



In Defense of Methodological Mechanism: the Case of Apoptosis

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I am not afraid of
mechanisms,
but I'm afraid of
the metaphysics of
mechanisms

1. Introduction

Main aim: propose a **minimal way** of understanding mechanisms and argue that this conception is sufficient in order to have an illuminating account of **scientific practice**.

discuss a central example of a biological mechanism, the **mechanism of cell death**, known as *apoptosis*.

use this case in order to advance the philosophical position of '**methodological mechanism**'

2. From Metaphysics to Practice: the **Truly Minimal Account of Mechanisms**

Until the 1980s, dominant view about mechanisms
metaphysical

- > Mechanism as a view about **causation**
- > Providing the **missing link** between cause and the effect.
- Various accounts: mark transmission (Salmon 1984), persistence, transference or possession of a conserved quantity (Mackie 1974; Salmon 1997; Dowe 2000).
- In the 1990s emergence of the **new mechanical philosophy**
Not a view about causation *per se*

-Three dominant accounts of mechanism:

Mechanisms are **entities and activities organized** such that they are **productive** of regular changes from start or set-up to finish or termination conditions

(Machamer, Darden, & Craver 2000, 3)

A mechanism for a behavior is a complex system that **produces** that behavior by the **interaction of a number of parts**, where the interactions between parts can be characterized by **direct, invariant, change-relating generalizations**.

(Glennan 2002, S344)

A mechanism is a structure performing a function in virtue of its **component parts, component operations, and their organization**. The orchestrated functioning of the mechanism is responsible for one or more phenomena.

(Bechtel & Abrahamsen 2005, 423)

Key claims of the New Mechanists:

1. The **world consists of mechanisms**.
2. A mechanism **consists** of **objects** of diverse kinds and sizes structured in such a way that, in virtue of their **properties and capacities**, they engage in a **variety of different kinds of activities and interactions** such that a certain behavior B or a certain phenomenon P is brought about.
3. To **explain** a certain behavior B or a certain phenomenon P in science is to offer the mechanism of it.

- Global** accounts of what a mechanism is
- a metaphysical aspect of the project of the new mechanists:
 - ‘**metaphysically inflated**’ accounts of mechanism
 - i.e. all committed to a certain **metaphysics of mechanisms**, and in particular to a certain “**new mechanical ontology**” (Glennan forthcoming)

This “**new ontology**” of entities, activities, interactions, organization of parts into wholes and the like creates the **further philosophical need**—which mechanists try to meet—to explain what they are and how they relate, if at all, with more traditional **metaphysical categories**.

Less metaphysically committed view of mechanisms:

“a mechanism for a phenomenon consists of **entities and activities organized in such a way that** they are responsible for the phenomenon” (Illari & Williamson 2012, 120).

Glennan's *Minimal Mechanism*:

A mechanism for a phenomenon consists of **entities (or parts) whose activities and interactions are organized so as to be responsible for the phenomenon.**

-> Glennan takes it that an advantage of this minimal account is that **mechanisms are everywhere** constituting “the causal structure of the world” (forthcoming, Ch. 2).

But these minimal accounts still invite a number of **metaphysical questions** that are **irrelevant to scientific practice.**

-> For instance, questions concerning the status of entities, their difference from activities, the need to introduce both activities and interactions, the role of the organization in the performance of the function etc.

-These questions are perhaps philosophically legitimate, but **need not be asked and answered for an understanding of the role of mechanisms in science.**

All these accounts **inflate the concept of mechanism as this is used in science.**

Pathologists on the causes and mechanisms of diseases:

-> **causal agents** (e.g. viruses) that constitute the **aetiology** of a disease

-> **pathogenesis**, which concerns the **mechanisms**, i.e. the *causal pathway* that leads from the causal agent to a disease state (e.g. Lakhani et al. 2009).

-In the practice of science, *the description of the causal pathway in the language of theory* is enough for the identification of the mechanism.

Little further interest in understanding it according to a certain theory of causation, or to characterize it in terms of entities bearing powers or engaging in activities, or being involved in activities *and* interactions and the like.

A very general way to understand what biologists mean by a 'mechanism' in most (if not all) contexts is this:

a mechanism is (simply) the way [causal pathway] a result is brought about.

Truly Minimal Mechanism (TMM).

(TMM): mechanism = causal pathway

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'Mechanism' concerns how causes (described in the language of theories) operate to bring about a certain effect.

-To identify a mechanism is to identify **a specific causal pathway** that connects an initial 'cause' (the causal agent) with a specific result.

if there is a cause for a specific effect, **there exists a mechanism that accounts for how the cause operates.**

The scientific task, then, is to identify the causal pathway.

-Identification of the causal pathway is crucial in order **to establish that a causal link exists** between a putative causal agent and a result (e.g. a disease state).

-But moreover, knowing the causal pathway makes **interventions possible** (and in the case of pathology, treatment).

3. Methodological Mechanism

Woodger on methodological mechanism

Part of the inspiration for TMM comes from what J. H. Woodger called “methodological mechanism” (MM).

-Woodger (1929): **two ways** a notion can be employed: a **metaphysical or ontological** way and a **methodological** one.

-The latter is when a notion is used for the purposes of description “independently of its metaphysical interpretation”.

-In this case, the notion “is employed methodologically, i.e. simply for the purpose of investigation” (1929, 31).

-The advantage of this use is that the notion can be used in a certain practice and cast light on it **independently of whatever difficulties (and controversies) are raised by the intricate metaphysical debates concerning what its worldly reference is really like.**

Woodger on methodological mechanism

-In adopting this view, Woodger noted that mechanism is a “methodological postulate” which as such “makes no assertions about the nature of the processes studied, but merely asserts that **they take place according to law, or ‘work in an orderly way’**” (1929, 258).

MM is not about the **metaphysics of mechanism** but about the use of the concept of mechanism in science and in particular about the **importance of identifying causal pathways**.

Our claim: **commitment to mechanism in science is adopting a methodological postulate which licenses looking for the causal pathways for the phenomena of interest.**

Hence, MM licenses adopting TMM.

Description of mechanisms in the language of theory

Brandon (1990, 185):

“A causal/mechanical explanation is one that explains the phenomenon of interest in terms of the mechanisms that produced the phenomenon. **What is a mechanism?** ... [T]his question has **no general metaphysical answer**, because the business of science is the discovery of mechanisms; so **we cannot delimit in any a priori manner the mechanisms of nature**. ... The best we can do is to give an open-ended answer: **a mechanism is any describable causal process**”.

Viewing mechanism as a **methodological** thesis allows that the sought-after identification of the **causal pathway** by which a specific result is produced, is fully captured in **the language of the specific theory, using deeply theory-laden concepts**.

MM philosophically neutral

- MM is non-committal about fundamental ontology.
- TMM allows for a rich understanding of the use of this concept in biology (and other sciences) without getting embroiled in a debate about what things in the world **mechanisms really are** and what kind of **metaphysical categories** their (theory-described) **components** fall into.

MM says **nothing about**:

- > how causation itself is to be understood
- > what the fundamental ontology of the world is
- > how the various levels of mechanisms relate to each other

No need to say something 'deeper' than TMM in order to have a useful concept of mechanism that elucidates practice.

MM not scientifically neutral

Are there alternative methodological standpoints
(i.e. standpoints which explain non-
mechanistically)?

Yes!

-> Boyle: explanations that use Aristotelian
substantial forms

-> vitalism

MM and the machine analogy

- Life scientists often talk about organisms or parts of organisms as kinds of **machines**
- Question: does this require that MM should be modified in some way?
- The **machine analogy** does not add much to MM

Lakhani et al. (2009):

They stress that they “will adopt a **strongly biomedical concept of disease**. This is a **mechanistic model** that regards the **body as a machine** with repairable or replaceable parts. It looks for **specific underlying biological causes** and places a high emphasis on the scientific evidence-base for untangling **cause and effect** in both the disease and its treatment, because this is important for patient care and prognosis” (2009, 4).

But although they adopt a mechanistic model, “it is a **complex model** with multiple parts that **interconnect**. A change in one area is likely to affect another. Thus maintaining homeostasis is not a simple single feedback loop and it is perfectly acceptable that a **new equilibrium** is achieved under a new set of circumstances, a new baseline; you do not have to return to the original state” (2009, 4).

To say that the body is a **machine** is to say that the body contains various **interacting parts** that underlie bodily functions and sometimes result in diseases, such that it is possible to identify **cause and effect relationships** and to **intervene** to treat parts that malfunction.

-Hence, the ‘mechanistic model’ mentioned by Lakhani et al. **is an instance of TMM.**

4. Methodological Mechanism at Work: the Case of Apoptosis

The best argument in favor of MM and TMM:

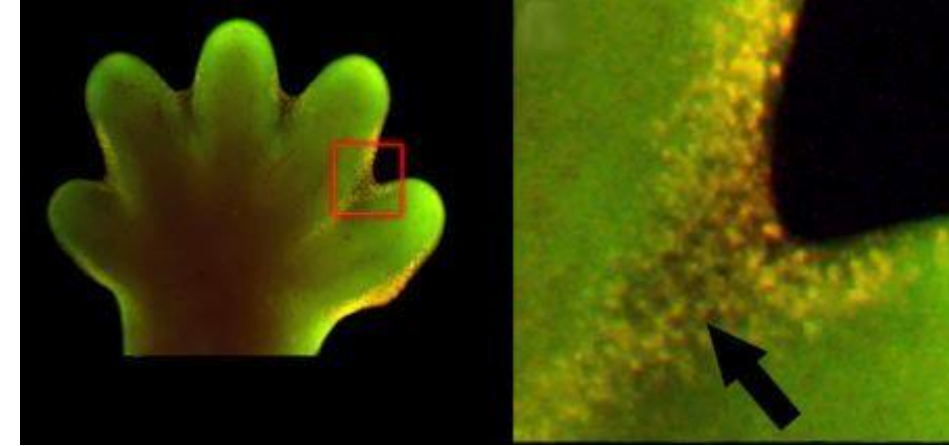
-> the **argument from scientific practice**:

This is the conception of mechanism one finds in scientific contexts where the language of mechanisms is used.

A central example of a type of biological mechanism, i.e. the **mechanisms of cell death**.

A case in which **a new mechanism**—what came to be known as **apoptosis**—was **identified**.

- Cell death known since the 19th century
- But until the 70s, **not much interest** from biologists



from Bandyopadhyay et al. (2006)

-> developmental biologists an exception

Saunders: “abundant death, often cataclysmic in its onslaught, is a part of early development in many animals; **it is the usual method of eliminating organs and tissues that are useful only during embryonic or larval life** or that are but phylogenetic vestiges” (Saunders 1966, 154).

-The reason is that biologists “tended to think that death was **accidental** and that mitosis was the active homeostatic process”—cell death was not yet viewed as a “**biological process**” (Lockshin 2008, 1092).

New era in the study of cell death after the 1960s due to new technological developments (e.g. electron microscopy, improved histological techniques)

John Kerr discovers shrinkage necrosis

Kerr, who had been working on the processes of cell death since the 1960s notes that at the time most researchers were “equating cell death with **cell degeneration**” (Kerr 2002, 472).

-So, an early hypothesis was that cell death was the **result of damaged lysosomes**, which were viewed as “**suicide bags**”.

-Kerr, by studying ischaemic liver injury, discovered a type of cell death that was “**non-degenerative** in nature” (because lysosomes were **preserved**; in classical necrosis they ruptured)

-He names it “shrinkage necrosis” (Kerr 1971)

-> **thinks that it is a type of necrosis**

“[s]hrinkage necrosis is a distinct and important type of cell death, which has received relatively little attention in the past. It probably results from **noxious stimuli that are insufficiently severe to produce coagulative necrosis**” (Kerr 1971, 19).

But soon Kerr noted that it was a different kind of mechanism—what he called “apoptosis”.

Description of apoptosis

Apoptosis was introduced in a seminal paper in 1972 (Kerr, Wyllie & Currie 1972)

It was described as “**a hitherto little recognized mechanism of controlled cell deletion**” (1972, 239).

-What did Kerr do to identify the mechanism of apoptosis?

He described it in the **language of theory** as a “vital biological phenomenon”, which is “**complementary to mitosis in the regulation of animal cell populations**” (241).

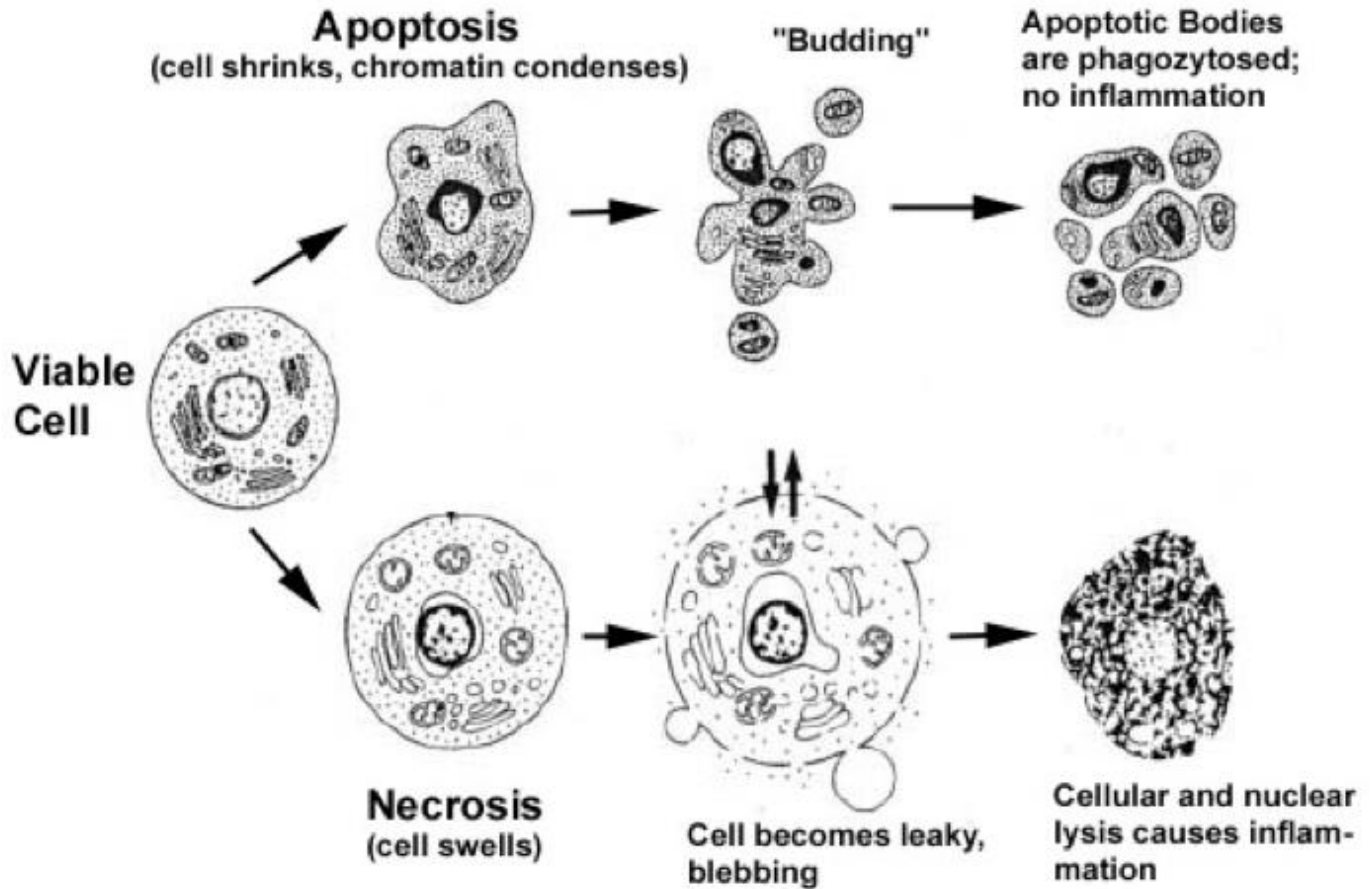
i) apoptosis is a **distinctive morphological process**

Main morphological changes during apoptosis (as shown by electron microscopy):

-> nucleus and the cytoplasm **condense**, nucleus **fragments** and **protuberances** are formed on the surface of the cell.

-> cell breaks apart and from the protuberances the **apoptotic bodies** are formed. (Spherical membrane-bound structures that contain condensed, but otherwise **intact and functional, cell organelles and fragments of nuclei**)

apoptotic bodies are **phagocytosed** and degraded by other cells.



ii) apoptosis is **ubiquitous**

-morphological changes that occur during apoptosis “essentially the same” (244) in **various types of circumstances** (both physiological and pathological), for example:

- > it occurs spontaneously in both treated and untreated **malignant tumours**
- > it is involved in cases of **pathological atrophy** but also of **normal involution** of tissues
- > in **normal development** (e.g. during the development of digits)
- > in general in **cellular turnover** in normal adults

Reconstruction of the argument in Kerr et al (1972):

- i) apoptosis is a **distinctive morphological process**
- ii) apoptosis is **ubiquitous**
- iii) apoptosis is **non-disruptive** (in contrast to necrosis, **absence of inflammation**)
- iv) apoptosis triggered by **physiological stimuli**
- v) Kerr et al: a form of “physiological cell death” that is at work **balancing divisions in cell populations** must exist
- vi) necrosis **cannot play that role**
- vii) apoptosis is **well suited to play that role**

-> Kerr et al: apoptosis “is well suited to a role in tissue homeostasis, since it can result in extensive deletion of cells with little tissue disruption” (250).

Conclusion: apoptosis has a crucial regulatory role within the organism

-> it “subserves a **general homeostatic function**” (Kerr 2002, 471).

So:

Apoptosis is “a **distinctive morphological process** (...) which **plays a complementary but opposite role to mitosis in the regulation of animal cell populations**” (255-6).

-> this is the most important **difference** with **necrosis**

-> so, now apoptosis is not described as a **type** of necrosis anymore, but it is **contrasted** with necrosis

-description of apoptosis shows that **full knowledge of the causal pathway not necessary for the identification of the mechanism.**

-> Kerr et al.: “the mechanism” of **condensation** “still **unknown**” (244).

-> also, little was known “of the **factors that initiate apoptosis or of the nature of the cellular mechanisms activated before the appearance of the characteristic morphological changes**” (255).

-But **enough of its causal pathway was known** to conclude that “[t]he ultrastructural features of apoptosis and its initiation and inhibition by a variety of environmental stimuli suggest to us that it is **an active, controlled process**” (256).

Apoptosis becomes an important biological mechanism

- Since its first conception in 1972, apoptosis has become a **fundamental research area** in biology.
- By the middle 1970s it was broadly recognized that “**cell death was as much a part of cell biology as mitosis**, extension of an axon, the enzymatic sequence of glycolysis, or secretion” (Lockshin & Zakeri 2001, 547).
- By the middle 1990s, cell death “was recognized as **an interesting and biological event**”; it was seen not just as “an incidental part of life”, but as “**a highly controlled and medically important element of existence**” (Lockshin & Zakeri 2001, 545).

The reason why apoptosis was transformed into a central field of biological research was the realization of its **central role in many functions within the organism.**

-> **First**, it was discovered that apoptosis was **much more common** than was initially thought.

-> **Second**, it was established that apoptosis was **genetically based**, with various **conserved genes** that control cell death identified.

-> **Third**, relation between apoptosis and fields such as **immunology** and **cancer research**.

realisation of **clinical relevance** of apoptosis

PERSPECTIVES



Figure 3 | **Scientists active since 1945 in the field of cell death.** Top panel: Viktor Hamburger (photo services, Washington University); John W. Saunders Jr.; J.R. Tata; R.A.L. at the 1995 Gordon conference. Bottom panel: H. Robert Horvitz at the 1995 Gordon conference; John Kerr; A. R. Currie (reproduced with permission from Lothian Health Services Archive); Andrew Wyllie, at the 1995 Gordon conference. Photos from the 1995 Gordon conference are courtesy of the Gordon Research Conferences Archives.

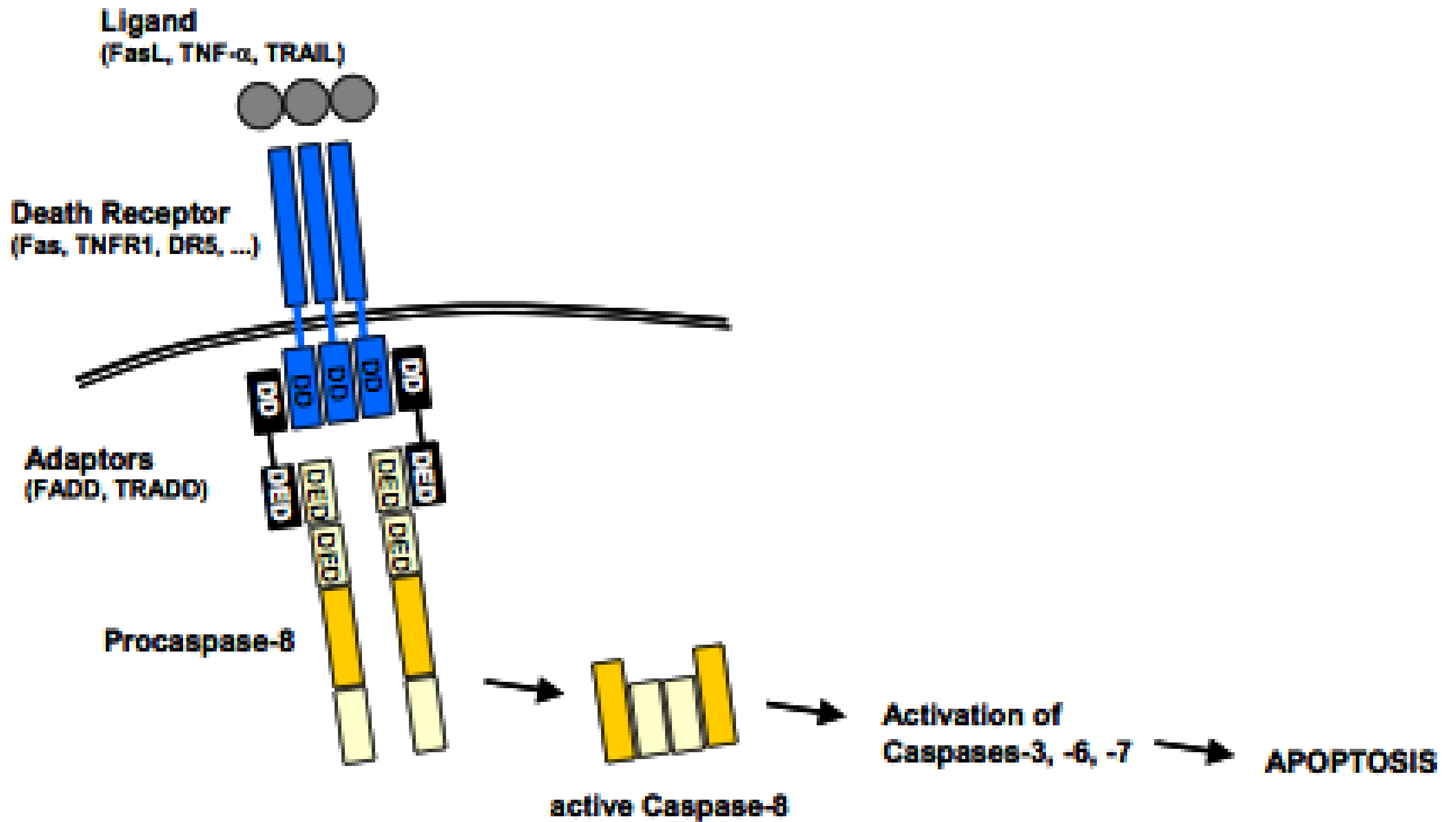
Signalling pathways of apoptosis

- > recent decades: **biochemical description** of the causal pathway of apoptosis
- > main events of the mammalian apoptosis pathway:
 - two distinct **signaling pathways**
 - intrinsic pathway** (apoptotic signal comes from **inside the cell**)
 - extrinsic pathway** (apoptotic signal comes from **outside**)
 - caspase cascade** common to both pathways
 - > caspases: **enzymes** that perform **proteolysis**
 - > they exist in the cytoplasm under **normal** conditions in **inactive form**
 - > for apoptosis to occur, some **caspases** need to be **activated**
 - > in turn, these active **caspases activate other caspases** -> **caspase cascade**

extrinsic pathway

extrinsic signal: binding of an extracellular **death ligand** to a **death receptor**, e.g. Fas ligand of T-lymphocytes binds to Fas receptor

- > **Fas ligand** binds to **Fas receptor** (protein located on cell surface)
- > **adaptor protein** binds to (intracellular domain of) Fas receptor
- > **procaspase-8 or 10** binds to adaptor protein
- > formation of **DISC** (Death Inducing Signalling Complex)
- > activates caspases-8 or 10
- > caspases-8 or 10 activate **effector caspases**
- > effector caspases destroy proteins

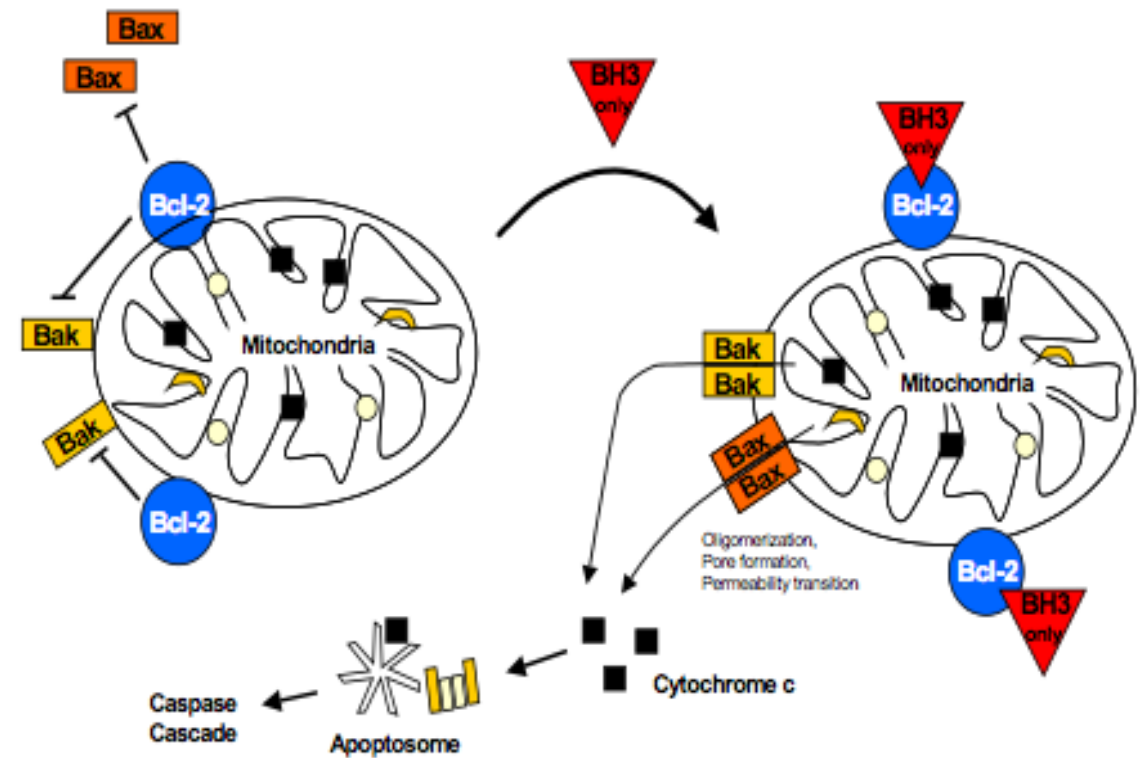


the extrinsic signalling pathway, from Gewies (2003)

intrinsic pathway

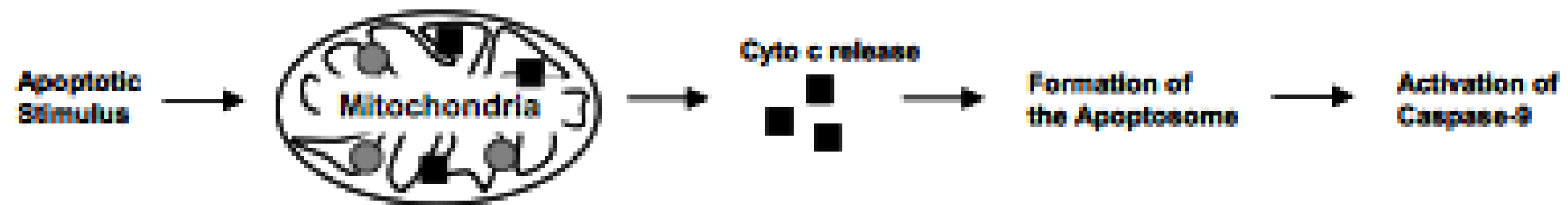
intrinsic signal, e.g. irreparable DNA damage
-> central components in the regulation of the intrinsic signaling pathway is the **bcl-2 family of proteins**

- > DNA damage
- > synthesis of **pro-apoptotic bcl-2** proteins (e.g. Puma, Noxa)
- > they inhibit **anti-apoptotic bcl-2** proteins (e.g. Bcl-2 and Bcl-xL)
- > **pro-apoptotic bcl-2** proteins (Bax, Bak) can form channels in outer mitochondrial membrane
- > release of **cytochrome c** (a mitochondrial protein) into the cytosol
- > cytochrome c binds to **Apaf-1** (Apoptotic protease activation factor 1)
- > Apaf-1 proteins form **apoptosome**
- > apoptosome activates **caspase-9**
- > caspase-9 activates the **effector caspases**
- > effector caspases destroy proteins

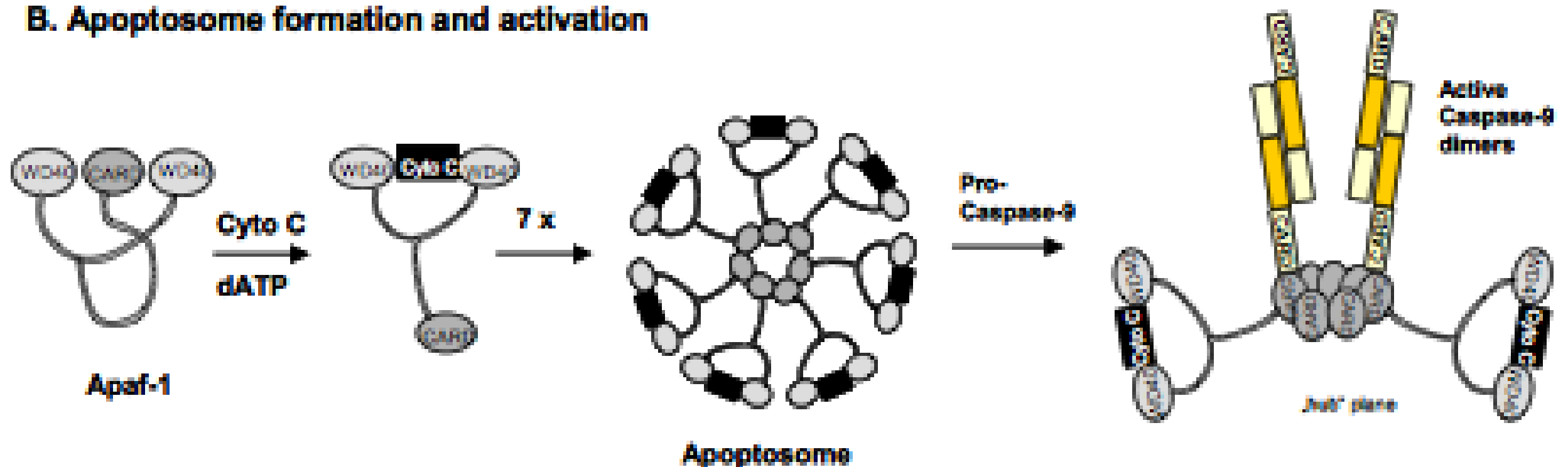


from Gewies
(2003)

A. Mitochondrial pathway of caspase activation



B. Apoptosome formation and activation



the intrinsic signalling pathway, from Acehan (2002)

5. Mechanisms of Cell Death

-An important issue that crops up here for MM is how the various causal pathways are **identified** and **distinguished** from each other.

Could it be the case that some causal pathways are **mechanisms in a more robust sense** (e.g. apoptosis) while others are **merely causal pathways** (e.g. necrosis)?

Apoptosis and necrosis

(Majno & Joris 1995):

Apoptosis: a process that leads to cell death

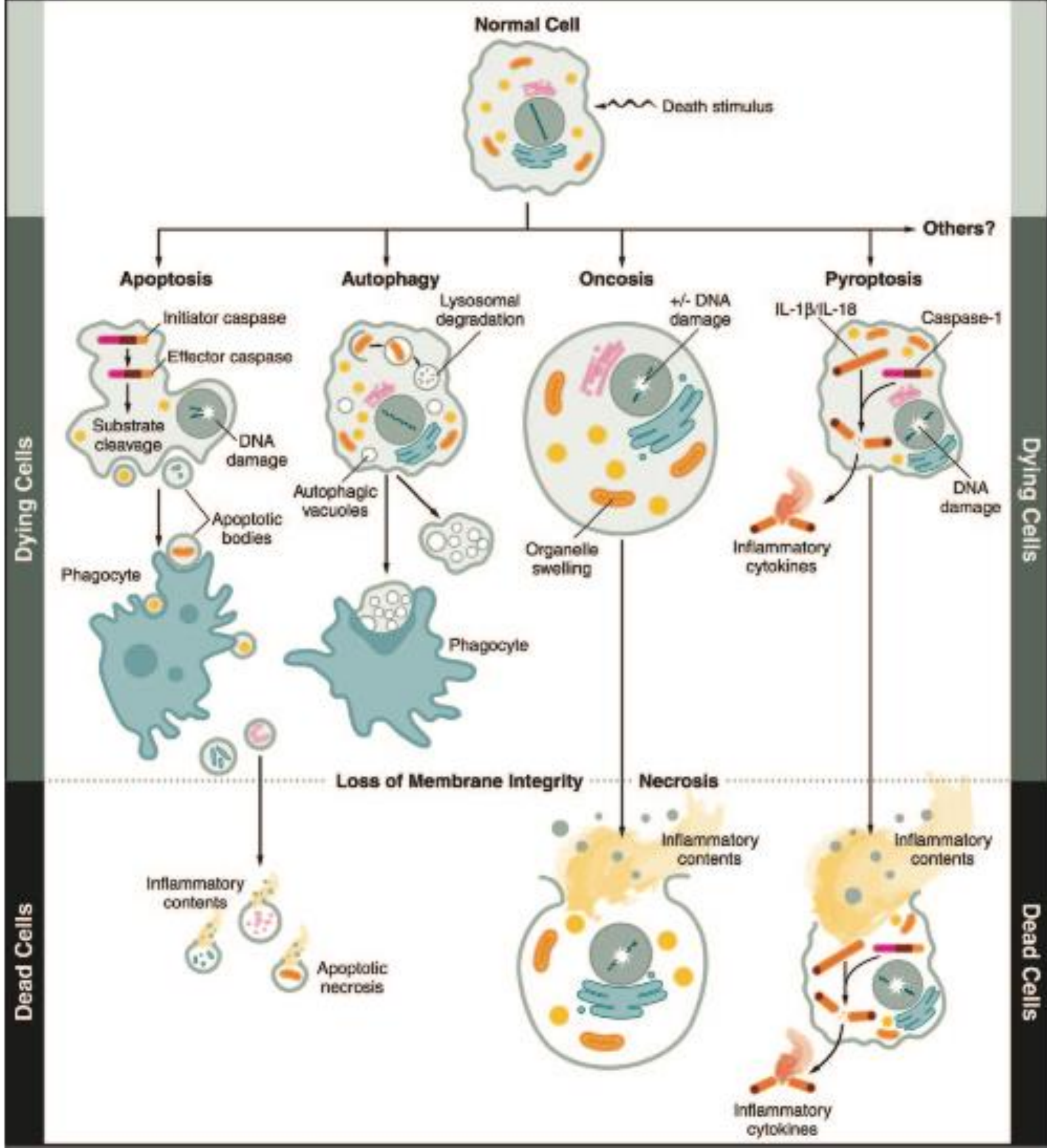
Necrosis: refers to changes that occur to cells after they die

Necrotic changes (for example, karyolysis, karyorrhexis, loss of structure in the cytoplasm) “are the features of a cell’s cadaver, **whatever the mechanism of the cell’s death**, be it ischaemia, heat, toxins, mechanical trauma, or even apoptosis” (Majno & Joris 1995, 11).

So: apoptosis and necrosis **should not be juxtaposed**

-According to Majno and Joris, “the major sore spot in the nomenclature of cell death is precisely the **lack of a suitable name** for cell death that occurs **not by apoptosis but by some external agent**” (Majno & Joris 1995, 11).

-So: cell death might have **different causal pathways** and the difference between them is not that one (or some) of them counts as a **mechanism** while the other **does not**; rather **the difference is in how they are described**.



from Fink & Cookson (2005)

Apoptosis and oncosis

Majno and Joris contrast apoptosis to what they call “oncosis” (1995, 12).

-Oncosis: **cell death by swelling** (apoptosis: cell death by **shrincage**)

-> typically activated by ischaemia

-> the **causal pathway of oncosis** can nowadays be characterized in detail: **reduced supply of oxygen and nutrients** leads to **protein denaturation, enzymatic digestion** due to damaged **lysosomes** and loss of integrity of the **plasma membrane**, **resulting in influx of water and calcium into the cell**, leading to **swelling** and ultimately **rupture of the cell**.

Question: can we distinguish apoptosis from oncosis such that **only the former counts as a mechanism?**

-We consider **three distinctions** used by researchers of cell death that might be used in order to do this:

- i) processes of **physiological** vs **accidental** cell death
- ii) process of **programmed** vs **non-programmed** cell death
- iii) **active** vs **passive** processes

The physiological - accidental distinction

physiological cell death: “such deaths are part of the normal function of the organism” (Lockshin & Zakeri 2001, 545)

accidental cell death: “accidental” causes, **not part of normal function of the organism**

-But: apoptosis can also be induced by a variety of “accidental” causes (e.g. heat, chemical agents, viruses).

So, contrast between physiological and accidental cell death,
not a contrast between mechanism and non-mechanism.

The programmed - non-programmed distinction

Programmed cell death: the phenomenon where cell **die 'on schedule'**, i.e. they are programmed to die at a specific time.

-> '**genetic clock**' that determines when the cells will die.

-But when the time comes for the cell to die, the specific 'programme' (e.g. apoptosis) that determines the form that cell suicide will take, is triggered.

As Majno and Joris stress: "The genetic programme of programmed cell death is **a clock specifying the time for suicide**, whereas the genetic programme of apoptosis specifies **the weapons (the means) to produce instant suicide**" (1995, 11)

-> **the weapon is precisely what we call the causal pathway**

-Again, one cannot use this distinction to distinguish apoptosis as a genuine mechanism.

The active - passive distinction

- Apoptosis** is described as an **'active'** process, **necrosis** as **'passive'**
- > can this distinction be used to differentiate between mechanisms and non-mechanisms?

Sloviter (2002, 23):

- active cell death requires “**active intracellular processes** for death to result”
- in passive cell death “**the cell plays no role in its own demise**”, that is, cell death is “immediate and involves no cellular activity”, the cause being **exogenous** to the cell such as “rapid freezing, aldehyde fixation, heat denaturation, and catastrophic physical destruction”.

-difference between 'active' and 'passive' is merely a difference concerning the details of each causal pathway

- > **no intrinsic difference** between the two causal pathways as such

-> The significant difference from a biological point of view is that because apoptosis involves a **'suicide programme'**, it can serve a homeostatic function (this was the argument in the paper by Kerr et al. 1972).

The active - passive distinction

Kanduc et al. say: “[i]t is frequently assumed that the death of cells can be **passive**. This **non-biological point of view** on cell death ignores the role of cell death in cell development and adaptation. It cannot be assumed that ‘ordinary’ cell death or ‘necrosis’ is a **passive process** while the presumed special form of cell death, ‘apoptosis’ is active. **Both the ante-mortem and postmortem changes are active since both are enzyme-catalysed biochemical reactions**”

(Kanduc et al. 2002, 167-168)

6. Is Mechanism more than the Causal Pathway?

-> Apoptosis and oncosis can **both be considered mechanisms in the TMM sense**: they are both **causal pathways** that produce a result

However, **the history of apoptosis might be used to argue that in biological practice what counts as a biological mechanism cannot just be a matter of identifying a specific causal pathway.**

-> Apoptosis **seems** to be a **special kind of causal process** with distinctive features which deserves to be labeled a mechanism.

But the reason apoptosis became a central biological mechanism is not due to some feature **internal to the sequence of events** that constitutes the apoptotic pathway

-but due to features that are **external to the pathway itself, i.e. because of its role within the organism**

What the case of apoptosis shows:

- > in the world there are **causal pathways for various phenomena**
- > all causal pathways of events are **mechanisms in the TMM sense**
- > not all those causal pathways are **biologically interesting or significant**, even if they occur frequently within organisms

biologically interesting or significant causal pathways are those pathways which have a **central function within the organism**; **that is, whether a causal pathway is biologically interesting has to do with features external to the pathway itself.**

But suppose one were to argue as follows:

We should certainly let **biological practice** itself decide what we should mean by a ‘**mechanism**’ in a **biological context**. If **practice has it that a causal pathway is deemed a mechanism** by an appeal to **external** features of the pathway, so be it.

So, TMM (the point would be) is **false**, since:

(P-TMM): mechanism=causal pathway +X,

where X is some **biologically significant external feature** of the causal pathway.

We can accept that features **external** to a causal pathway, that can be established by looking at **biological practice**, determine whether a specific **theory-described causal pathway** counts as a **biological mechanism**.

This would entail that **‘mechanism’ is an honorific term attached to causal pathways which have certain (external) features.**

The **further scientific question** then is whether **there is evidence that a causal pathway is a ‘mechanism’ in this sense or not.**

The choice between TMM and P-TMM is **not particularly significant**

To adopt P-TMM is to claim that we allow a **distinction** between a **causal pathway** for a phenomenon P, and a **specifically biological mechanism**, where the difference between the two concerns an **external feature** of the relevant causal pathways.

The **important point**: both views licensed by **methodological mechanism**: to be committed to either option, one **need not be committed to some metaphysical view about causation, or the ontology of mechanisms.**

-Could someone insist that there is some **other feature** that differentiates a **causal pathway** from a **mechanism**?

-> A possibility here is to adopt the requirement of **causal modularity** (cf. Woodward 2002).

-> Causal modularity may be seen as the criterion that determines whether a process counts as **machine-like** or not; so, perhaps 'mechanism' should be used **only for causal processes that exhibit causal modularity**.

-The **major disadvantage** of this view is that many instances of 'mechanisms' in biology turn out not to be such, since they are **not modular**; apoptosis is a case in point (cf. Cassini 2016).

So, adopting this view necessitates **abandoning taking scientists' talk of mechanisms at face value**.

7. Conclusions

- Most philosophical accounts of mechanisms are '**inflated**' accounts of mechanisms
- We have defended a **deflationary** account of mechanisms: according to what we called *Truly Minimal Mechanism*, a mechanism **just** is a **causal pathway** that produces a particular effect.
- We argued that commitment to mechanism means adopting a certain **methodological postulate**, i.e. that one should always look for the causal pathways producing the phenomena of interest.
- The case of apoptosis shows that several distinctions used by biologists in order to differentiate between causal processes (e.g. physiological vs accidental, programmed vs non-programmed, active vs passive) do not correspond to internal features of causal pathways, but concern an external feature, i.e. the role those processes play within the organism.**
- Main conclusion: **a truly minimal understanding of mechanisms is sufficient for understanding biological practice.**

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