

Brain-Apparatus Communication: A Journal of Bacomics

Journal homepage: <https://www.tandfonline.com/loi/tbac20>

Dezhong Yao, Yun Qin, Yangsong Zhang (2022) From psychosomatic medicine, brain-computer interface to brain-apparatus communication, *Brain-Apparatus Communication: A Journal of Bacomics*, 1:1, 66-88, DOI: 10.1080/27706710.2022.2120775

从心身医学、脑机接口到脑器交互

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摘要

心身医学中, 和谐的脑-身体互动是人类健康的重要基石。近代提出的脑机接口(BCI), 大脑和非生物设备之间的交互, 将无限智慧的人脑和功能强大的计算机相连, 为人类的发展提供了更广阔的可能和想象。而我们新近提出的脑器交互(BAC)在认可上述两种相互作用的独特价值的基础上, 进一步描述了它们之间的依赖性。这种相互依存关系如何使人们更好地保持生理和心理健康, 促进人与环境的和谐共处, 值得深入探讨研究。本篇综述对这三种类型的交互进行了概述, 并讨论了可能的未来趋势。

关键词: 心身医学, 脑机接口, 脑器交互

背景

人类的大脑和各种器官在遗传密码的指导下，从受精卵发育开始就建立了不可分割的联系。出生后，新生儿面对来自外界环境的听觉、视觉和触觉刺激，刺激通过感觉器官传递到大脑，使得大脑快速发育，并迅速建立起大脑感知外部环境的方式。由于这两种相互作用（即脑-身体和脑-环境）都以大脑为中心，因此可统称为脑器交互（BAC）[1]；这里的“器”可以是内部器官（BAC-1），也可以是外部设备/环境（BAC-2）。聚焦于BAC-1的心身医学最初建立于大约200年前，随着对BAC-1的越来越深入的理解，使得众多患者因此受益；自20世纪60年代中期以来，不同BAC-2类型与计算机紧密联系，促进了脑机接口技术（BCI）的产生与发展。

BAC-1和BAC-2在日常生活中必不可少，也密不可分。例如，在打篮球时，BAC-2反映了大脑与篮球及与团队成员的互动，而BAC-1反映了大脑与肌肉、心脏、肺等器官的互动。高强度的电子游戏也是一个例子，它涉及到大脑和电子游戏内容之间的相互作用，也涉及到大脑与许多器官之间的相互作用。由于这两种相互作用是互相依赖、互为支撑的，因此我们称之为BAC-3。在本文中，我们首先介绍了心身医学和BCI，为读者报告了BAC-1和BAC-2的历史和进展。接下来，介绍了BAC的概念和示例。最后，我们讨论了BAC对于跨物种大脑多样性的重要性和独特性。我们认为，提升BAC-3的有效性，包括BAC-1和BAC-2，将贡献于人类的健康和福祉，甚至能够启发扩展人类能力边界的有效途径。

1. 心身医学:概念和历史

早在1900年前的中医《黄帝八十一难经》中，就记载了蕴含古老智慧的四诊方法：“望、闻、问、切”，将身心合一的概念用于诊断疾病。1818年，Heinroth引入了“心身医学”这个术语，而实际上心身医学概念的根源可以追溯到古希腊。近代，心身医学作为一门正式学科诞生，此后便获得了迅速发展。其中心思想，即大脑和身体是人类所有功能的组成部分，医生能够通过评估个人的心理因素以及疾病的发展过程，应用特定心理疗法来治疗身体疾病。因此，心身医学试图解释非物质性事件是如何转化为身体变化的，如对心理社会刺激的行为或心理反应在解剖结构、酶促、神经、内分泌等身体变化上的反应。图1列举了现代心身医学史上的部分代表性研究。现代心身医学的基础通常认为是在20世纪的10-20年代奠定的，当时Cannon研究了特定情绪伴随发生的身体变化[2, 3]，提出了丘脑和下丘脑在情绪反应中的重要作用，形成Cannon - Bard理论，推动了研究从先前的James - Lange理论到研究情绪背后的中枢大脑机制的转变[4-8]。基于此理论，Papez探讨了情绪的脑机制，Maclean提出了心身疾病和“内脏大脑”之间的关系[9, 10]。于是，人们认识到情绪紧张是身体疾病的重要原因[11, 12]，并描述了人格特征和生活情境之间的心身关系[13]，阐明了压力和身体疾病，尤其是心血管疾病之间的相互影响[14, 15]。在这些研究的基础上，Engel等建立了一种评估受试者心理状态的方法，提出了疾病的多因素模型，认为疾病是细胞、组织、机体、人际和环境水平相互作用的结果[16-18]。在这一阶段（20世纪30-60年代），心身医学研究的重点从疾病的发生逐渐转移到其发生相关的情景方面。

20世纪60年代后，会诊-联络精神病学（consultation-liaison psychiatry）的发展进一步推动了世界范围内的心身研究，丰富了该领域的精神病学内涵。在这个阶段，心身医学在会诊精神病学中的初步应用得以确立[19-21]。同时，行为医学也得到了发展和越来越多的应用。有研究强调了某些行为对疾病发展的风险[22, 23]以及家庭因素在儿童严重身心问题的发展和维持中的重要性[24, 25]。压力、创伤和敌意也被认为是心身疾病的重要诱因[26-28]。此外，人们提出了心身综合症的诊断标准[29, 30]，并概述了与精神病学

的关系[31, 32]。在这一阶段, 行为疗法兴起, 并在疾病治疗中展示出了巨大的潜力[33-36]。

在过去的二十多年里, 心身医学持续发展, 为临床实践提供了新的有效策略和方法[37-40]。心身医学把精神病学和生理系统联系起来, 并逐渐扩展到新的领域。人们发现, 心理社会应激源或其干扰的免疫调节可能是各种疾病背后的关键因素[41], 炎症、氧化和亚硝化应激途径与慢性疲劳等心身疾病密切相关[42]。脑-肠轴的存在以及肠道微生物群与神经发育和抑郁等精神类疾病的关系展示了另一条重要的心身途径[43, 44]。到今天, 心身疾病及其治疗方法获得了越来越多的科学证据的支持, 相关的临床实践指南已逐渐完善[45-48]。

随着信息科学、智能科学、环境科学和生物科学的进步发展, 当前的环境和人类生活方式正在经历深刻的变化[49]。心身医学提供了疾病和身心相互作用的微观视角, 也为维持、改善和增强人类行为健康提供了基础。

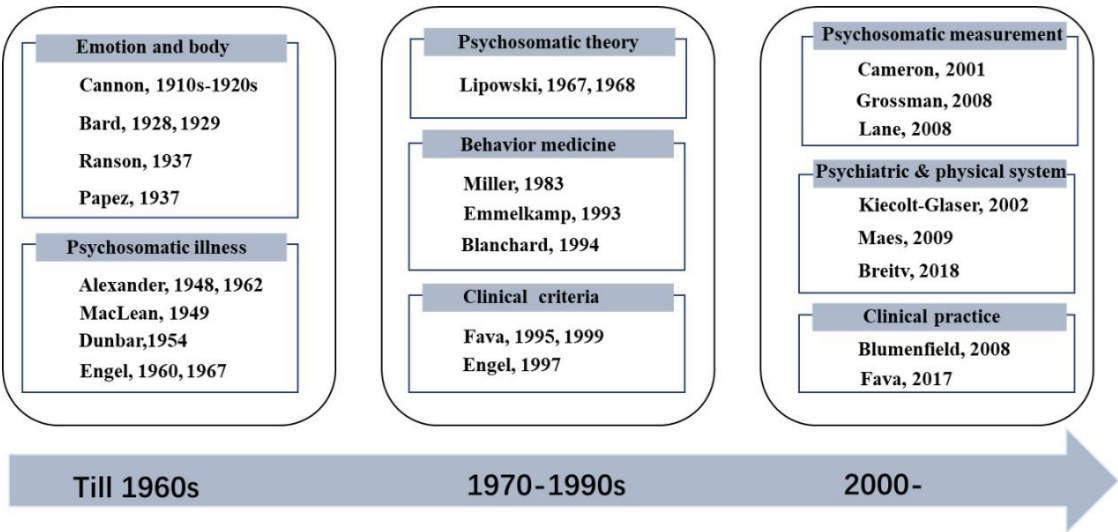


图1. 心身医学领域发展的代表性研究。

在20世纪初, Cannon实验室开展了二十余年的情绪生理学研究, 融合Bard的研究形成Cannon - Bard理论, 建立了情绪和生理反应的联系。20世纪中期(40年代到60年代), 人们进一步界定了不同疾病的相关心理因素及其伴随的生理变化。20世纪60年代后, 人们重点提出并讨论了精神病学的内涵、心身机制、行为治疗和临床标准。在过去的二十多年中, 心身医学扩展到了更多的精神和生理系统疾病, 其临床治疗和实践应用的重要性越来越突出。

2. 脑机接口: 历史与进展

人类与自然环境如何互动是进化的结果。然而, 某些疾病会干扰或破坏这种互动方式, 如瘫痪等严重运动障碍的人群。脑机接口(BCI/BMI(brain-machine interface))的出现一定程度上就是为了应对这种干扰或破坏, 试图在大脑和外部设备之间提供双向链接, 旨在帮助障碍人群恢复运动功能。目前, BCI作为大脑和设备之间的重要互联, 已经衍生出了众多类型和应用, 在神经康复和疾病干预中显示出巨大的潜在应用价值[50-58]。

基于EEG的BCI可以追溯到20世纪60年代中期, 如由Edmond Dewan展示的脑控开灯[59]。“脑机接口”这个术语最早是由Vidal在1973年提出[60], 在接下来的近50年里, BCI逐渐成为科学研究的热点。其中, Fetz (1969)发表了第一篇关于动物皮层棘波串的操作性条件反射的论文[61]。随后, 研究者基于无创EEG记录的慢皮层电位(SCP)开发了BCI系统[62], 并于1979年用于自我调节和外部控制[63-70]。1991年, Wolpaw等利用感觉运动节律(SMR)实现了光标控制, 近年来, SMR相关的节律被广泛应用于BCI系统的构建[51, 52, 71-73]。事件相关电位(ERPs)和诱发电位(EPs)能够表征大脑对外部和内部刺激的反应, 如P300、稳

态视觉诱发电位 (SSVEP) 和运动诱发视觉诱发电位 (mVEP)，基于这些电位的BCI应用也越来越广泛[74-76]。Farwell和Donchin开发了第一个基于P300的BCI打字系统，在BCI过程中如何最佳呈现刺激和提取单次试验响应等方法也不断发展[74, 77]。此外，SSVEP由快速连续视觉呈现来诱发[76]，而且SSVEP-BCI不需要特别的训练，具有可靠的分类特征，因此基于SSVEP的快速拼写BCI已成为一种重要的BCI模式[78-85]。

随着大脑信号获取技术的发展，基于功能性近红外光谱 (fNIRS)、功能性磁共振成像 (fMRI) 和脑磁图 (MEG) 的BCI系统涌现出来[86-88]，同时出现了一些新的BCI交互类型，如BCI与虚拟现实的结合，以及可进行多人协作控制的多脑BCI系统等 [89-92]。更重要的是，BCI的范式出现了从运动到情绪、认知BCI，从主动到反应或被动BCI的快速发展，其中不同种类的认知和情感BCI范式为脑疾病干预和脑功能增强提供了更多的潜在应用[93-107]。此外，融合人工智能的算法在解码不同尺度大脑信号中发挥了更加重要的作用 [108-110]。

BCI的发展历程表明，其核心技术是特定范式，包括用何种大脑信号采取什么技术解决什么问题。一个新的范式，能够推动所需支撑技术的进步，包括数据获取分析、传输、编解码、特征提取等，并发展出新的应用，建立起新的领域。因此，未来的BCI研究应更多地考虑人类的实际需求和发展生态友好型范式，关注实施这些范式所需的支撑技术。图2显示了自1973年以来BCIs的主要进展。其中早期BCI主要关注运动功能，最近的BCI有望为全球数百万患有神经和精神疾病的患者提供非药物个性化治疗[111]。

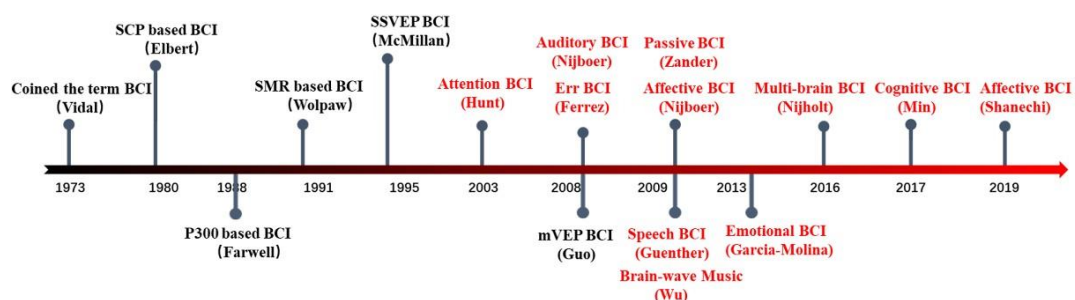


图2. BCI主要研究范式。早期的范式(黑色)集中于运动控制，近几年的范式(红色)侧重于各种监测和调控模式。

3. 脑器交互

我们亲身体验这个世界并与之互动，推动了我们智能行为的表达[39, 112]。外界刺激作用于综合的生理系统——中枢神经系统、外周神经系统、内分泌系统和免疫系统等，从而启动生理反应网络，产生身心互动。如前文所述，心身研究的重点是心理-身体的互动。而身体-心理互动包括的领域有：具身认知，强调生理状态对认知过程的重要性[113, 114]；躯体精神障碍的研究，强调躯体精神障碍是由躯体障碍引起或加剧的精神障碍 [115, 116]。相比而言，BCI专注于大脑和外部设备之间的交互。这两种相互作用看似有明显区别，但事实上，在大脑不断地与身体器官发生关系的同时也与环境相互作用。为了涵盖以上所有交互内容，我们在2010年提出了“脑器交互”（BAC）这一概念，并于2020年提出了Bacomics (BAC+omics)这一名词，旨在构建一个整合大脑、身体和外部环境的统一框架[1, 117]。BAC可以分为三种不同类型的交互：脑-器官交互 (BAC-1)、脑-外部环境/设备交互 (BAC-2) 以及这两种交互的融合 (BAC-3) (图3)。

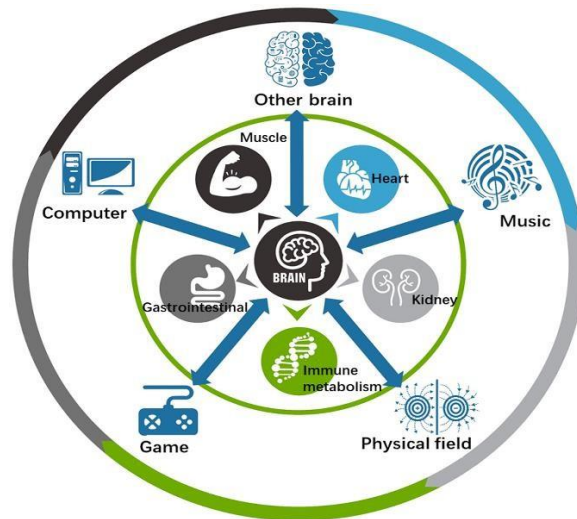


图3. BAC的概念： 大脑和身体器官之间的相互作用 (BAC-1) 在内部圆圈表示，大脑和外部设备/环境之间的相互作用 (BAC-2) 在外部圆圈中表示，同时内部和外部相互作用 (BAC-3) 由重叠部分表示。

BAC-1中脑和身体的整合构成了人类生长和发育的生理学基础。如大脑和心脏之间的相互作用近年来引起了越来越多的关注，相关研究也促进了心血管和脑血管疾病的诊断和治疗[118-125]。图4提供了大脑-内脏双向作用的示意图。脑肠轴理论提出，肠道微生物在神经发育和神经退行性疾病中起着关键作用，并可能调节神经精神疾病的发生和发展[126-132]。大脑与其他器官的活动也密切相关，如肌肉、胃、肺、肝和肾[133-139]。BAC-1还强调了大脑和免疫系统在神经免疫学和神经精神疾病中的相互依赖性[140]，不同类型的身体-大脑互动，如体育活动和舞蹈有益于大脑健康[141-144]。大脑和身体之间的相互作用涉及了中枢和众多外周系统的整合，BAC-1的深入活跃研究将为相关疾病的临床治疗干预带来新的选择[145]，也为打破认知、情感和意识之间，精神和身体之间的界限提供了独特的新理论。

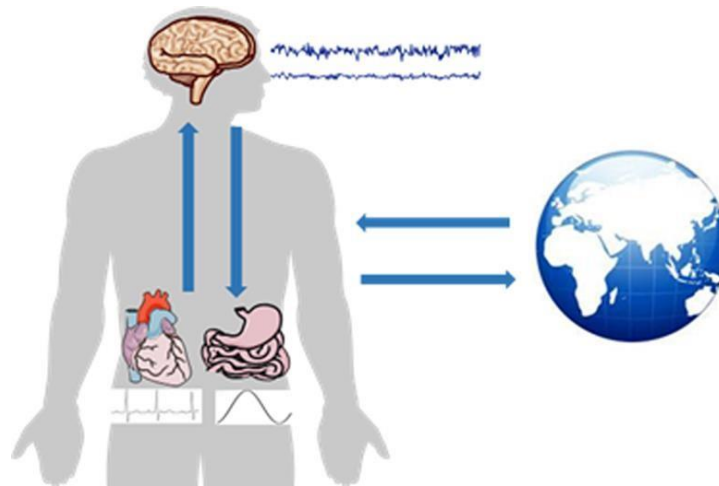


图4. 大脑与内脏的相互作用。

BAC-2代表大脑和非生物器官之间的互动，如上节中介绍的BCI，能够解析大脑信息并构建新的通道，实现大脑和外部设备之间的直接通信。图5给出了一个例子，脑瘫儿童通过运动想象BCI进行神经康复。近几年，闭环BCI受到越来越多的重视[146-148]。其中，经颅磁刺激(TMS)和经颅电刺激(tES)作为常见的神经调节技术，能够影响大脑区域和回路的兴奋性或抑制性，无创性地调节感知觉和认知能力，为临床干预和认知增强提供了重要选择[149-153]。此外，基于功能磁共振成像的神经反馈，能够实现皮层下-皮层回路的自我调节，为情绪调控提供了新手段[154]。总结众多关于BCI/BMI的评论或书籍[51, 78, 155-165]，我们认为BCIs发展的四大趋势在于：BCI已经从最初的基于电的范式发展到集成电、磁、声、光、代谢和其他输入和输出的范式；BCI硬件已经转向更灵活、无线、小型化、高通量和低功耗的设备；BCI的应用场景已经从运动功能的康复逐渐扩展到神经/精神疾病的干预和治疗，以及感知和认知能力增强；BCI与人工智能、大数据、数字医学、云技术相结合，实现从交互到智能编码/解码和智能集成的发展。



图5. 脑瘫儿童使用运动想象BCI进行神经康复治疗。

BAC-3代表BAC-1和BAC-2的融合，即融合智能。一方面，人类可以依靠大脑与外界的交互(BAC-2)完成技能获得和智力增强(BAC-1)；另一方面，BAC-2可以促进人体内自然通路的充分整合(BAC-1)，例如，在自然的运动通道不改变的情况下控制“第三只手”，可望有助于多任务处理[166]。除了面向大脑本身的研究之外，融合监测和调节外周器官的外周接口也已经成为诊断和治疗神经、代谢和免疫疾病的新选择[167]。在控制假肢方面，虽然BAC-2提供了一种有前途的方法，但将人工通道整合到用户的自然通道中可能仍是恢复残肢感觉的最佳解决方案[168]。因此，一些研究试图整合身体现有的视觉、感觉和运动通路，并通过对中枢或外周通路施加物理刺激来模拟感觉知觉，控制假肢或残肢，提高运动能力[169, 170]。此外，BAC-3可以将类脑智能(BAC-1)纳入BCI中(BAC-2)。通过将大脑的神经形态和功能特征与深度学习相结合，有望产生新的类脑网络模型，为人工智能和脑器智能(BAI)模型的发展提供新的途径。BAC1与BAC2的融合方式多样，如音乐、视频游戏(图6)、基于计算机的训练、针灸，这些方式在促进身心健康方面发挥着重要作用。例如，基于计算机的认知训练被证明对大范围的认知功能提升有利[171]；情感游戏作为一种新兴的调节方法，涉及广泛的生理互动和大脑-游戏双向互动[172]；具有穴位特异性的低强度电针激活迷走神经-肾上腺轴，可抑制全身炎症，证实了针灸的神经解剖学基础[173]。

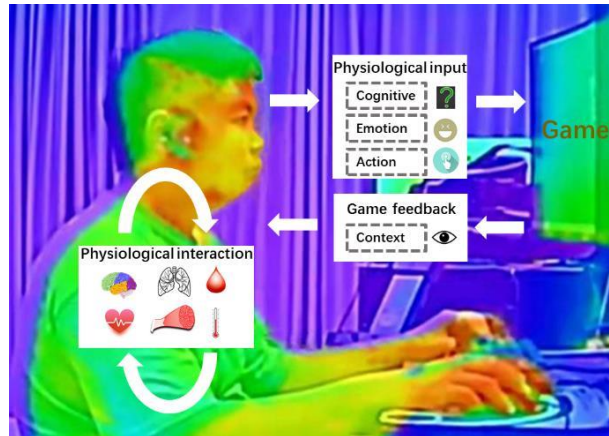


图6. 电子游戏过程中的红外图像。游戏过程涉及心理和生理(例如, 认知、情感和动作)输入、基于情境的反馈, 以及大范围的生理交互(例如, 大脑、心率、呼吸、肌肉、新陈代谢和皮肤温度)。

4. 大脑多样性和脑器交互

真实世界中的脑形态与功能各异。例如, 水母没有中央神经系统, 只拥有分散的神经元; 蚯蚓的大脑很小, 主要通过感知光线而不是控制肌肉来引导运动; 新杆状线虫有302个神经元, 决定了其行为的如趋化性和趋热性; 蟑螂有两个“大脑”, 分为前脑和后脑, 一个长在尾巴上, 失去头(前脑)的蟑螂仍可以存活约一周; 海豚在睡眠时“一心二用”, 大约2个小时会交换左右两侧大脑承担的任务; 章鱼是非常聪明的海洋生物, 它们的触手上也有大脑网络, 神经元数量超过了很多哺乳动物; 没有大脑或神经细胞的海绵已经存在了数亿年, 海绵被认为在其进化史中曾拥有神经细胞, 但后来由于缺乏使用而放弃了它们(因为它们只是停留在海床上, 滤食从它身旁流过的食物); 海星的手臂末端有眼睛, 可以察觉光照的差异, 感知光明和黑暗, 从而巧妙地避开捕食者, 但它们其实没有大脑或中枢神经系统。

大自然的丰富多彩启示我们大脑的出现与消失, 在相当程度上取决于脑与身体器官、外界环境的交互需要。可以想象, 我们人类大脑的演化过程也是遵循了类似的规则。如今我们的大脑越来越大, 内部的组织结构越来越复杂, 这是我们不断战胜自然灾害, 战胜其它物种的挑战, 从而进化到目前食物链顶端的生物基础。然而, 在人类面临日益复杂的内外环境, 包括越来越复杂精巧的人工产品, 以及太空、深海等全新自然环境, 与此同时, 人类和人脑的进化速度似乎略显蹒跚, 同时也受到生理、生化、能量供给、营养等生物学方面的约束限制。我们需认识到, 单纯进化的道路已经无法满足人类现实的发展需求。从这个意义上说, BCI的出现可以认为是突破生物学限制的尝试, 试图解决内部和外部的多重挑战。

目前, BAC-1无疑是人类关注的焦点, 但有一天大脑可能会完全依赖BAC-2的发展。当大脑和外部设备消除了生物限制, 一个真正意义上的“超人”可能会出现。因此, 理论上来说, 发展出具有纯粹BAC-2的赛博格是可能的, 但这需要很长时间, 并会引发许多伦理问题。如果我们摆脱了生物学的约束, 交互仅发生在外部环境和“虚拟大脑或数字孪生脑”之间[174], 一个纯粹的机器人世界可能最终会出现。如果这个机器人展示出自然进化的能

力，它最终可能会统治世界。然而，是否存在有大脑却没有身体的生物呢？宇宙学家提出的假设中，认为低熵宇宙可以产生许多低熵意识，即玻尔兹曼大脑，这些大脑摆脱了生物有机体的束缚，可能是比人类更具普遍性的存在[175]。

最后，我们对BAC的演化进行了推测，提出了图7中的五个演化模型。模型1代表一个没有大脑的身体；模型2代表具有脑-身体相互作用的有机体(BAC-1)；模型3代表大脑、身体和外部物体的协调(BAC-3=BAC-1*BAC-2)，这是目前的存在模式；模型4代表智能机器人的大脑(BAC-2)；而模型5代表高度智能的智能体(即只有大脑)。目前，我们正处于BAC发展中最令人兴奋的模式3，美好真实的世界在我们身边，无限可能的未来在等着我们创造。

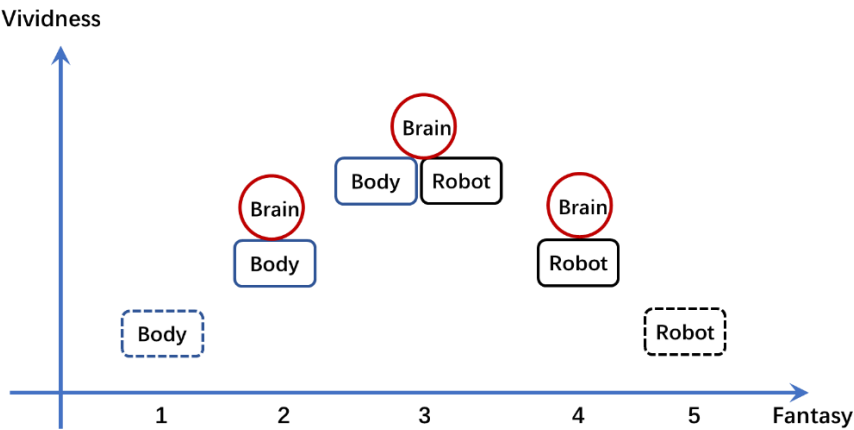


图7. BAC的五种模型。其中模型1和模型5是假设的，模型3反映了当前的现实。

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