

# 生理科学实验**研究型**实验课程

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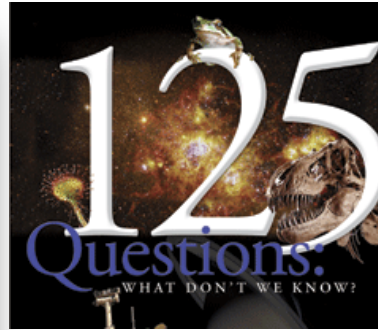
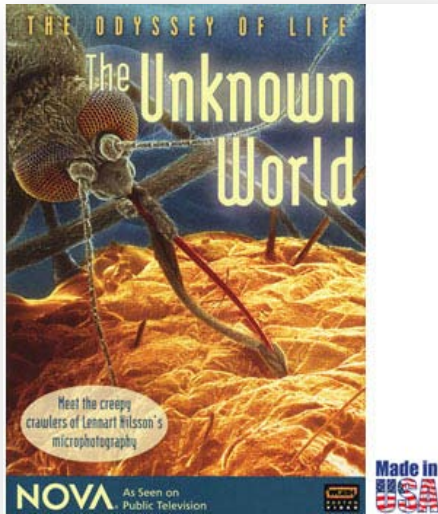
Email: [xiangnan\\_zhang@zju.edu.cn](mailto:xiangnan_zhang@zju.edu.cn)

Tel: 88208227

# 希望与大家分享什么

- ▶ 为什么做研究
- ▶ 什么是研究
- ▶ 怎样做研究

# 为什么做研究？



- 56、太阳系的其他星球上现在和过去是否存在生命？
- 58、能否预测蛋白质折叠？
- 59、人体中的蛋白质有多少种？
- 60、蛋白质如何发现其合作对象？
- 61、细胞死亡有多少种形式？
- 62、是什么保持了细胞间的通行顺畅？
- 63、为什么细胞组件可以独立于DNA而自行复制？
- 64、基因组中功能不同于RNA的角色是什么？
- 65、基因组中端粒和丝粒的作用是什么？

- 1、宇宙由什么构成？
- 2、意识的生物学基础是什么？
- 3、人类的基因为什么如此之少？
- 4、遗传变异与人类健康在多大程度上彼此相关？
- 5、物理定律能否统一？
- 6、人类寿命可以延长多久？
- 7、是什么控制着器官再生？
- 8、皮肤细胞如何变成神经细胞？
- 9、单一体细胞怎样成为完整植株？
- 10、地球内部如何运行？
- 11、我们在宇宙中是孤独的吗？
- 12、地球生命是在哪里、如何诞生的？
- 13、什么决定了物种的多样性？
- 14、何种基因改变造就了独特的人类？
- 15、记忆如何存储和提取？
- 16、合作行为如何发展？
- 17、怎样从海量生物学数据中获得大的图形模式？
- 18、我们能在化学自组织方面走多远？
- 19、常规计算的极限在哪里？
- 20、我们能否有选择地切断某些免疫反应？
- 21、量子不确定性和非局部性背后是否有更深刻的原理？
- 22、能否研制出有效的HIV疫苗？
- 23、温室效应会使地球变得多热？
- 24、什么时间用什么能源可以替代石油？
- 25、马尔萨斯会一直错下去吗？

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<http://www.sciencemag.org/site/feature/misc/webfeat/125th/>

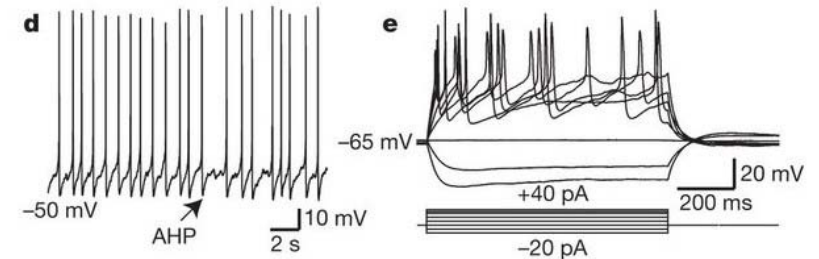
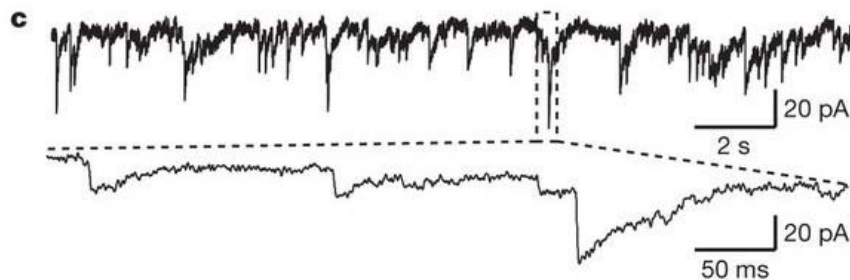
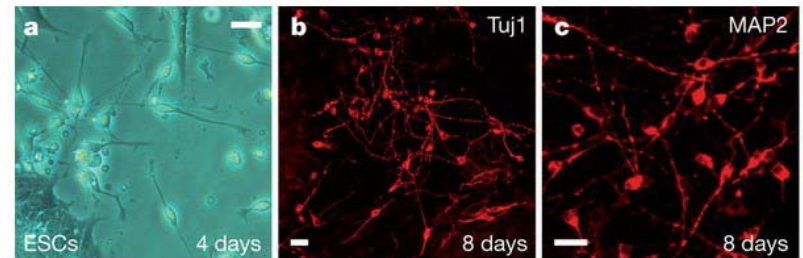
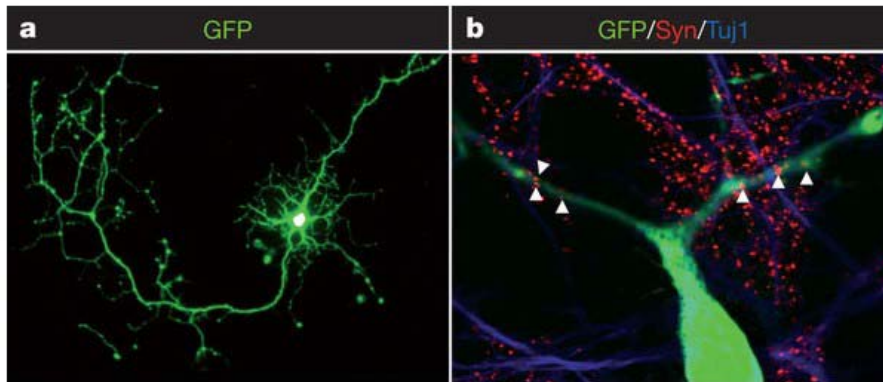
# Induction of human neuronal cells by defined transcription factors

Zhiping P. Pang, Nan Yang, Thomas Vierbuchen, Austin Ostermeier, Daniel R. Fuentes, Troy Q. Yang, Ami Citri, Vittorio Sebastiano, Samuele Marro, Thomas C. Südhof & Marius Wernig

Affiliations | Contributions | Corresponding author

Nature (2011) | doi:10.1038/nature10202

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一项令HIV研究重获新生的临床试验名列本杂志2011年科技进步名单之冠。感染了HIV的人如果服用抗逆转录病毒药物（ARVs）的话，他们将病毒传播给其伴侣的可能性要降低96%。

隼鸟号太空使命

揭开人类起源之谜

捕捉一种光合蛋白

太空中原始的气体

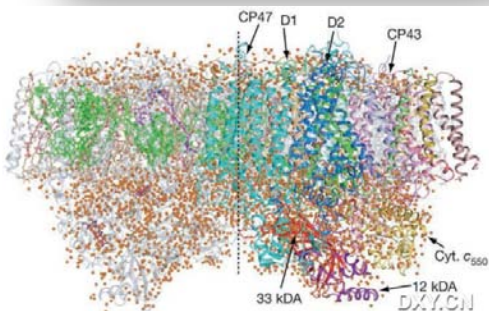
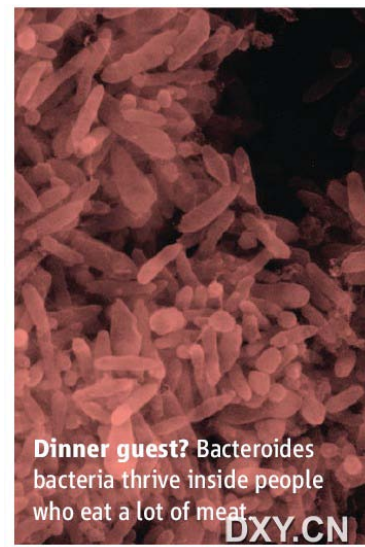
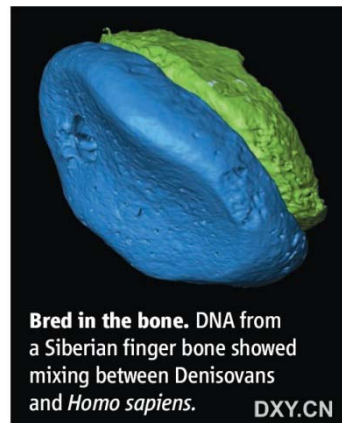
对微生物组的逐步了解

一种有前途的疟疾疫苗

奇怪的太阳系

专门设计的沸石

清除衰老细胞





1. 发现希格斯玻色子
2. 丹尼索瓦人基因组
3. 让干细胞形成卵子
4. 好奇号的着陆系统
5. X射线激光解开蛋白质的结构
6. 基因组的精密工程 (TALENs)
7. 马约拉纳费米子
8. ENCODE项目
9. 大脑/机器界面
10. 中微子混合角



Controlling Bionics

Majorana Fermions

Eggs from Stem Cells

# 什么是科学研究？

1、我国国家教育部定义是：“科学研究是指为了增进知识包括关于人类文化和社会的知识以及利用这些知识去发明新的技术而进行的系统的创造性工作”

文献来源

2、美国资源委员会对科学研究的定义是：“科学研究工作是科学领域中的检索和应用包括对已有知识的整理、统计以及对数据的搜集、编辑和分析研究工作”

文献来源

Google

科学



搜索

找到约 131,000,000 条结果 (用时 0.28 秒)



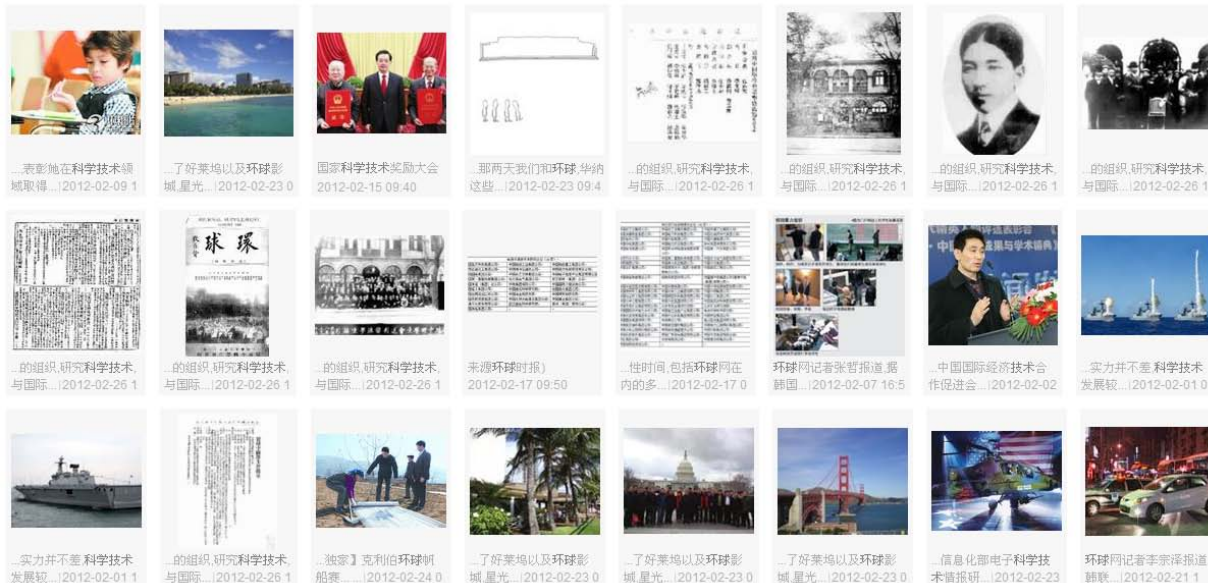
Baidu 图片

新闻 网页 贴吧 知道 MP3 图片 视频 地图 百科

科学



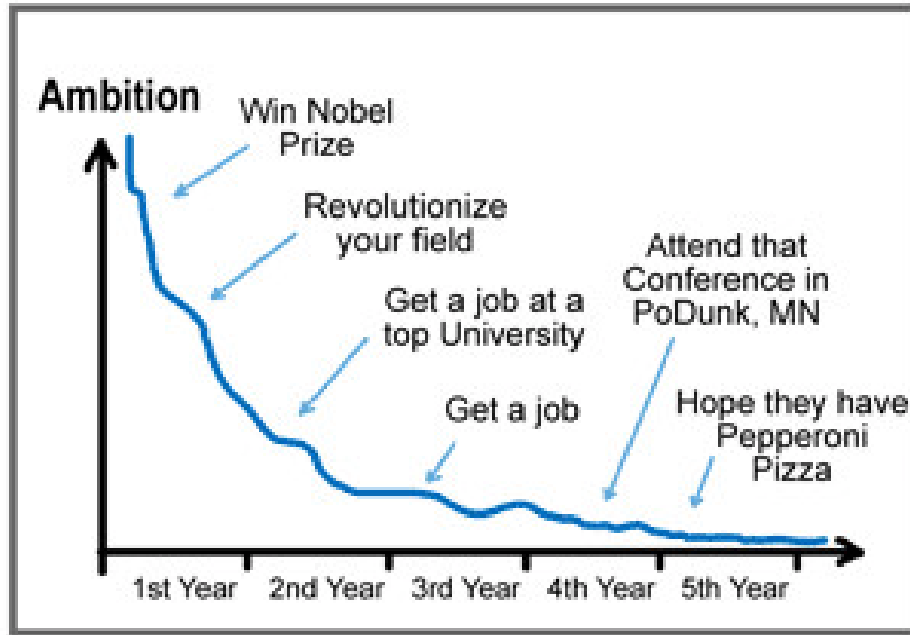
百度一下





# Ambition

## YOUR LIFE AMBITION - What Happened??

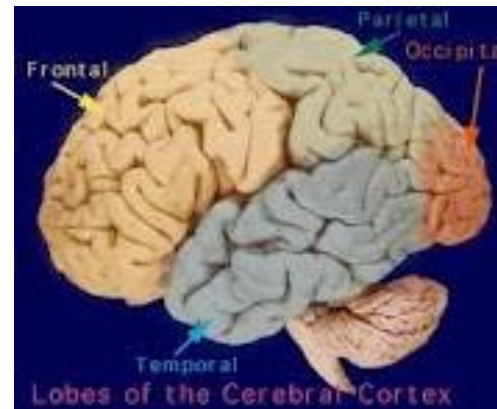
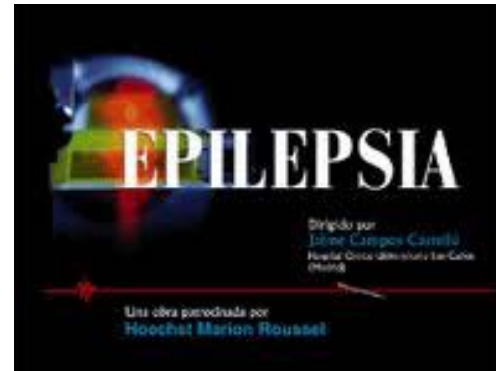
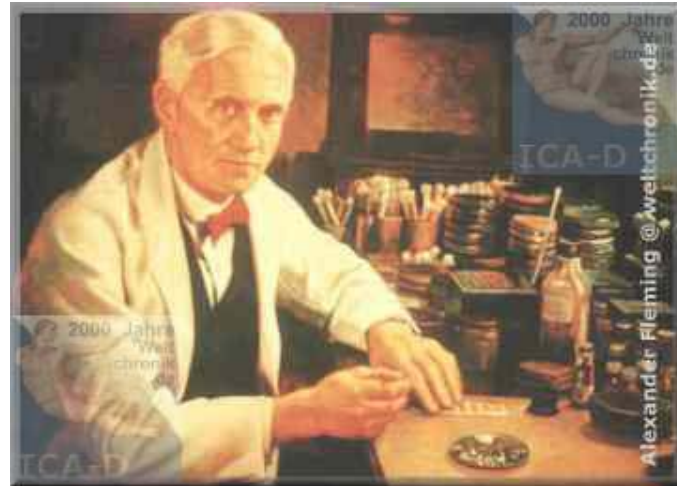


JORGE CHAM © 2008

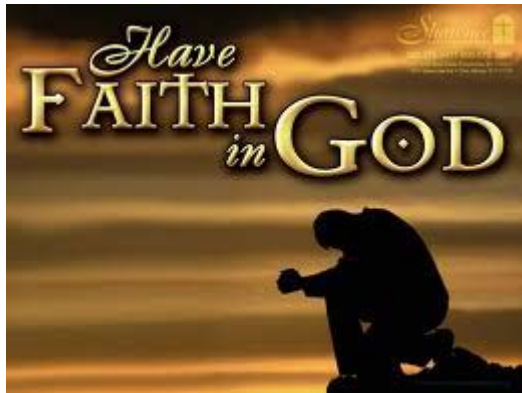
WWW.PHDCOMICS.COM

# Observation!

Are You  
Paying  
Attention?



# Duration



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教 教 教 教

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## PRAYER PUPS BY JEFFREY SMITH



SCIENCE IS BELIEF THAT IS BASED ON PROOF. FAITH IS BELIEF THAT IS BASED ON YOUR HEART.

www.PrayerPups.com

# 生物医学科研的任务

- ▶ 探索生物医学中未知事物及其未知过程
- ▶ 揭示已知事物中的未知规律
- ▶ 研究已知规律的应用前景
- ▶ 不断检验和更新已有的理论和学说

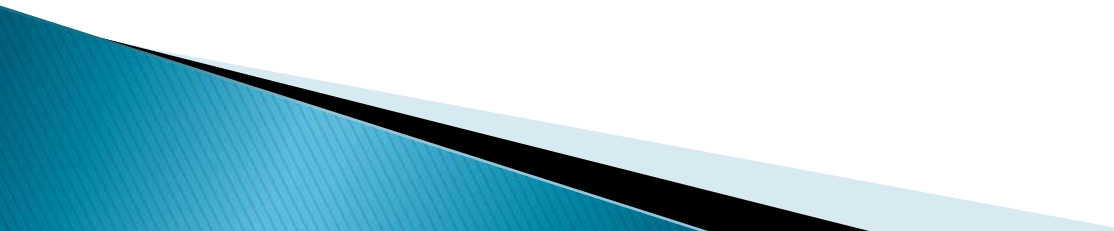
# 生物医学科研的分类

- ▶ **基础研究 (fundamental research)**
  - 纯基础研究
  - 应用基础研究
- ▶ **应用研究 (applied research)**
- ▶ **发展研究 (development research)**

# 科学家应当具备的素质

- ▶ 忠于真实  
两大戒律：剽窃  
作假
- ▶ 勤于思考
- ▶ 作风严谨
- ▶ 执着追求
- ▶ 合作精神
- ▶ 善于表达

# 科学研究的步骤

- 提出构想、假说（课题的选择）
  - 实验设计
  - 实验研究
  - 撰写论文
- 

# 研究课题的选择的原则

- ▶ 课题的理论意义
- ▶ 课题的应用前景
- ▶ 课题具备的创新性、科学性和可行性



# 如何提出科研构想

科学依据，科学思维

查资料



假说、构想  
(大胆并符合科研选题的条件)

查资料



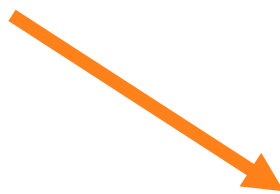
有无同类研究



没有



有，但仍有问题



已研究清楚

# 查资料（医学文献检索）

▶ 图书

▶ 期刊

网站搜索引擎、文献检索（Medline, elsevier, 维普资讯, etc）

▶ 科技报告

▶ 学位论文

▶ 专利文献

▶ 病历档案

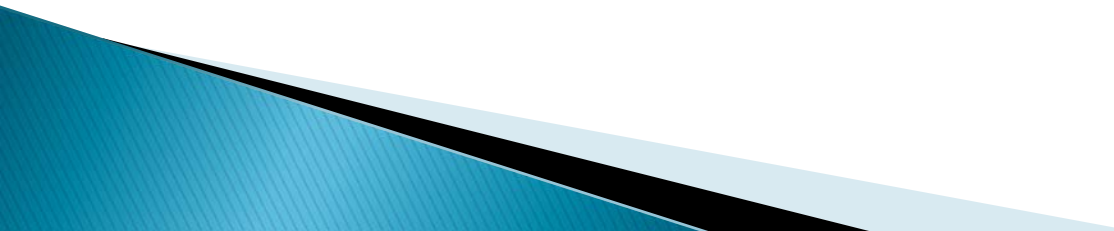
▶ 政府出版物

▶ 产品资料

# 实验设计

- ▶ 确立题目
- ▶ 阐明题意，提出假说
- ▶ 处理因素
- ▶ 受试对象
- ▶ 方法和观察指标
- ▶ 观察效应
- ▶ 预算及预期效果

# 论文书写

- 题目、作者、通讯地址  
(title, authors and address)
  - 摘要(abstract)
  - 前言(introduction)
  - 材料与方法(materials and methods)
- 

# 论文书写

- 结果(results)
  - 讨论(discussion)
  - 结论(conclusion)
  - 致谢(acknowledgement)
  - 参考文献(references)
- 

# 医学文献检索

# 医学文献检索

- 一、概述
- 二、检索语言
- 三、医学主题标引
- 四、检索方法
- 五、数据库类型
- 六、检索基本规则
- 七、数据库检索示范
- 八、文献检索与管理软件：endnote

# 一、概述

## 基本概念：

利用检索工具，准确、全面地查询与特定研究课题有关的文献资料的过程

## 意义：

- 1.提高探索知识的本领，增强解决实际问题的能力
- 2.学习和借鉴他人研究成果，避免重复研究
- 3.利用信息资源，促进管理决策科学化



# 一、概述

## 检索系统

- 1.文献存储：检索工具的编制（输入）
- 2.文献检索：检索工具の利用（输出）

## 二、检索语言

**1.基本概念：**根据文献检索的需要创造的人工语言，是在文献标引、文献检索工作中用来描述文献外部特征或文献主题特征及检索提问的一种专门语言。

**2.意义：**是文献存储和文献检索的桥梁，在信息存储和检索过程中，检索语言起规范和转换作用，以及知识组织和知识表示的作用

## 二、检索语言

### 3.检索语言类型

#### 3.1分类检索语言：

国际：杜威十进分类法

国内：中国图书馆图书分类法

#### 3.2主题检索语言：

主题词

关键词

#### 3.3分类主题一体化检索语言：

中国分类主题词表

## 二、检索语言

### 3.1 分类检索语言

#### 《中国图书馆图书分类法》

1. 1995年出版第一版，到1998年已出版第四版。
2. 分为5个基本部类、二十二个基本大类（A-Z）

#### 3.R<sub>557</sub>

R: 医药卫生

千位的5: 内科学

百位的5: 血液系疾病

个位的7: 白细胞疾病

## 二、检索语言

### 3.2 主题检索语言

#### 基本概念

- 1. 主题词(叙词):** 是经过严格规范化的词和词组，是词和概念单一对应，排除同义词以保证文献集中归入一个主题词下。
- 2. 关键词:** 从文献题目或文摘、正文中提取出来具有实质意义、能代表文献主题内容的词汇，是非规范性的自然语言。

## 二、检索语言

### 3.2 主题检索语言

《医学主题词表》(medical subject headings, MeSH)

1. 是目前最权威、最常用的标引与检索的标准主题词表，包含18 000个词和词组，分十五个大类 (A-N, Z)
2. 词的形式：单个词和复合词 (顺装和倒置)
3. 词的种类：主题词 (叙词) 包括主要叙词、次要叙词  
款目词  
非主题词  
特征词  
副主题词：限定主题概念的一类规范化词汇  
(词目有82个)

## 三、医学主题标引

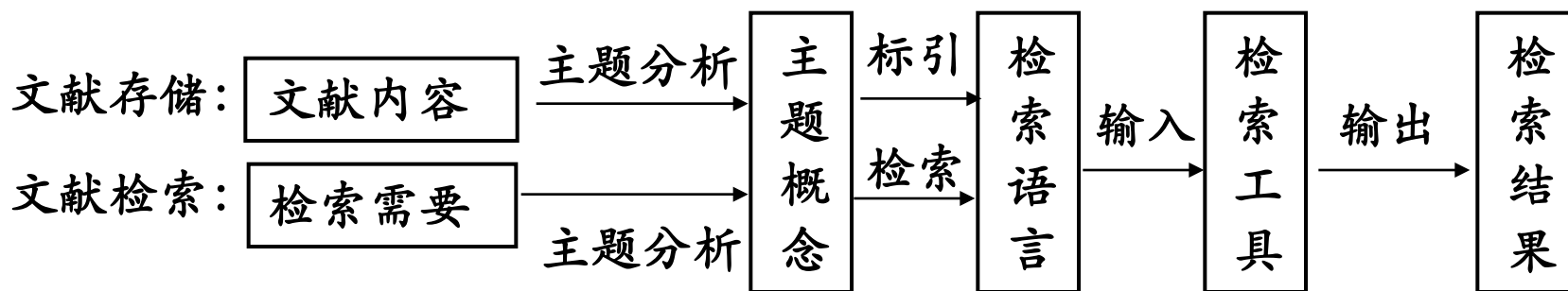
### 基本概念

**标引：**对文献进行主题分析，用规范化的检索语言代替自然语言来表达文献主题内容的过程

**类型：**主题标引和分类标引

### 三、医学主题标引

#### 标引与检索的关系





## 三、医学主题标引及标引规则

### 主题标引的基本原则

1. 一般原则：客观性、准确性、专指性、全面性和一致性
2. 选词原则：主题词的规范化
  - 先组主题词
  - 靠词标引
  - 自由词标引
3. 组配标引
  - 主题词-主题词交叉组配
  - 主题词-副主题词组配

## 四、检索方法

1.利用检索工具书图书馆检索

2.光盘数据库检索

3.网络数据库检索

## 四、检索方法

### 常用的中文检索工具书

1. 《中文科技资料目录》
2. 《国外科技资料目录》
3. 《中国医学文摘》
4. 《中国药学文摘》

### 常用的外文检索工具书

1. 美国 《医学索引》
2. 荷兰 《医学文摘》
3. 美国 《生物学文摘》
4. 美国 《化学文摘》

## 四、检索方法

### 光盘数据库检索

#### 1.光盘检索分类:

单机检索

局域网检索

#### 2.中国的学术期刊光盘 (CAJ-CD)

#### 3.美国的MEDLINE光盘 (美国银盘公司生产) 检索

## 四、检索方法

### 网络数据库检索

1.中国生物医学文献数据库Web版

2.PubMed检索

## 五、数据库类型

1.文摘索引型数据库

2.全文数据库

3.引文数据库

## 五、数据库类型

常用的文摘索引型数据库

- 1、MEDLINE 《美国全科医学文献数据库》 1966-
- 2、EMBASE 《荷兰医学文摘》 1989-
- 3、CBMDISC 《中国生物医学文献数据库》 1980-
- 4、CMCC 《中文生物医学期刊文献数据库》 1994-

## 五、数据库类型

### 常用的全文数据库

- 1、ScienceDirect OnSite 《Elsevier 电子期刊全文数据库》 1998-
- 2、Kluwer Online 《Kluwer 电子期刊全文数据库》 1986-
- 3、其他：LWW、OVID Technologies、Springer LINK、John Wiley 等
- 4、中国期刊网专题全文数据库 1994-
- 5、万方数字化期刊数据库 1986-



## 五、数据库类型

### 常用的引文数据库

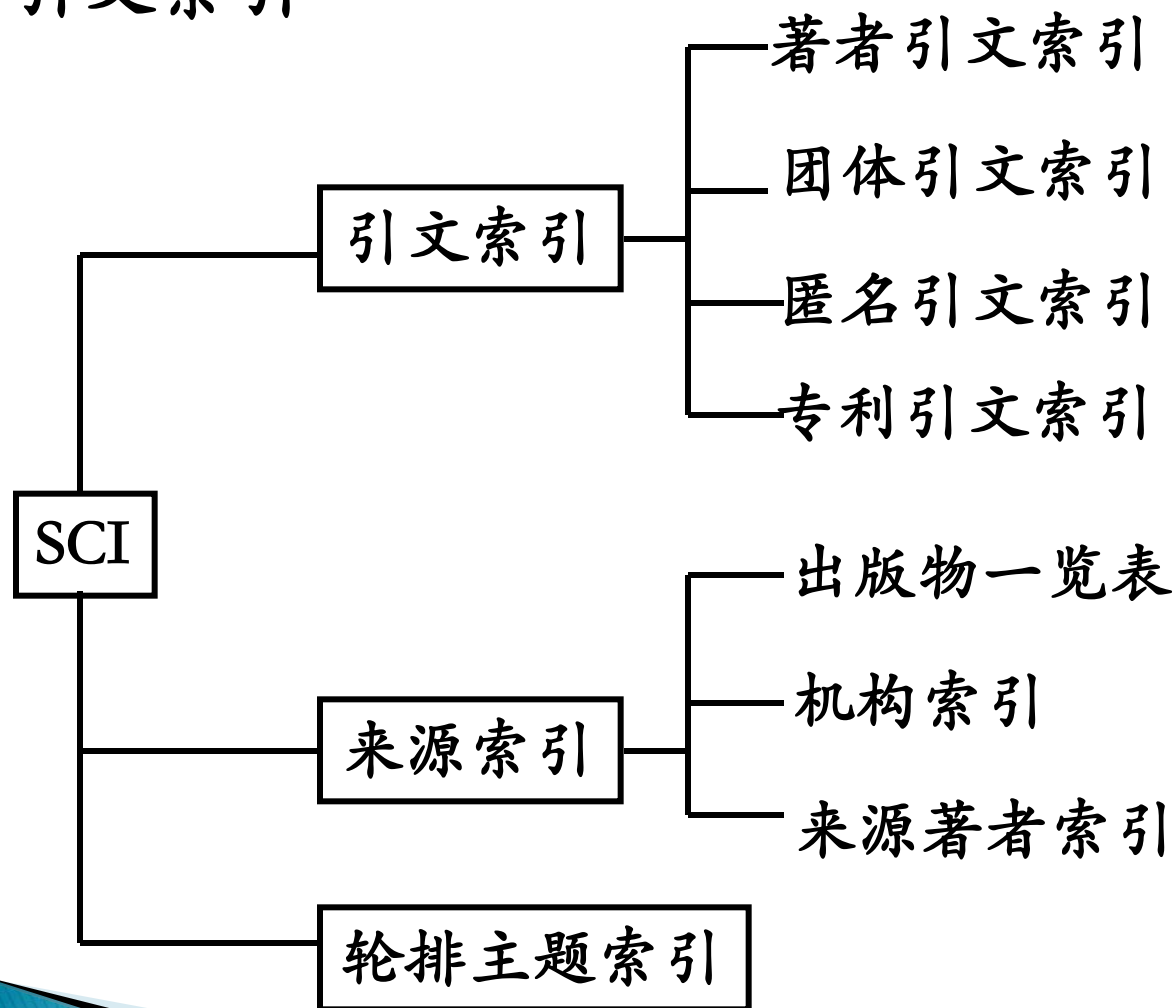
- 1、Web of Science 《美国科学引文索引(SCI)网络数据库》 1973-
- 2、Journal Citation Reports (JCR) 《期刊引文分析数据库》 Current
- 3、CSCS 《中国科学引文数据库》 1998-

## 五、数据库类型

### 引文索引

- 1.是揭示科技文献之间引用和被引关系的检索工具
- 2.美国《科学引文索引》(Science Citation Index, SCI).
- 3.三部分组成：引文索引(A、B、C分册) 来源索引(D分册) 和轮排主题索引(E分册)

# 引文索引



## 六、检索基本规则

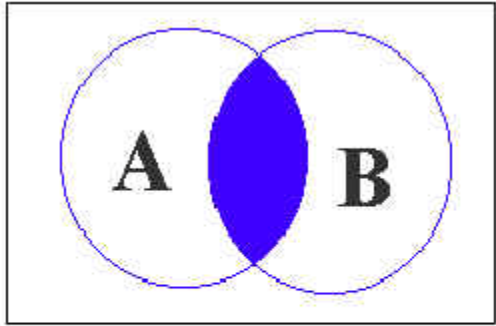
布尔逻辑算符 (AND, OR, NOT)

截词符 (? 或\*或\$)

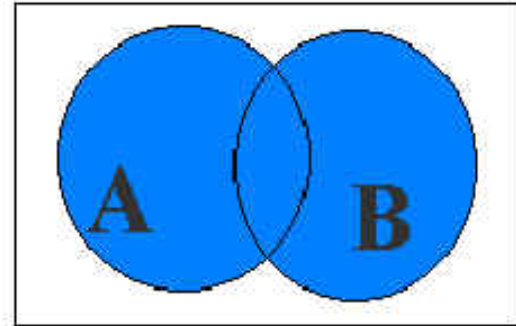
位置算符 (ADJ 或NEAR)

“A ADJ B”表示A和B两个检索词相邻，在ADJ后还可跟数字，如information adj5 retrieval则表示information和retrieval相邻至多5个词。检索式“A near B”表示检索词A和检索词B不仅要同时出现在一条记录的同一段落里，还必须在同一个子字段（一句话）里的文献才是命中文献。

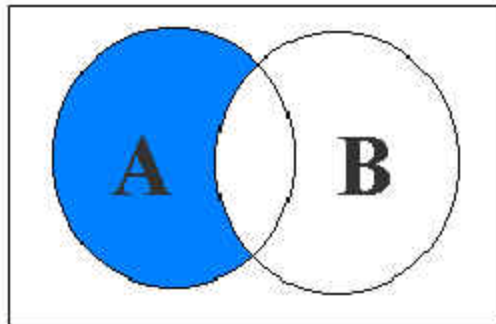
其它算符 (如词组用引号)



**A and B**



**A or B**



**A not B**

## 七、数据库检索示范 (PubMed)

<http://www.ncbi.nlm.nih.gov/sites/entrez>

## 八、文献检索与管理软件:

**endnote, reference manager**



A service of the U.S. National Library of Medicine and the National Institutes of Health

www.pubmed.gov

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All Databases PubMed Nucleotide Protein Genome Structure OMIM PMC Journals Books

Search PubMed for Go Clear Advanced Search (beta)

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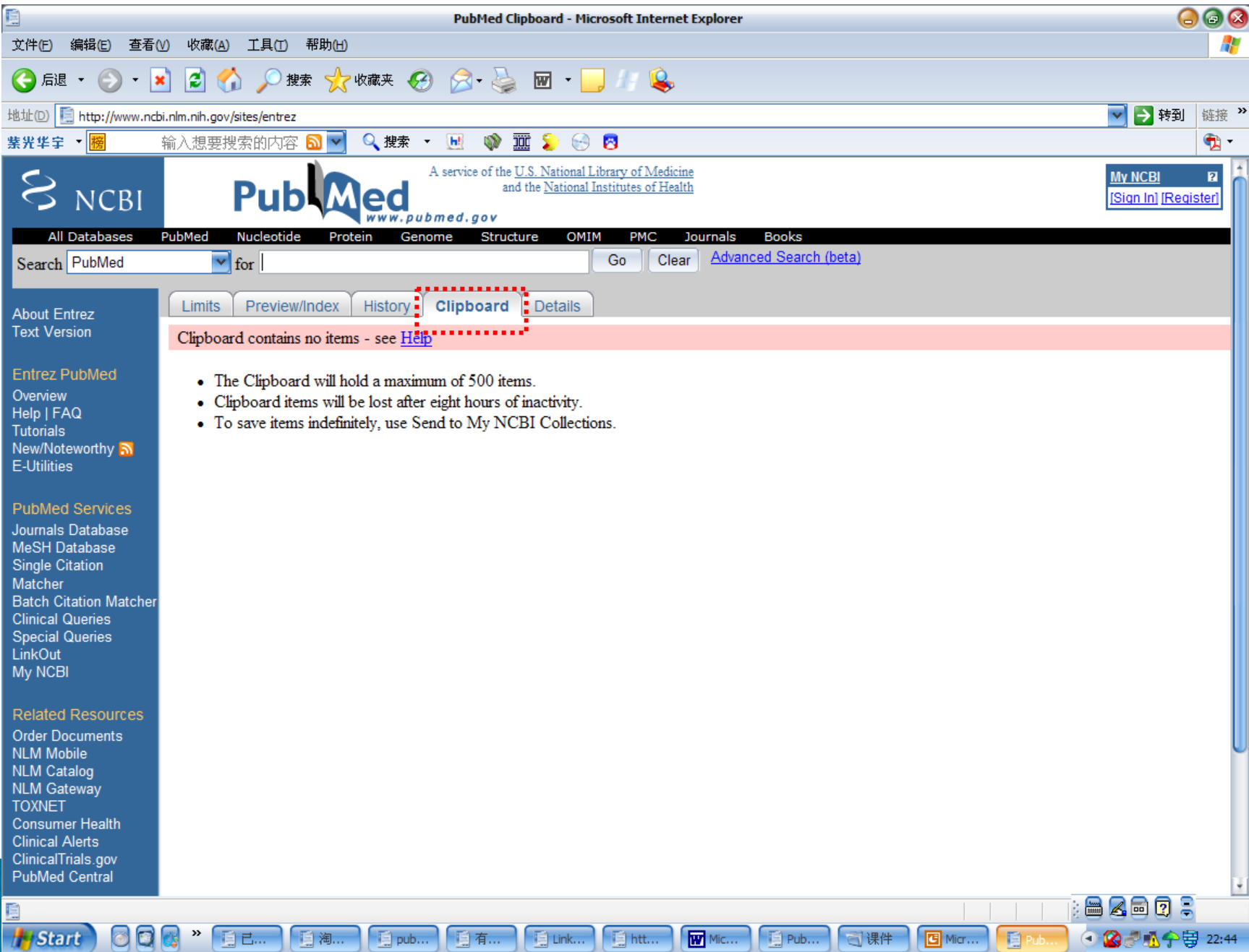
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**Avignone E, Ullmann L, Levavasseur F, Rassendren F, Audinat E.**

Inserm U603, and Université Paris Descartes, Unité Mixte de Recherche (UMR)-S603, Centre National de la Recherche Scientifique (CNRS) UMR 8154, 75006 Paris, France, CNRS UMR 5203, Institut de Génétique fonctionnelle, Universités Montpellier 1 et 2, UMR-S661, and Inserm U661, 34094 Montpellier, France.

Microglia cells are the resident macrophages of the CNS, and their activation plays a critical role in inflammatory reactions associated with many brain disorders, including ischemia, Alzheimer's and Parkinson's diseases, and epilepsy. However, the changes of microglia functional properties in epilepsy have rarely been studied. Here, we used a model of status epilepticus (SE) induced by intraperitoneal kainate injections to characterize the properties of microglial cells in hippocampal slices from CX3CR1(eGFP/+) mice. SE induced within 3 h an increased expression of inflammatory mediators in the hippocampus, followed by a modification of microglia morphology, a microglia proliferation, and a significant neurodegeneration in CA1. Changes in electrophysiological intrinsic membrane properties of hippocampal microglia were detected at 24-48 h after SE with, in particular, the appearance of new voltage-activated potassium currents. Consistent with the observation of an upregulation of purinergic receptor mRNAs in the hippocampus, we also provide pharmacological evidence that microglia membrane currents mediated by the activation of P2 receptors, including P2X(7), P2Y(6), and P2Y(12), were increased 48 h after SE. As a functional consequence of this modification of purinergic signaling, motility of microglia processes toward a source of P2Y(12) receptor agonist was twice as fast in the epileptic hippocampus. This study is the first functional description of microglia activation in an in vivo model of inflammation and provides evidence for the existence of a particular microglial activation state after a status epilepticus.

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- Pathophysiological roles of extracellular nucleotides in glial cells: differential expression of purinergic receptors [Brain Res Brain Res Rev. 2005]
- ATP-induced chemotaxis of microglial processes requires P2Y receptor-activated initiation of outward potassium currents. [Glia. 2007]
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