also organize the cortical actomyosin cytoskeleton in syncytial structures, i.e. the *Drosophila* embryo and, in the case of ANI-2, the *C. elegans* oogenic gonad.

Do anillins act early or late in cytokinesis? *Drosophila* and *C. elegans* anillins recruit septins during contractile ring assembly. Via septin recruitment, ANI-1 is responsible for furrow asymmetry throughout ingression in the *C. elegans* zygote. Furrow initiation and ingression occur with comparable kinetics in *C. elegans* blastomeres depleted of ANI-1. However, when ANI-1 and Rho-kinase or ZEN-4 (the *C. elegans* MKLP1 homologue) are simultaneously depleted, cytokinesis is severely perturbed, suggesting that the early functions of anillins in cytokinesis can be compensated by other proteins. In contrast, human cells injected with anti-anillin antibodies displayed slow and abortive furrowing and, consistent with this, the ingression rate of the cellularization front is slower in *Drosophila* anillin mutant embryos. The idea that anillin's primary role is late in cytokinesis is supported by the observations that, in human and *Drosophila* cultured cells depleted of anillin, the majority of furrowing occurs normally, but later in cytokinesis the actomyosin cytoskeleton oscillates wildly along the spindle axis, and cytokinesis failure ensues.

How are anillins regulated? *S. pombe* Mid1p is hyperphosphorylated (probably by the Polo kinase Plo1p) upon relocation from the interphase nucleus to the cortex during mitosis. Metazoan anillins are also heavily phosphorylated, but the kinase(s) responsible is not known. In *Drosophila* and human cultured cells, anillin recruitment to the equatorial cortex depends on RhoA activity, but is independent of other cytoskeletal Rho downstream targets, including Rho-kinase, myosin and F-actin. Interestingly, post-anaphase activation of Rho is itself dependent on Polo kinase; thus, a parallel can be drawn between metazoan and fission yeast anillin regulation. After mitotic exit, proteolysis of human anillin is triggered by the anaphase-promoting complex/cyclosome (APC/C). *S. pombe* Mid2p is also regulated by ubiquitin-mediated proteolysis, indicating that its activity is actively limited to cell division. Anillins can be sequestered in the nucleus during interphase, with the exceptions of *Drosophila* anillin and *C. elegans* ANI-1 in early embryos, ANI-2 in the *C. elegans* oogenic gonad, and Mid2p in fission yeast. Thus, some anillins may regulate cytoskeletal dynamics in contexts other than the cytokinetic contractile ring.

Is anillin implicated in any diseases? Because it is essential for cell division, anillin is critical for development and homeostasis in metazoans. Anillin expression levels correlate with metastatic potential of human tumors from many different tissue origins. Inhibition of anillin expression suppressed the growth of lung cancer cells in culture. Considering that human anillin is normally degraded after mitotic exit and sequestered in the nucleus during interphase, its overexpression may overwhelm these normal regulatory mechanisms, freeing anillin to have an impact on the actomyosin cytoskeleton during events besides cytokinesis, including, for example, cell motility, and thus directly contribute to cancer progression.

Where can I find out more?

D'Avino, P.P. (2009). How to scaffold the contractile ring for a safe cytokinesis – lessons from Anillin-related proteins. J. Cell Sci. *122*, 1071–1079.
Field, C.M., and Alberts, B.M. (1995). Anillin, a contractile ring protein that cycles from the nucleus to the cell cortex. J. Cell Biol. *131*, 165–178.
Hall, P.A., Todd, C.B., Hyland, P.L., McDade, S.S., Grabsch, H., Dattani, M., Hillan, K.J., Russell, S.E. (2005). The septin-binding protein anillin is overexpressed in diverse human tumors. Clin. Cancer Res. 11:6780–6786.
Hickson, G.R.X. and O'Farrell, P.H. (2008). Anillin: a pivotal organizer of the cytokinetic machinery. Biochem. Soc. Trans. *36*, 439–441.
Maddox, A.S., Habermann, B., Desai, A. and Oegema, K. (2005). Distinct roles for two C. elegans anillins in the gonad and early embryo. Development *132*, 2837–2848.
Maddox, A.S., Lewellyn, L., Desai, A., and Oegema, K. (2007). Anillin and the septins promote asymmetric ingression of the cytokinetic furrow. Dev. Cell *12*, 827–835.

[1]Cytoskeletal Dynamics and Cell Division Laboratory, Institute of Research in Immunology and Cancer, Université de Montréal, C.P. 6128, Succ Centre-ville Montréal, QC Canada H3C 3J7.
[2]Département de Pathologie et de Biologie Cellulaire, Université de Montréal, C.P. 6128, Succ Centre-ville Montréal, QC Canada H3C 3J7.
*E-mail: amy.maddox@umontreal.ca

Primer

Working memory

Alan Baddeley

Working memory refers to the system or systems that are assumed to be necessary in order to keep things in mind while performing complex tasks such as reasoning, comprehension and learning. Over the last 30 years, the concept of working memory has been increasingly widely used, extending from its origin in cognitive psychology to many areas of cognitive science and neuroscience, and been applied within areas ranging from education, through psychiatry to paleoanthropology.

The term working memory was coined in 1960 by Miller, Galanter and Pribram in their classic book '*Plans and the Structure of Behaviour*', used in 1968 by Atkinson and Shiffrin in an influential paper [1], and adopted as the title for a multicomponent model by Baddeley and Hitch [2]. It is this use of the term that will concern the rest of the discussion. It is important to note, however, that the term working memory was adopted independently by Olton [3] in connection with the performance of animals, typically rats, in a multi-arm radial maze in which each arm was baited: the animals were given several trials per day and needed to remember which arm had already been visited on that day, in order to maximise reward. Within the human context, this would be regarded as a long-term memory task, demanding more than the brief limited capacity system that is assumed to comprise human working memory. Olton's concept is still sometimes used in studies based on animals, although primate studies typically use the term in the same way as it is used in studies on humans.

This concept of working memory evolved from that of short-term memory, the temporary storage of small amounts of material over brief periods of time. It became a topic of major interest during the 1960s, linked to an information-processing approach to psychology, in which the digital computer served as a theoretical basis for the development of psychological theories. This approach became known as cognitive psychology and has, in one form or another, become increasingly widely applied in subsequent years.

A very fruitful development stemmed from applying the concepts and methods of cognitive psychology to patients with brain impairment, an approach termed cognitive neuropsychology. While most brain-damaged patients typically suffer from a number of deficits, cases occasionally occur in which a single isolated cognitive function is impaired, while other functions are preserved, allowing theories to be tested directly. A very influential case was that of H.M. [4], who, following bilateral hippocampal surgery to relieve intractable epilepsy, became densely amnesic and unable to form ongoing memories. He could, however, perform normally on short-term memory tasks such as hearing and repeating back a telephone number. This dissociation between impaired long-term and preserved short-term memory also proved applicable to patients whose pure amnesia resulted from a number of different aetiologies. It was also shown to extend to a range of other tasks that were assumed to distinguish between long-term and short-term memory. Other patients, with damage to the left temporo-parietal cortex rather than the hippocampus, were reported to have exactly the opposite pattern of deficits, suggesting preserved long-term but impaired short-term memory.

This led to a conceptualisation of memory as comprising a succession of storage systems in which information flows from the environment, into a series of temporary sensory buffers, which are essentially part of perceptual processes, before being passed on to a limited capacity short-term memory store, which then feeds long-term memory. In the most influential of these models, Atkinson and Shiffrin [1] proposed that this short-term system acts as a working memory, controlling the flow of information into and out of long-term memory, and playing a crucial role in learning and in cognition more widely.

This model, however, ran into two problems. The first concerned the assumption that the mere maintenance of material in short-term

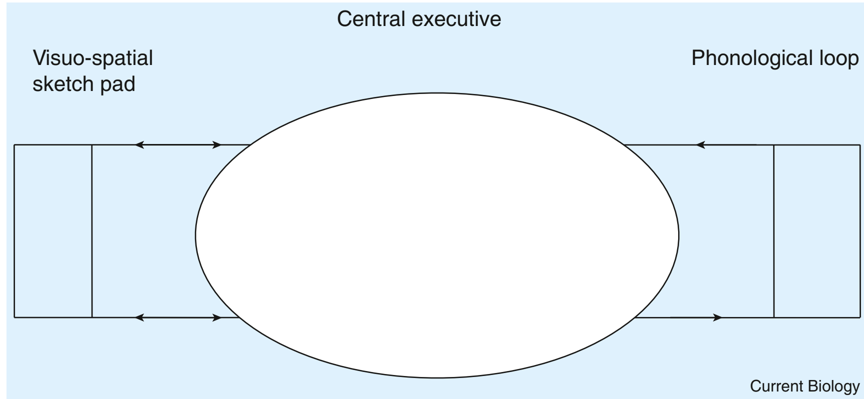

Figure 1. The model of working memory proposed in 1974 [2].

The earlier concept of the short-term memory has been elaborated to include an attentional controller and two modality based temporary stores. The components are assumed to interact, and to be linked to both perception and long-term memory.

memory would guarantee long-term learning. This proved incorrect, with degree of learning depending much more on the nature of the processing. Hence, processing a word in terms of its perceptual appearance or spoken sound is much less effective for subsequent learning than encoding the material on the basis of its meaning or its emotional tone [5]. The second problem came from the study of patients with a very specific short-term memory deficit as described by Shallice and Warrington [6]. According to the Atkinson and Shiffrin [1] model, in the absence of an adequate short-term memory, information should be rapidly lost and hence such patients should not be able to learn. Furthermore, if this system did indeed function as a working memory, patients with impaired short-term memory should be seriously cognitively handicapped. In fact, these patients appeared to show normal long-term learning and to live intact lives, one as a secretary, another as a taxi driver and a third running a shop.

Baddeley and Hitch [2] attempted to tackle this paradox by studying the effect of disrupting short-term memory on the capacity of normal people to perform complex tasks such as reasoning, comprehending and learning. We did so by combining such tasks with a concurrent activity that was assumed to depend on short-term memory, namely remembering and repeating back sequences of digits such as a telephone number. As the length of the sequence increases, the remaining available capacity of short-term memory should be reduced, and performance on the concurrent cognitive task progressively disrupted. We found that there was indeed a consistent effect, with speed of performance declining with sequence length, but impairment was far from catastrophic even with long digit sequences, and error rate was low and unchanged. In order to explain our results, we abandoned the unitary model, proposing instead a three-component model illustrated in Figure 1. This assumes an attentional control system, the central executive, aided by two short-term storage systems, one for visual material, the visuo-spatial sketchpad, and one for verbal-acoustic material, the phonological loop. We assumed that short-term memory patients had damage to the loop, and that in simulating such patients using concurrent digit memory, we had systematically loaded up the loop, at the same time as placing only a modest load on the rest of working memory.

Our model differed from that of Atkinson and Shiffrin [1] in a number of ways. Most obviously, we replaced the concept of a single system with one comprising at least three separable, but interacting, subsystems. Secondly, this form of interaction abandoned the assumption of a series of successive stages for a model capable of parallel processing across the subsystems. This is methodologically very important, as it rules out the use of methods in which the first

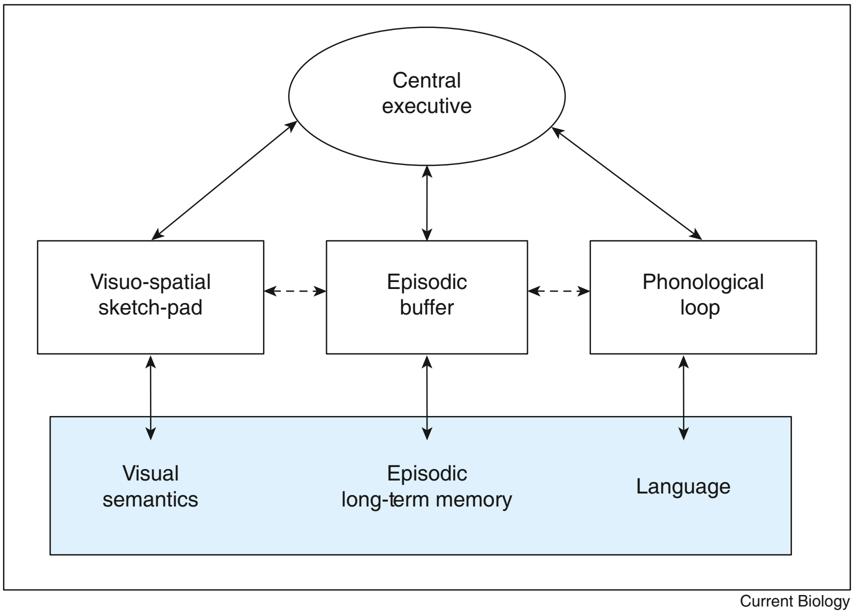

Figure 2. A later development of the multicomponent model.

It includes links to long-term memory and a fourth component, the episodic buffer that is accessible to conscious awareness.

few seconds are assumed to reflect pure short-term or working memory, and later measures pure long-term memory, an assumption that is still made in far too many studies. Long-term memory may well influence performance at every stage, meaning that other methods must be used to separate the two or more memory components that are likely to influence early performance.

The multicomponent model was offered as a broad theoretical framework that, if successful, would allow more detailed modelling of the three components. In choosing the term working memory, we aimed to stress that its role went beyond simple storage, allowing it to play an important role in cognition more generally, hopefully providing a framework and a set of techniques that could be applied practically to the wide range of activities for which working memory might be important.

The model has subsequently proved both useful and resilient, but has had to be supplemented by a fourth component, the episodic buffer (Figure 2). This is episodic in that it is capable of holding multidimensional episodes or chunks, which may combine visual and auditory information possibly also with smell and taste. It is a buffer in that it provides a temporary store in which the various components of working memory, each based on a different coding system, can interact through participation in a multidimensional code, and can interface with information from perception and long-term memory. The episodic buffer is assumed to have a limited capacity of about four chunks or episodes, and to be accessible through conscious awareness [7]. In its initial form, the buffer was assumed to play an active and attentionally-demanding role in binding together information from different sources, but further investigation suggests that it serves as a passive store rather than an active processor [8].

This broad theoretical framework has proved durable and has been widely used within both basic and applied psychology and in neuroscience more generally [7,9,10]. One reason for the survival of this broad framework is its simplicity, allowing more detailed theoretical development within the model, without the need for constant change. At this more detailed level, there have been many theoretical developments, some mainly behavioural, others based on detailed mathematical modelling while yet other approaches have been more neurobiologically oriented [9,10]. Rather than attempting to review this wide area, I will describe two topics that are relatively close to the multicomponent model and that have seen development, controversy and practical application. One concerns the concept of a phonological loop and the other involves the study of individual differences in working memory capacity as a means of investigating the basis of executive control.

We proposed in our initial theorising that the phonological loop has two major features. The first is a store in which speech-like memory traces are registered and will spontaneously fade within about two seconds. The second is a process whereby such traces can be refreshed by verbal or subvocal rehearsal, an activity that takes place in real time. Blocking rehearsal by requiring the continuous utterance of an irrelevant sound — for example, repeatedly saying the word ‘the’ — will prevent the transformation and storage of a visual stimulus, such as a printed letter or word, as a phonological encoded spoken item. Evidence for reliance on a speech-like memory store comes from the phonological similarity effect. Immediate recall of a sequence of words is grossly impaired when they are similar in sound. Hence the sequence Map, Cat, Cap, Mat, Can is harder to recall immediately than Pit, Day, Cow, Tub, Pen. Similarity of meaning on the other hand, as in the sequence Huge, Wide, Long, Big, Tall, has little effect on immediate recall. But when list length is increased to ten words, and several learning trials are allowed, forcing reliance on long-term memory, the pattern reverses, with meaning becoming the crucial factor [2].

Evidence for the importance of subvocal rehearsal comes from the word length effect, whereby immediate recall declines as the length of the words to be remembered increases [11]. The longer it takes to say the words in the sequence, the more the forgetting that will occur. Uttering a sequence of irrelevant sounds stops you rehearsing the words and hence abolishes the word length effect. Evidence from the study of neuropsychological patients fits the model well [12], as illustrated in Figure 3.

An attempt to investigate the possible evolutionary significance of the phonological loop led to the hypothesis that it facilitates the new phonological learning that is necessary for learning to produce new words. Patients with phonological loop impairment can learn meaningful material at a normal rate, but have great difficulty in learning foreign language vocabulary. Further evidence for the language learning function of the loop comes from a range of further sources. Children with specific language impairment typically have poor short-term memory, and are slower in acquiring new vocabulary. In the case of normal children, size and rate of increase in vocabulary during early years is influenced by phonological loop capacity [13].

Aspects of this evidence remain controversial. More specifically, it is by no means generally accepted that forgetting within the short-term store reflects a fading memory trace, rather than some form of interference from other material. It is also the case that older children can typically cope with a phonological-loop deficit without major language acquisition problems, so long as they have good executive processing. These are issues of both theoretical and practical importance, but do not present a major challenge to the overall concept of a phonological loop. Other critics argue that the phonological loop should be regarded simply as part of the language processing system, rather than regarding it as a supplementary store. However, while the loop has almost certainly evolved from mechanisms for speech perception and production, the fact that patients with grossly impaired phonological short-term memory may have normal speech perception and production argues for a separate system, although this is strongly linked to language processing [12].

My second example is linked to the concept of a central executive, a term that refers to the system whereby working memory is controlled, leaving open the question of whether this involves a single unitary controller, or as seems more likely, an emergent alliance of executive processes. An influential approach to this issue uses correlational methods in which differences between individuals on specific working memory tasks, typically referred to as working memory span, are linked to more general measures of cognition such as prose comprehension or academic performance. The classic initial study in this area [14] required college students to read out a sequence of unrelated sentences, and then recall the last word of each sentence. People can usually manage only three or four sentences; this comprises their working memory span. Surprisingly, this simple measure proved to correlate well with the prose comprehension component of a widely used college aptitude test. This finding has been replicated many times, and extended to many other ways of measuring working memory span, provided they require simultaneous storage and processing. Such span measures have been shown to predict performance on many cognitive tasks, ranging from rate of learning programming skills to performance on the type of reasoning task used in intelligence testing [15].

Gathercole and colleagues [16] have used variants of the working memory span measure as part of a broader working memory battery that is proving useful in education, where it is able to identify children at risk of subsequent academic difficulties, enabling teachers to anticipate future problems and provide help. But despite the success of the individual difference-based approach to working memory, there is no widely accepted explanation of precisely what processes underpin the predictive capacity to these complex working memory tasks. Engle and Kane [15] emphasise the role of inhibition in suppressing interference from irrelevant information, while others stress the

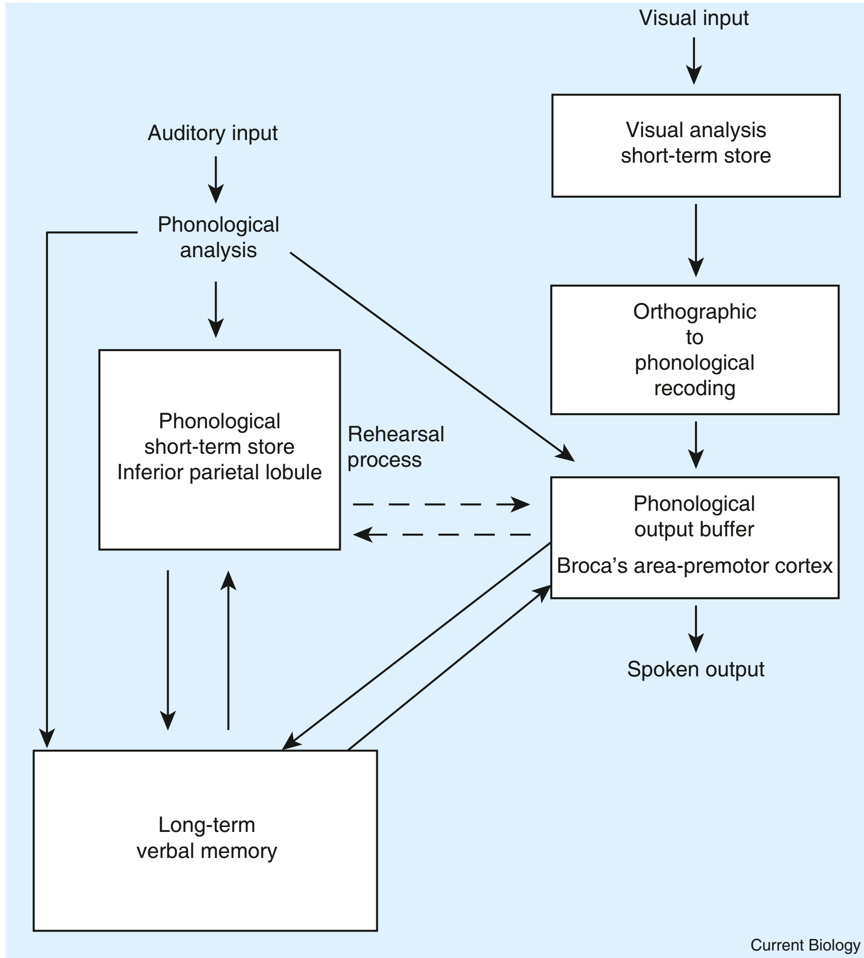

Figure 3. A more detailed formulation of the phonological loop model based on both behavioural and neuropsychological evidence [12].

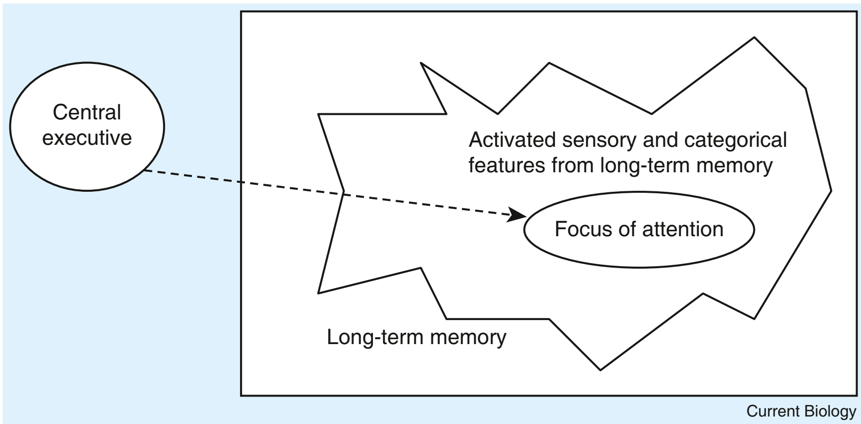

Figure 4. Cowan's model, which treats working memory as the temporary activation of areas of long-term memory.

capacity to divide or switch attention [17], or to update and maintain information [18].

This is clearly an important and lively area that can readily be fitted into the broader multicomponent model of working memory, although not all investigators would necessarily choose to do so. Some prefer an alternative framework proposed by Cowan [19], whose influential embedded processes model is illustrated in Figure 4. Cowan defines working memory as "cognitive processes that retain information in an unusually accessible state". Activation occurs in long-term memory, is temporary, and fades unless maintained by verbal rehearsal or continued attention. Cowan [19] emphasises the focus of attention, which he suggests has a limit of about four items or chunks.

Cowan's model is often seen as inconsistent with our own. It can, however, be interpreted as an attempt to specify the interface between the attentionally-limited central executive and the storage-limited episodic buffer components of the multicomponent model. Cowan accepts the importance of verbal rehearsal, has made important contributions to its analysis and takes a position broadly similar to the phonological loop concept. Furthermore, although Cowan's model appears to assign everything outside the attentional focus of his model to activated or inactive long-term memory, this seems to be a kind of shorthand for declaring it outside his central remit, rather than proposing that this constitutes a developed theory.

There is no doubt that working memory does depend on activated long-term memory in many ways. For example, memory for a telephone number spoken in your native language is substantially better than that for a number spoken in a foreign language, reflecting the importance of long-term phonological knowledge in short-term verbal memory. The capacity to remember and repeat a string of unrelated words is about five items, but if they comprise a meaningful sentence, the span is around 15 words, reflecting a contribution from grammar and meaning, both depending on different aspects of long-term memory. Hence, it is unsurprising that neuroimaging studies of short-term or working memory tasks also tend to activate areas associated with long-term memory. The crucial question is not whether long-term memory is involved in working memory, but how. In what ways do long-term and working memory interact? [7]. Hence, in practice, Cowan and I tend to agree with each other on most aspects of our respective theories, despite using very different theoretical metaphors, his derived from an initial focus on attention, my own influenced by studies of short-term verbal memory.

In conclusion, in surviving for over 30 years, the concept of a multicomponent working memory has provided a useful theoretical framework for investigating a wide range of human activities, at the same time generating both controversy and progress in the task of understanding the role of memory in our capacity to think.

References

1. Atkinson, R.C., and Shiffrin, R.M. (1968). Human memory: A proposed system and its control processes. In K.W. Spence and J.T. Spence (Eds.), The Psychology of Learning and Motivation: Advances in Research and Theory. (Vol. 2, pp. 89–195). New York: Academic Press.
2. Baddeley, A.D., and Hitch, G.J. (1974). Working memory. In G.A. Bower (Ed.), Recent Advances in Learning and Motivation (Vol. 8, pp. 47–89). New York: Academic Press.
3. Olton, D.S. (1979). Mazes, maps, and memory. Am. Psychol. *34*, 583–596.
4. Milner, B. (1966). Amnesia following operation on the temporal lobes. In Amnesia, C.W.M. Whitty and O.L. Zangwill (Eds.) (London: Butterworths) pp. 109–133.
5. Craik, F.I.M., and Lockhart, R.S. (1972). Levels of processing. A framework for memory research. J. Verb. Learn. Verb. Behav. *11*, 671–684.
6. Shallice, T., & Warrington, E. K. (1970). Independent functioning of verbal memory stores: A neuropsychological study. Q. J. Exp. Psychol. *22*, 261–273.
7. Baddeley, A.D. (2007). Working Memory, Thought and Action (Oxford: Oxford University Press.)
8. Baddeley, A.D., Hitch, G.J., and Allen, R.J. (2009). Working memory and binding in sentence recall. J. Mem. Lang. *61*, 438–456.
9. Miyake, A., and Shah, P. (eds.). (1999). Models of Working Memory: Mechanisms of Active Maintenance and Executive Control (New York: Cambridge University Press).
10. Repovs, G., and Bresjanak, M. (2006) Special Issue: Cognitive neuroscience of working memory. Neuroscience *139*, 1–413.
11. Baddeley, A.D., Thomson, N., and Buchanan, M. (1975). Word length and the structure of short-term memory. J. Verb. Learn. Verb. Behav. *14*, 575–589.
12. Vallar, G. (2006). Memory systems: The case of phonological short-term memory. A festschrift for cognitive neuropsychology. Cogn. Neuropsychol. *23*, 135–155.
13. Baddeley, A.D., Gathercole, S.E., and Papagno, C. (1998). The phonological loop as a language learning device. Psychol Rev. *105*, 158–173.
14. Daneman, M., and Carpenter, P.A. (1980). Individual differences in working memory and reading. J. Verb. Learn. Verb. Behav. *19*, 450–466.
15. Engle, R.W., and Kane, M.J. (2004). Executive attention, working memory capacity, and a two-factor theory of cognitive control. In The Psychology of Learning and Motivation, B. Ross (ed.) (New York: Elsevier) Vol. 44, pp. 145–199.
16. Gathercole, S.E., Lamont, E., and Alloway, T.P. (2006). Working memory in the classroom. In Working Memory and Education, S. Pickering (ed.) (London: Elsevier Press) pp. 220–241.
17. Barrouillet, P., Bernardin, S., and Camos, V. (2004). Time constraints and resource sharing in adult's working memory spans. J. Exp. Psychol. Gen. *33*, 570–585
18. Miyake, A., Friedman, N.P., Emerson, M.J., Witzki, A.H., Howerter, A., and Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: a latent variable analysis. Cogn. Psychol. 41, 49–100.
19. Cowan, N. (2005). Working Memory Capacity (Hove: Psychology Press).

Department of Psychology, University of York, York YO10 5DD, UK.
E-mail: a.baddeley@psych.york.ac.uk