date, field-affiliations and document type). Citation data: CWTS, Leiden University; data source: Thomson Scientific/ISI.

First author	Abbreviated title	Relative citation frequency	Citation interval (months)
Shaw	Cerebrospinal Fluid Biomarker Signature …	24	37
Blennow	Alzheimer's disease…	18	69
Mattsson	CSF biomarkers and incipient Alzheimer d…	17	34
Abbott	Astrocyte-endothelial interactions at th…	13	76
Faux	PBT2 Rapidly Improves Cognition in Alzhe…	8	27
Klyubin	Amyloid beta protein dimer-containing hu…	8	49
Li	Protective role of reactive astrocytes i…	8	50
Bergman	PITX3 polymorphism is associated with ea…	7	28
Curtis	Human neuroblasts migrate to the olfacto…	7	62
Draganski	Temporal and spatial dynamics of brain s…	7	71
Hansson	Evaluation of plasma A beta(40) and A be…	7	26
Lindgren	l-DOPA-induced dopamine efflux in the st…	7	26
Lucassen	Regulation of adult neurogenesis by stre…	7	28
Brys	Prediction and longitudinal study of CSF…	6	36
Melke	Abnormal melatonin synthesis in autism s…	6	52
Eriksson	Consensus guidelines for the management …	5	42
Loken	Coding of pleasant touch by unmyelinated…	5	36
Ohrfelt	Cerebrospinal fluid alpha-synuclein in n…	5	39
Galluzzi	Mitochondrial membrane permeabilization …	4	34
Svedin	Matrix metalloproteinase-9 gene knock-ou…	4	63
Zhu	Different apoptotic mechanisms are activ…	4	75

Table 2. Journal (two year) impact factors from *Journal Citation Report* 2010 for journals in which papers in Set *A* were published.

First author	Journal name	JIF
Blennow	Lancet	33,6
Curtis	Science	31,4
Mattsson	Jama-Journal of the American Medical Association	30,0
Abbott	Nature Reviews Neuroscience	29,5
Galluzzi	Nature Reviews Neuroscience	29,5
Melke	Molecular Psychiatry	15,5
Loken	Nature Neuroscience	14,2
Shaw	Annals of Neurology	10,7
Draganski	Journal of Neuroscience	7,3
Svedin	Journal of Neuroscience	7,3
Klyubin	Journal of Neuroscience	7,3
Brys	Neurobiology of Aging	6,6
Bergman	Neurobiology of Aging	6,6
Hansson	Neurobiology of Aging	6,6
Li	Journal of Cerebral Blood Flow And Metabolism	4,5
Zhu	Journal of Neurochemistry	4,3
Lindgren	Journal of Neurochemistry	4,3
Faux	Journal of Alzheimers Disease	4,3
Lucassen	European Neuropsychopharmacology	4,2
Eriksson	Neuroendocrinology	3,3
Ohrfelt	Neuroscience Letters	2,1

Table 3. First and co-authors of 21 papers: First authors in bold and authors affiliated with University of Gothenburg underlined.

Authors
Abbott, Hansson, Rönnbäck
Zhu, Blomgren, Hagberg, Shibata, Uchiyama, Wang, Xu
Draganski, Buchel, Gaser, Kempermann, May, Kuhn, Winkler
Blennow, de Leon, Zetterberg
Svedin, Hagberg, Mallard, Sävman, Zhu
Curtis, Anderson, Axell, Björk-Eriksson, Dragunow, Eriksson, Faull, Frisen, Holtås, Kam, Nannmark, Nordborg, van Roon-Mom, Wikkelsö
Eriksson, Ahlman, Arnold, Auernhammer, Kloppel, Korner, Krenning, Plockinger, Rindi, Wiedenmann, Wildi
Melke, Anckarsäter, Betancur, Botros, Bourgeron, Chabane, Chaste, Chevalier, Collet, Delorme, Drouot, Durand, Fauchereau, Gillberg, Gillberg, Launay, Leboyer, Mouren-Simeoni, Nygren, Råstam, Ståhlberg
Li, Andersson, Aprico, Blomstrand, Carmeliet, Davies, Fotheringham, Kubista, Larsson, Lundkvist, Maragakis, Moons, Nagai, Nilsson, Nodin, Pardo, Pekna, Pekny, Schwartz, Stahlberg, Wilhelmsson, Yabe
Klyubin, Anwyl, Betts, Blennow, Cullen, Lemere, Peng, Rowan, Selkoe, Wallin, Walsh, Welzel, Wisniewski, Zetterberg
Öhrfelt, Andreasen, Blennow, Grognet, Wallin, Vanmechelen, Zetterberg
Brys, Blennow, de Leon, De Santi, Glodzik-Sobanska, Mehta, Mosconi, Pirraglia, Pratico, Rich, Rolstad, Saint Louis, Switalski, Wallin, Zinkowski
Löken, McGlone, Morrison, Olausson, Wessberg
Shaw, Aisen, Blennow, Clark, Dean, Knapik-Czajka, Lee, Lewczuk, Petersen, Potter, Siemers, Simon, Soares, Trojanowski, Vanderstichele
Galluzzi, Blomgren, Kroemer
Mattsson, Andreasen, Blankenstein, Blennow, de Leon, Ewers, Hampel, Hansson, Herukka, Jonhagen, Jonsson, Kaiser, Marcusson, Minthon, Mulugeta, Parnetti, Pirttila, Rich, Rosen, Scheltens, Schroder, Tsolaki, Wallin, van der Flier, Verbeek, Winblad, Visser, Zetterberg
Bergman, Belin, Eriksson, Håkansson, Holmberg, Nissbrandt, Nordenstrom, Olson, Sydow, Westberg
Lucassen, Czeh, Dayer, Fuchs, Meerlo, Naylor, Oomen, van Dam
Lindgren, Andersson, Cenci, Lagerkvist, Nissbrandt
Hansson, Andreasson, Blennow, Londos, Minthon, Wallin, Vanderstichele, Vanmechelen, Zetterberg
Faux, Bedo, Blennow, Bush, Cummings, Gunn, Harrison, Herd, Ingelsson, Lannfelt, Masters, Rembach, Ritchie, Tanzi, Tsatsanis, Zetterberg

Collaboration

Collaboration on the institutional level

On the institutional level, a total of 82 unique institutions contributed with at least one author to papers in **Set *A***, GU excluded. Of these, 69 institutions occurred in only one paper and only four institutions occurred more than twice (Sahlgrenska University Hospital, Lund University, NYU and Karolinska Institution). The mean number of institutions for a paper was six. Summing up, the distribution of collaborating institutions is quite even and nothing really stands out. A way of comprehending the collaborative patterns of these papers is to assign them to different collaboration types. We may for instance partition all papers in two groups; papers produced in collaboration with Anglo-Saxon countries (Australia, UK, USA, New Zealand, Ireland) and papers *not* produced in collaboration with Anglo-Saxon countries. The ratio of Anglo-Saxon papers to non Anglo-Saxon papers was 4:3. A more informative grouping of papers may be accomplished using four different labels where *local* indicates papers exclusively produced by GU, *nation* papers with a Swedish address (other than GU) , *Europe*, papers with a European address and *Global*, papers with an address outside Europe. Combining these labels eight mutually exclusive groups are generated (Table 4). We conclude that most papers are produced in collaboration with institutions outside Sweden, that no paper was produced entirely by GU and that more than half of the papers are co-authored with a European institution.

Table 4. The distribution of collaboration types.

Collaboration-type	Frequency
Local+Europe	4
Local+Europe+Global	4
Local+Global	4
Local+Nation	3
Local+Nation+Europe	3
Local+Nation+Europe+Global	2
Local+Nation+Global	1
Local	0
Total	**21**

Collaboration on the author-level

We may apply specific measures in order to comprehend the underlying co-author network. For this end we use graph-theoretical concepts and terms and consider the underlying network of collaborative relations an undirected graph *G*. In such a graph we consider authors *nodes* or *vertices* and the association between two authors based on co-authorships *arcs* or *edges*.

The first measure captures the density of the graph, that is, the general level of connectedness of the graph. The density *D* is defined as:

$$D = \frac{2\ (\#L(G)}{N(N-1)}$$

where

N = number of nodes

#*L*(*G*) = number of arcs in a graph *G*.

(Otte & Rousseau, 2002).

In this case *D* for the total graph with 202 nodes (authors) was 0,08. This means that 92 % percent of all possible arcs (based on co-authorships) in the network is missing. Indeed, this is a sparse network. However, there are methods to generate more dense and informative networks (graphs), which lead us to the next measure. This measure captures the number of co-authors in the graph for a certain author and is called *degree centrality*. Specifically, degree centrality of a node *j* measures the number of edges adjacent to *j*:

$$d(i) = \sum_j m_{ij}$$

where m_{ij}= 1 if there is a link between nodes *i* and *j* and m_{ij}= 0 when there is no link.

Degree centrality for a node in an N-node network can be standardized as :

$$d_s(i) = d(i)/(N-1)$$

(Otte & Rousseau, 2002)

Applying the standardized degree centrality, we can identify the more central authors in the network constituted by the 21 outstanding papers. Applying a threshold where $d_s \geq 0{,}14$, a total of 29 out of 202 authors form a collaboration network where identified (Table 5). This filtering out of less central authors lead to an increase of the density of the network so that *D* = 1,00. This means that we have a *complete graph* where every node is connected to every other node. In Figure 1, a graph based on the selected 29 authors and their co-authorship relations is depicted using MDS. In the graph, the distance between nodes is inversely related to the frequency of co-authorship between authors. For instance, the distance between Wallin A and Kaiser E is longer than the distance between Wallin A and Blennow K due to more co-authored papers for the latter author pair. Hence, the two agglomerations in the upper respective lower part of the graph are due to variations of the co-author frequency. Note that there is no analytical value in left-right or up-down, the only analytical use relates to the grouping of related nodes and the relative distances between them. Hence, the usefulness of this type of collaboration- graph is to *explore* relations in the underlying network and various algorithms and thresholds may be used.

Table 5. Standardized degree centrality for the most central authors in the network of 21 outstanding papers.

Author	d_s
Blennow K	0,42
Zetterberg H	0,30
Wallin A	0,28
Rich K	0,20
Hansson O	0,16
Minthon L	0,16
Andreasen N	0,15
Aarsland D	0,14
Blankenstein MA	0,14
de Leon M	0,14
Ewers M	0,14
Hampel H	0,14
Herukka SK	0,14
Jonhagen ME	0,14
Jonsson M	0,14
Kaiser E	0,14
Marcusson J	0,14
Mattsson N	0,14
Mulugeta E	0,14
Parnetti L	0,14
Pirttila T	0,14
Rosen E	0,14
Scheltens P	0,14
Schroder J	0,14
Tsolaki M	0,14
van der Flier WM	0,14
Verbeek M	0,14
Winblad B	0,14
Visser PJ	0,14

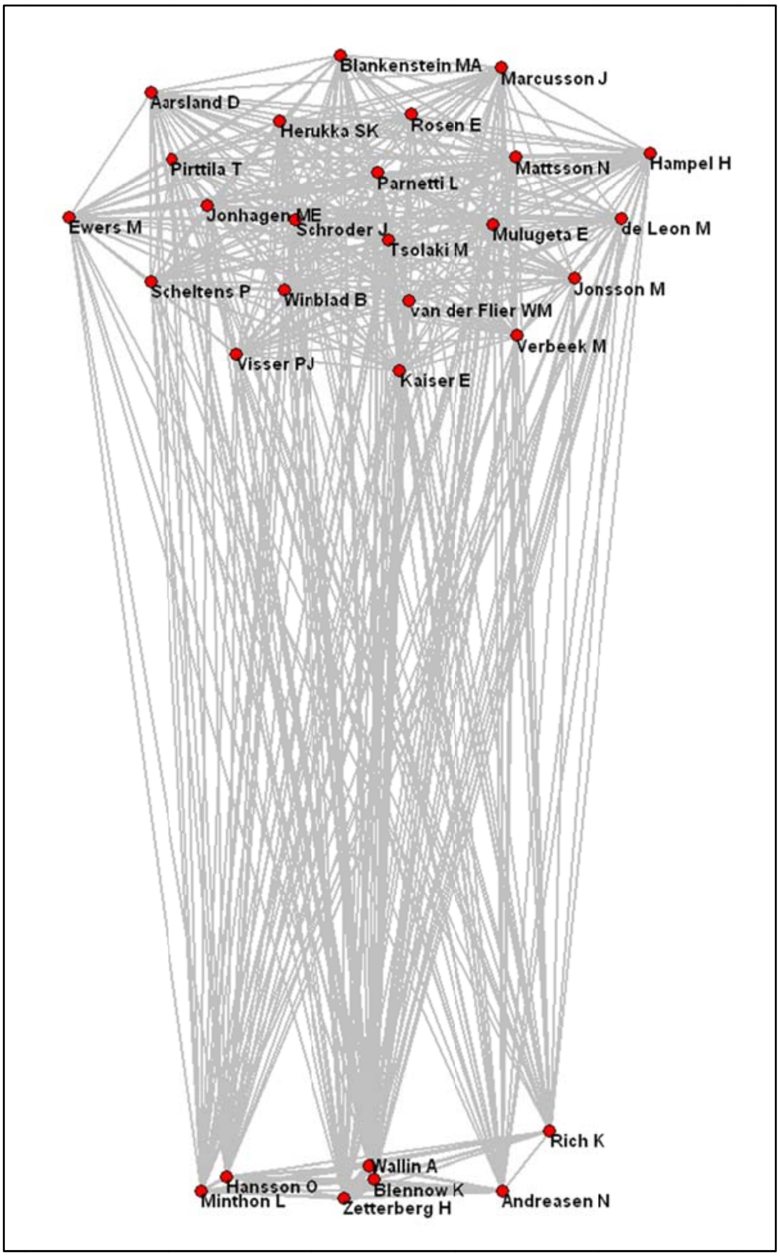

Figure 2. Co-author network based on 29 authors with the highest degree centrality mirrored by MDS. Kruskal's stress I = 0 %.

Mapping the cognitive context of outstanding papers

A variety of multivariate statistical methods combined with different measures were tested for the mapping of the cognitive context of papers in **Set *A*** . The basic problem was to find a measure of similarity (proximity) for the entities under investigation, here papers, and a method for the grouping of the same. As accounted for in the method section, various citation relations may be used or combinations thereof.

One may apply practical (technical) aspects when deciding on methods as time or economy required may influence the choices. Also, the ability to repeat methods consistently (aspect of reliability) needs to be considered. In this case we chose a simple cluster algorithm implemented in the preferred bibliometric software (Bibexcel). For sure, there exist more complex algorithms that may (from one or another aspect) perform better, however, we believe that given an existing structure in data, also more simplistic methods may suffice.

A cluster analytical approach

A total of 1980 direct citation links between papers in **Set *C*** (article or proceedings-papers) were converted to WDC-links connecting a total of 1009 papers. In order to create a more manageable, but still intelligible citation network, a threshold of 2 WDC-scores was set. This reduced the network to 254 papers connected by 377 links. Applying the cluster routine of the preferred bibliometric software (Bibexcel version 2012-05-03), a total of 19 clusters was created with sizes ranging from 4 to 52 cluster members. In this way, we expanded the cognitive context of 19 (out of 21) selected source papers by 231 additional papers. An overview of the resulting cluster structure is given next, in addition, clusters are represented by search-keys, title, journal name, publication year and times cited (up to 2012, April) in the Annex. The following variables were used to describe the generated clusters:

- **labels** identifying the major research theme of a cluster as may be concluded on basis of titles and key-words on a lay-man level.
- **titles**
- **size** (number of papers)
- **the average publication year**
- **source papers** included as cluster members
    - Such papers are presented by the following variables: search-key, title, journal name and publication year.

Cluster 1. Alzheimer's Disease and biomarkers

This cluster is about Alzheimer's Disease and biomarkers.

The cluster contains 52 papers and the average publication year is 2010.

A total of three papers also belong to the set of source papers in *A*:

- Shaw, 2009, V65, P403; Cerebrospinal Fluid Biomarker Signature in Alzheimer's Disease Neuroimaging Initiative Subjects, *Annals of Neurology;*
- Mattsson, 2009, V302, P385; CSF Biomarkers and Incipient Alzheimer Disease in Patients With Mild Cognitive Impairment, *Jama-Journal of The American Medical Association;*
- Brys, 2009, V30, P682; Prediction and longitudinal study of CSF biomarkers in mild cognitive impairment, *Neurobiology of Aging.*

Cluster 2. Brain structure and cognition

This cluster concerns the relation between the morphology of the brain and mental processes (in a general sense). It focuses on cognitive aspects like mediation and learning (memory) but also deals with processes like aging and illnesses.

The cluster contains 24 papers and the average publication year is 2009.

One of its papers belongs to set *A*:

Draganski, 2006, V26, P6314;Temporal and spatial dynamics of brain structure changes during extensive learning, *Journal of Neuroscience*.

Cluster 3. Apoptotic mechanisms and gender

This cluster focuses on gender differences with regard to brain-hypoxemia. It also comprises aspects on neonatal-hypoxia .

The cluster contains 15 papers and the average publication year is 2008.

One paper also belongs to set A:

Zhu, 2006, V96, P1016; Different apoptotic mechanisms are activated in male and female brains after neonatal hypoxia-ischaemia, *Journal of Neurochemistry.*

Cluster 4. Neurogenesis and the olfactory bulb

This cluster concern neurogenesis in general, and in particular with regard to the olfactory bulb.

The cluster contains 33 papers and the average publication year is 2009. One paper also belongs to set *A*:

Curtis, 2007, V315, P1243; Human neuroblasts migrate to the olfactory bulb via a lateral ventricular extension, *Science*.

Cluster 5. Amyloid-beta and Alzheimer

This cluster concerns the role of amyloid-beta proteins as neurotoxicants with a specific focus on Alzheimer's disease. Non-disease activities of these proteins are also covered.

The cluster contains 28 papers and the average publication year is 2010. One paper also belongs to set *A*:

Klyubin, 2008, V28, P4231; Amyloid beta protein dimer-containing human CSF disrupts synaptic plasticity: Prevention by systemic passive immunization, *Journal of Neuroscience*.

Cluster 6. Alzheimer's diagnostics

This cluster also deals with Alzheimer's disease but with a slant to diagnostics.

The cluster contains 13 papers and the average publication year is 2011. No paper from set *A* is a member of this cluster.

Cluster 7. Clinical trials and Alzheimer-therapy

This cluster deals with Alzheimer-therapy and clinical testing.

The cluster contains 5 papers and the average publication year is 2010. One paper from set *A* is a member of this cluster:

Faux, 2010, V20, P509; PBT2 Rapidly Improves Cognition in Alzheimer's Disease: Additional Phase II Analyses RID C-4423-2011 RID A-1186-2007, *Journal of Alzheimers Disease*.

Cluster 8. Biomarkers for Parkinson Disease

This cluster specifically focuses on alpha-synuclein and dementia; in particular with regard to Parkinson's disease.

The cluster contains 11 papers and the average publication year is 2010. One paper from set *A* is a member of this cluster:

Ohrfelt, 2009, V450, P332; Cerebrospinal fluid alpha-synuclein in neurodegenerative disorders-A marker of synapse loss? *Neuroscience Letters*.

Cluster 9. PITX3 and Parkinson's disease

This cluster specifically deals with the association of polymorphisms in the PITX3 gene with Parkinson's disease.

The cluster contains 10 papers and the average publication year is 2011. One paper from set *A* is a member of this cluster:

Bergman, 2010, V31, P114; PITX3 polymorphism is associated with early onset Parkinson's disease, *Neurobiology of Aging*.

Cluster 10. Neuroendocrine tumors

This cluster is about the diagnosis and treatment of neuroendocrine tumors. The deviating subject-content of this cluster is for all due to the assignment of the journal *Neuroendocrinology* to the field of Neurosciences & Neurology and to the fact that Thomson Reuters includes research covering the neuro-endocrine and neuro-immune systems in the journal subject field *Neurosciences*.

The cluster contains 10 papers and the average publication year is 2010. One paper from set *A* is a member of this cluster:

Eriksson, 2008, V87, P8; Consensus guidelines for the management of patients with digestive neuroendocrine tumors - Well-differentiated jejunal-ileal tumor/carcinoma, *Neuroendocrinology*.

Cluster 11. The physiology of touch.

This cluster specifically addresses the physiology of sensory receptors; in particular the processes associated with "pleasant touch".

The cluster contains 7 papers and the average publication year is 2010. One paper from set *A* is a member of this cluster:

Loken, 2009, V12, P547; Coding of pleasant touch by unmyelinated afferents in humans, *Nature Neuroscience*.

Cluster 12. Levodopa and dyskinesia

The effects of L-dopa administration are modeled in rat-models, hence, this cluster is associated with Parkinson's disease.

The cluster contains 5 papers and the average publication year is 2010. One paper from set *A* is a member of this cluster:

Lindgren, 2010, V112, P1465; l-DOPA-induced dopamine efflux in the striatum and the substantial nigra in a rat model of Parkinson's disease: temporal and quantitative relationship to the expression of dyskinesia, *Journal of Neurochemistry*.

Cluster 13. Plasma-A-beta and diagnosis of Alzheimer's

Amyloid-beta peptides in plasma are evaluated in the context of prediction and diagnosis of Alzheimer's disease. Hence, this cluster is related to cluster 5, where these proteins are studied as neurotoxicants .

The cluster contains 4 papers and the average publication year is 2011. One paper from set *A* is a member of this cluster:

Hansson, 2010, V31, P357; Evaluation of plasma A beta(40) and A beta(42) as predictors of conversion to Alzheimer's disease in patients with mild cognitive impairment, *Neurobiology of Aging*.

Cluster 14. Neuro imaging and the olfactory bulb

This cluster specifically treats the pathology and imaging of the olfactory bulb.

The cluster contains 5 papers and the average publication year is 2010. No paper from set *A* is a member of this cluster.

Cluster 15. Astrocytes and ischemia

This cluster deals with astrocytes in the context of brain-ischemia and spinal cord injury.

The cluster contains 5 papers and the average publication year is 2008. One paper from set *A* is a member of this cluster:

Li, 2008, V28, P468; Protective role of reactive astrocytes in brain ischemia, *Journal of Cerebral Blood Flow and Metabolism.*

Cluster 16. Plasma Amyloid-beta as a biomarker

Again, we see a cluster focusing on amyloid-beta as a biomarker in the context of Alzheimer's disease (cf. Cluster 13).

The cluster contains 4 papers and the average publication year is 2011. No paper from set *A* is a member of this cluster.

Cluster 17. Melatonin and children with Autism

This cluster specifically focuses on autistic children's' sleep behaviors.

The cluster contains 5 papers and the average publication year is 2009. One paper from set *A* is a member of this cluster:

Melke, 2008, V13, P90; Abnormal melatonin synthesis in autism spectrum disorders, *Molecular Psychiatry*.

Cluster 18. Cortical changes and training

This cluster focuses on changes of gray matter due to training.

The cluster contains 5 papers and the average publication year is 2011. No paper from set *A* is a member of this cluster.

Cluster 19. MMPs and brain pathology

This cluster concerns the contribution of Matrix metalloproteinase (MMP)-9 to brain disease.

The cluster contains 9 papers and the average publication year is 2009. One paper from set *A* is a member of this cluster:

Svedin, 2007, V27, P1511; Matrix metalloproteinase-9 gene knock-out protects the immature brain after cerebral hypoxia-ischemia, *Journal of Neuroscience*.

Overview

A total of 19 clusters were generated. Though there is mostly *some* topic drift in clusters, on the whole, clusters seemed subject consistent. However, some clusters appeared to represent similar topics. For this reason, the clustering was iterated, joining some of the clusters by the strongest link between papers in clusters (Figure 1). As can bee seen, we arrive at three larger clusters of clusters, while remaining clusters (not depicted) are singleton clusters, i.e. they do not join with any other cluster. Beginning with the largest cluster consisting of 5 sub-clusters (c1, c5, c6, c,13, c16), a total of 101 papers represent various aspects of research on Alzheimer's disease. Research on bio-markers is a common theme for the whole aggregate and any decisive differences between the Alzheimers' clusters with regard to subject content should be decided on a field-expert's level. Suffice it to say, research on Alzheimer's is a major theme. Moving to the left-lower quadrant of the map, cluster c2 joins with cluster c 18, both cognitively related with brain structure and (mental) training/activity. This structure involves a total of 29 papers. The fusion of the two remaining clusters (c4 and c14) in the right-lower quadrant of the map represents various researches involving the olfactory bulb and comprises a total of 38 papers.

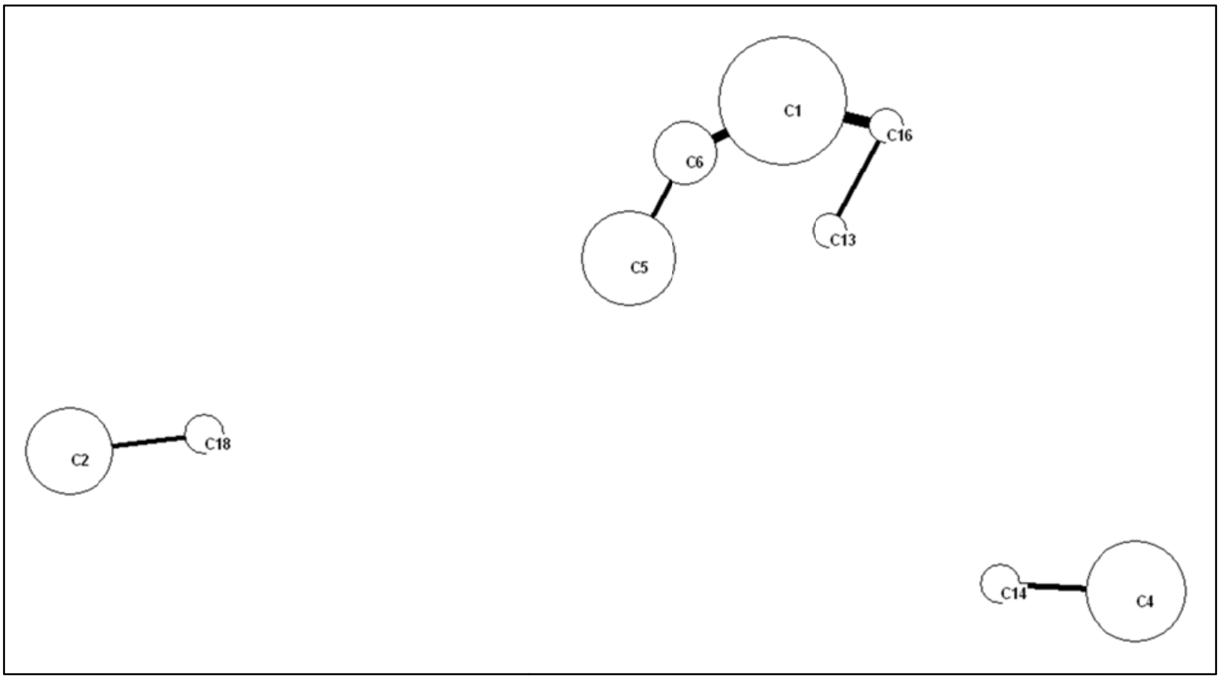

Figure 3. Repeated clustering where 9 clusters are connected through 6 links. Sizes of circles representing clusters are proportional to the number of cluster members of a cluster, and the width of connecting links to the WDC between papers connecting clusters.

On the single-cluster level, the distribution of publication years is not varying much and the modal as well as the mean "average publication year" for a cluster is 2010. Deviations are, however, interesting and the oldest clusters are c3 (apoptotic mechanisms) and c15 (astrocytes and ischemia), both having an average publication year of 2008.

Notably, some of the clusters (c6, c14, c16, c18) lack source papers (Set *A*). However, in all instances these clusters join with other clusters when the clustering process is iterated. Hence, they do not represent isolated research themes.

A term-analytical approach

A complementary method for the mapping of cognitive contexts applies words (terms) in papers rather than references. This method is called co-word analysis (Callon et. al, 1983) and basically the number of co-occurrence of key-words (title words, abstract terms or descriptors of any kind) in papers decides the similarity or distance between important concepts. Commonly some kind of normalization with regard to the term frequency is applied, in this case the *Jaccard measure* (*J*), where the similarity between two terms *i* and *j* is defined as:

$J_{ij} = c_{ij}/(c_i+c_j-c_{ij})$

where

c_i = the frequency for *i*

c_j = the frequency for *j*

c_{ij} = the co-occurrence frequency of *i* and *j*

The Interval is [0,1] and if $i=j=c_{ij}$ max is obtained.

Selecting the 75 most frequent descriptors (Key-word plus in WoS[4]) of the papers in **Set *C*** (N = 1011), corresponding to the 98th percentile, the ambition was to provide with a snap-shot of the core of the cognitive content from the perspective of term use and concepts. Admittedly, this technique only captures a fraction of all research themes but has the advantage of highlighting topical research themes. The MDS-map in Figure 4 pictures densities of key-words, indicating important themes. Most central in the map is the concept of Alzheimer's-disease connecting with more than 60 other nodes (key-words). As can be seen this term is closely associated with terms like *Dementia, Mild Cognitive Impairment, Cerebrospinal-Fluid and In-Vivo*. In the left-lower part of the map less central, but highly frequent and closely associated, terms related with the *hippocampal formation* are seen (e.g. *olfactory bulb*). Several other research themes are recognizable (e.g. *astrocytes* and *spinal cord injury*) but further interpretation should be the task of the field-expert. It should be pointed out that specific concepts could be mapped more in detail by selecting a concept (term) of interest and then zooming in on associated terms of lower frequency. Conclusively, the usability of this type of map should be tried out in collaboration with the field-expert.

[4] KeyWords Plus are words or phrases that frequently appear in the titles of WoS-articles' references.

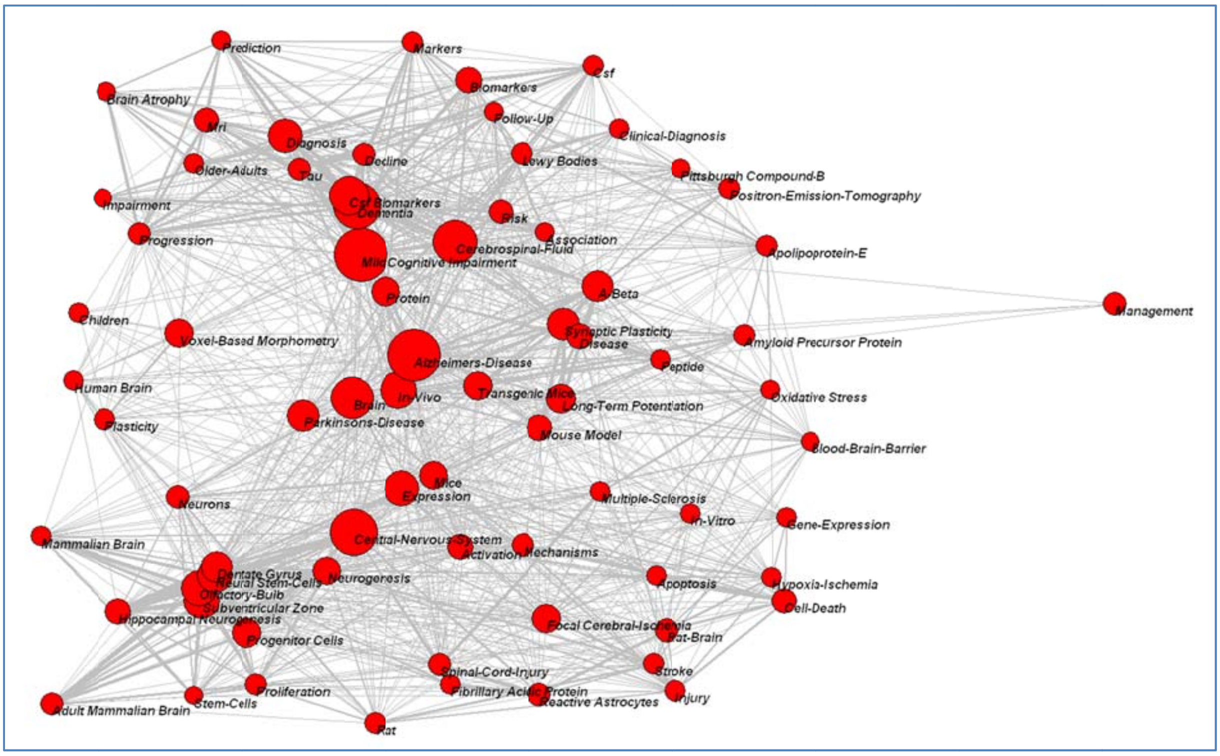

Figure 4. Co-word analysis: 75 top-descriptors depicted by MDS. Circle-sizes are proportional to the number of papers in which a term occurs. Kruskal's stress I = 15 %.

Summary

A set of analytical tools were tested with the objective of identifying and mapping outstanding GU-papers published in journals classified as neuro-science. As a measure of "outstandingness" a citation score of at least four times the field normalized citation frequency was applied. This meant that a paper had to be cited at least four times the world (field) standard in order to be included. This mode of selection brought about 21 papers when using the Web of Science (Thomson Reuters) as the data source. Pertinent information (author names, journal titles, citation frequency) was presented and complementary information made available in an annex.

Investigation the aspect of collaboration between universities respectively authors revealed that the distribution of collaborating universities was even and no concentration of collaboration to specific universities was found. Hence, a large number of unique universities or other institutions contributed with citations. Elaborating on the geographical aspect of institutional collaboration it was concluded that more than half of all papers were produced in collaboration with a European university and no paper was produced solely by GU. Applying a graph theoretical approach, measures of centrality was applied identifying a set of highly connected authors which were depicted graphically.

The mapping of papers linked to the set of outstanding papers through citation resulted in 19 subject-coherent clusters and a total of 231 additional papers, enlarging the cognitive context. Repeated clustering resulted in three clusters with one large cluster representing research on Alzheimer's disease and two smaller clusters dealing with research on brain structure and mental activity respectively research on the olfactory bulb. Cluster labels should be considered preliminary as they were accomplished on a layman-level and other interpretations are certainly plausible.

A term-analytical approach was also presented in the context of cognitive depiction of research themes. The analytical value of this type of map could not be established here, but needs to be further investigated.

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