Chapter 8
Crisp Islands in Vague Seas: Cases of Determinate Parthood Relations in Biological Objects

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8.1 Introduction

Parts are important for describing (types of) biological organisms: Mammals have lungs, fishes do not. Most cells have nuclei, red blood cells do not. Parthood is generally considered a fundamental relation both in formal ontology and in knowledge representation. As a complement to a taxonomic view on organizing things by categories, an (orthogonal) mereological view often constitutes an additional organizational principle for the representation of biological entities. Comprehensive representations of mereological hierarchies can be found in many biomedical terminology systems. Parthood relations are represented, e.g., in the anatomy branch of the MeSH thesaurus (Medical Subject Headings National Library of Medicine 2013), but there they are not formally distinguished from taxonomical relations. They are represented formally in the Foundational Model of Anatomy (Rosse and Mejino 2008), the Gene Ontology (Ashburner et al. 2000), ChEBI (Chemical Entities of Biological Interests; Hastings et al. 2013) and other OBO Foundry (Smith et al. 2007) ontologies that describe biological structures. In the huge clinical ontology SNOMED CT (International Health Terminology Standards Development Organisation (IHTSDO) 2013), an extensive mereological hierarchy describing anatomy classes is represented as a taxonomy of reified parthood relations, according to the structure-entity-part (SEP) triple architecture proposed by Schulz and Hahn (2005), where auxiliary classes like, e.g., *Heart structure* are introduced to model a partonomic statement like "The myocardium is part of the

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heart" as a subclass relation between the class *Myocardium* and the class *Heart structure*.

Philosophical accounts of parthood (Simons 1987; Varzi 2014) have attracted much attention in the analysis of ontological problems in biology and medicine; and numerous use cases have driven the development of domain ontologies that depend on formal descriptions of biological structures. Controversial issues include the transitivity of part-of and the so-called propagation of attributes via partonomic hierarchies (Horrocks et al. 1996; Schulz and Hahn 2005; Schulz et al. 2006). These issues are crucial wherever mereology hierarchies are expected to support generalisable inference mechanisms. For example, a disease or injury being part of an anatomical entity could imply a disease or injury of the whole: A disorder of the retina is a disorder of the eye and a fracture of an elbow is a fracture of an upper extremity. On the other hand, if a part is lacking, this does not imply that the whole is lacking. Such patterns could be used in medical decision support systems or in other intelligent applications in life sciences and health care where we have to account for the broad range between normal and abnormal constitution, shape and function, as well as for the developmental stages that characterize the life cycle of organisms (Schulz and Hahn 2007; Schulz and Johansson 2007). They could also be used to test whether we deal with parthood or not. In both cases, of course, the inference patterns in question need to be valid ones. In this paper, we will discuss a number of candidates for such patterns and assess their scope.

When it comes to its application to biomedical domains, mereology opens up a multifaceted problem space, which has been repeatedly addressed both in philosophy and biomedical informatics. In order to prepare the ground for our discussion in this paper, we will discuss some of these dimensions in the remainder of this introduction.

Domain thesauri, as well as ontology-like artefacts derived from them, often represent taxonomies together with *parthood statements on class level* as opposed to particular things. These statements on class level are expressed in seemingly straightforward formulations like:

$$\textit{part-of}(\textit{Finger}, \textit{Hand}) \tag{8.1}$$

Although this statement closely resembles natural language sentences like "A finger is part of a hand", its precise semantic is a matter of debate. Several competing interpretations for such statements have been suggested. Some read them as universal statements (Smith et al. 2005), others read them as set-theoretical statements (Schulz and Hahn 2002) and yet others – less explicitly – as prototypical statements (Rosse and Mejino 2008). Out of these different possibilities, the first one has been integrated into the Relation Ontology (RO) as a suggested standard for biomedical ontologies (Smith et al. 2005). It takes the time-indexed instance-level relation **part-of** (a, b, t) as a primitive and defines class-level parthood as follows:

$$\begin{aligned} \textit{part-of}(A, B) =_{def} \forall a, t(\textbf{instance-of}(a, A, t) \rightarrow \\ \exists b(\textbf{instance-of}(b, B, t) \wedge \textbf{part-of}(a, b, t))) \end{aligned} \tag{8.2}$$

Of course, this leaves open the interpretation of instance-level parthood relations. It has, indeed, been debated whether standard mereology is appropriate for modelling this relation within the biomedical domain. To start with, the standard mereological **part-of** relation is the reflexive, antisymmetric and transitive proper-or-improper parthood relation (Simons 1987), whereas in biomedicine there is an *implicit restriction to proper parthood*, which is irreflexive and asymmetric. Biological and medical terms containing "partial" are, indeed, generally opposed to terms containing "total". E.g., SNOMED CT contains 804 preferred terms with the modifier "partial" in their name, like "partial larynx" or "partial agenesis of pericardium". In all of these cases, "partial" is opposed to and explicitly excludes "total" or "complete". For instance, "total mastectomy" is never seen as a special case of "partial mastectomy". To generalise, there is no use of the word "part" in biological or medical discourse that would contradict irreflexivity (Schulz et al. 2006). However, this is only a terminological issue: It is an empirical linguistic fact that the scientific language of biomedicine uses "part of" to denote an irreflexive relation, whereas from an logical point of view it is a mere matter of convention whether to use the reflexive "(proper or improper) part" or the irreflexive "proper part" as a primitive.

More substantial is an attack on the transitivity of the standard mereological proper-or-improper parthood: Some authors have argued for the *non-transitivity of parthood* in biology (Johansson 2004; Varzi 2006). E.g., the sheep is part of the flock, the sheep's stomach is part of the sheep, but the sheep's stomach is not part of the flock. However, if we leave aside the use of "part" in ordinary discourse, which must not be considered to be an exact fit to the formal-mereological parthood relation, there are no convincing arguments against the transitivity of the most general parthood relation, for the alleged counterexample can be dissolved if we analyse "part of" in the first premise as a linguistic substitute for "member of", which is a more specialised mereological relation that is not transitive. Below, we will discuss in more detail intransitive subrelations of **has-part**, such as **has-granular-part** or **has-component** (Beisswanger et al. 2008).

More of a problem is the domain-specific application of the parthood predicate. Anatomy, for example, needs to talk about *immaterial parts of material objects*, like cavities and one- or two-dimensional boundaries (Schulz et al. 2006). Biology also talks about *disconnected parts of non-connected wholes*, such as the molecules in a volume of gas, the sheep in a herd or a component of an organ system such as the thyroid gland as part of the endocrine system. Though not physically connected, these entities are considered parts of their wholes as long as they fulfil certain other criteria. We will analyse this later in more detail. General discourse about parts also includes *removed or lost parts*, e.g. a lost hair, a blood sample taken from the body, or a fallen apple, as well as *future parts*, such as car parts. In cases of self-connected wholes, the loss of connection is a clear criterion for the loss of parthood, whereas this is less clear with regard to, e.g. a sheep that has moved away from its herd or a gas molecule that dissipates from the remainder of a volume of gas.

There are a number of phenomena that make the decision about biological parthood a non-trivial problem. The first of these is the *continuous mereological* *change of biological objects over time*, without which life would not even be possible. My body remains numerically the same even after my hairs have been cut and probably all of a body's molecules are being replaced during life. Mereological essentialism (Simons 1987) postulates that if an object loses a part, it is no longer the same entity. This may hold, e.g., for information entities; a word from which you remove a letter is, indeed, no longer the same word. But mereological essentialism is counterintuitive when it comes to living entities: The loss of a hair does not make me a different individual and metabolic processes in organisms are not feasible without the exchange of matter. Such questions of identity and mereological change lead up to well-known paradoxes, like the infamous Ship of Theseus or the Paradox of Tibbles and Tib (Rea 1995); however, these do not surface in current endeavours to develop biomedical ontologies.

Another issue is the *indeterminacy in the spatial demarcation of biological objects*, with their surfaces exhibiting the most diverse shapes of cavities, tunnels etc. An object located, e.g., in a microscopic cavity of a biological surface structure like the intestinal mucosa, is therefore located within this surface structure. If the cavity were not part of the wall, then the object would be outside the wall and, as a consequence, outside the object that "hosts" it. Especially the condition of some object being "in" a biological object often reflects a situation of being located in some not fully enclosed immaterial part (Schulz and Johansson 2007). Moreover, biomedicine combines the analysis of *different granular partitions* where parthood across different such partitions is often difficult to determine, as in parthood predications with regard to countable objects vs. homogeneous collections of particles of heterogeneous "chunks of stuff" (Jansen and Schulz 2011; Schulz et al. 2006).

All this raises the hypothesis that parthood statements are complicated both by ontological vagueness and by epistemic indeterminacy. In Table 8.1, we list a number of examples of objects that are spatially included within other objects and for which common sense arguments in favour and against the assertion of parthood are collected. For spatial inclusion without parthood we will introduce a new relation, *containment*, which will be formally described below. This allows us to harvest intuitions that we will analyse with more scrutiny in the following sections. However, it also shows that our intuitions are not unambiguous.

8.1.1 Vagueness and Indeterminacy of Biological Parthood

Important inference patterns are sensitive to the interpretation of the parthood predicate. Therefore, the question whether something is part of, e.g., a cell or an organism, or merely contained by it, has noteworthy implications: Radiologists identify a certain structure in a medical image and ask themselves whether this depicts a modified structure of the body or rather something contained in it as a foreign body. Also, the distinction between "own" and "alien" is fundamental to the functioning of an organism's immune system. It can even be of legal and ethical

Table 8.1 Biological problem cases, with arguments in favour and against parthood, given a spatial inclusion relation between objects

Case	Arguments in favour of parthood	Arguments against parthood
(A) My body presently includes a certain portion of urine. Is this portion of urine a part of my body?	(i) The portion of urine is the result of a biological process that occurred in my body, (ii) It contains organic material with my body's genetic identity, (iii) It is completely surrounded by body parts.	(iv) The urine does not contribute to the functioning of the body, (v) Its presence in the body is short-lived, (vi) Most of the urine volume is of an inorganic nature (H_2O), (vii) A longer presence in the body will negatively affect the functioning of the body.
(B) A cell contains a certain volume of water. Is this water part of the cell?	(i) The cell would not be functional if this water volume were removed. Furthermore, it would probably be completely destroyed.	(ii) The water volume is inorganic.
(C) This H_2O molecule is now included in one of my cells. Is it part of this cell?	(i) The molecule contributes (together with many others) to the functioning of the cell.	(ii) H_2O is inorganic and does not require a biological process to be synthesised, (iii) It does not necessarily come into being in the cell, (iv) Its presence therein may be very short.
(D) A brain now includes this brain metastasis. Is this (ill-formed; Schulz and Hahn 2007) object a part of this brain?	A metastasis derives from malignant tissue that originates elsewhere. (i) It shares the genetic identity with the brain, (ii) It is tightly connected with the brain, (iii) It exchanges matter with it.	(iv) It did not originate there, (v) It is a non-canonical structure, body part, (vi) it negatively affects the function of the brain.
(E) My body now includes this E. coli population. Is it a body part?	(i) Intestinal bacteria contribute to canonical body functions, (ii) Every organism hosts a bacteria population.	(iii) The bacteria are genetically different, (iv) They are not attached to the organism.
(F) This single bacterium is included in my body. Is it a part of my body?	(i) The bacterium is part of a larger bacterial population bearing important body functions.	(ii) The bacterium may not have started its life within my body and may cease to exist outside (cf. (E).(i)).

relevance whether something is part of a human organism or merely located within it. If we subscribe to the principle that a defect of a part is also a defect of the whole, we will have to accept that a defect of an artificial heart valve implies a defective heart if this artificial valve is considered to be a part of the heart. On the other hand,

Fig. 8.1 A virus is ingested by a cell. When do virus components become part of the cell? (Schulz and Johansson 2007)

it would be counterintuitive to interpret a structure abnormality of an embryo as an abnormality of the maternal organism.

As opposed to parthood, containment is a matter of mere spatial location, like cookies are contained in a box without being a part of it. Later in this section, we will introduce a formal definition of containment. To be sure, containment is itself a matter of vagueness and it is not at all clear where parthood starts and containment ends (Schulz and Johansson 2007).

One example from biology is phagocytosis, i.e. the gradual incorporation and re-use of foreign material by a cell, such as depicted in Fig. 8.1. Similar problems arise with ingestion and digestion processes in general: We could trace the fate of a single carbon atom which is taken in into the body as part of some piece of food and later becomes part of an animal's tissue (Donnelly 2009). At which time does it become part of the animal's body?

In the following, our discussion of such phenomena will be based on a number of assumptions. Of some of these assumptions we are convinced that they are true, although we will not argue for them in this paper. Foremost, we subscribe to a notion of biological objects, according to which they are independent continuants (Grenon and Smith 2004) that either are living three-dimensional material beings or material parts thereof (Schark 2005). In addition, we will make some methodological restrictions for the sake of simplicity. E.g., this paper will only consider objects at the times they are included in or constituting some living organism. That is, we will not discuss, e.g., dead bodies, fossils, tissue samples and processed biological material like food items, leather, cotton, timber etc., as long as they are not included in living biological systems. Moreover, we will assume that every biological object occupies at any time an exactly one spatial region. That is, we will not consider vague boundaries here, although they are typical for many biological surfaces as mentioned above.

We take into consideration, however, the possibility that biological objects may have "fiat boundaries", i.e. that they may be arbitrarily delineated by human fiat (Smith and Varzi 2000; Vogt et al. 2012). Material objects may also have immaterial objects as parts, especially cavities, in line with the current specification of BFO version 2 (Smith et al. 2013). We will, however, not consider zero to two-dimensional boundaries (i.e. points, lines and planes), which could also be considered to be parts of their hosts (Donnelly 2011).

We also assume that when asserting parthood between two objects, this assertion refers to the current state of affairs, despite the common extension of the word "part" to denote past and future parthood, such as in calling something a car part because it is being produced with the intention to become part of a car (intended part), or calling something a body part because it has been severed from the body (past part). Our fundamental assumption in this paper is that, in accordance with (Bittner 2004), spatial inclusion is a necessary condition for material parthood. Standard material parthood, that is, implies spatial inclusion:

$$\textbf{has-part}(I, i, t) \rightarrow \textbf{includes}(I, i, t) \tag{8.3}$$

with "I" ("includer") and "i" ("includee") denoting individuals.

We need to say more about spatial inclusion, however. Any three-dimensional entity can be included in any other three-dimensional entity, be they material objects, immaterial spatial objects or spatial regions. We use the term "inclusion" instead of the more common term "location" because the latter is normally used for the relation of an object to a spatial region only and not, as we need, to another material object. The conception of inclusion is thus broader than the standard notion of spatial location (Casati and Varzi 1999) where the range is restricted to spatial regions. This extension of the concept of location is in line with the ongoing BFO 2 specification (Smith et al. 2013), as well as with the BioTop upper domain ontology (Beisswanger et al. 2008).

The inclusion predicate can formally be defined in terms of overlapping regions, where the region of a thing is, in turn, the set of points in space occupied by this thing. If we follow this strategy, talk about an object I including another object i is a simplified way of stating that, at a given time, all of i's parts are located in I's region or, even more simple, i is located within I's region.

We can give a formal semantics for the inclusion relation using notions from mathematical topology. On this account, each physical object c occupies exactly one spatial region at a time t, namely **region**(c, t). This spatial region is, by definition, exactly occupied by c at time t. Using **has-part** as a primitive, we can then define the relation of material inclusion and containment as follows:

$$\textbf{includes}(I, i, t) =_{def} \textbf{point-subset-of}(\textbf{region}(i, t), \textbf{region}(I, t)) \tag{8.4}$$

$$\textbf{contains}(I, i, t) =_{def} \textbf{includes}(I, i, t) \wedge \neg\textbf{has-part}(I, i, t) \tag{8.5}$$

$$\textbf{part-of}(i, I, t) =_{def} \textbf{has-part}(I, i, t) \tag{8.6}$$

The relation **includes** is defined in terms of topologic (point-set) inclusion, whereas containment is defined as spatial inclusion without parthood. As **has-part** has been introduced as a primitive term, we cannot expect any sufficient criteria for parthood with general applicability. The question, however, is, whether we can state necessary conditions or conditions that are sufficient for certain subdomains. All of these three relations (i.e. **has-part**, **includes** and **contains**) are considered to be transitive (Bittner 2004), but we will later discuss intransitive sub-relations of **has-part**.

On this basis, the main question of the deliberations in the remainder of this paper can be phrased as follows: What distinguishes full-blown parthood from mere containment? Are there criteria that can be added to inclusion in order to get parthood? And are there criteria that can be added to inclusion to get containment?

8.2 Soft Criteria: Function, Origin and Genetic Identity

In this section, we discuss an extended list of criteria and explore whether they support either parthood or containment. The assessment is, above all, guided by cognitive adequacy. In Sect. 8.3, we strive for clearly delineated, ontological criteria, aware, however, that we can, at most, identify "islands" of ontological certainty within an ocean of vagueness. These criteria will be mostly categorial criteria, i.e. criteria that refer to the kind of beings includer and includee belong to. In this section, however, we will explore a number of prima facie criteria referring to origin, function and genetic identity.

We will now start our quest for such criteria by revisiting a decision algorithm that has been suggested by Schulz et al. (2005). This algorithm makes use of a set of simple decision rules (see Table 8.2): (i) Is the includee an artefact? (ii) Is the function of the includee relevant for the integrity of the includer? (iii) Do includee and includer have the same genetic origin? (iv) Has the includer hitherto been located in the includer or in a part of the includer?

Of these, the first criterion appears to be a monadic criterion, asking for a property of the includee alone. It is based, however, on the assumptions that the includer is a biological entity and that no artefact can be part of a biological entity. However, the distinction between biological and artificial entities is not as clear-cut as would be necessary for successfully applying this criterion (Jansen 2013). Engineered cells and genetically modified mice are both artefacts and biological entities. Moreover, the question whether something of artificial origin can be part of a biological entity will be answered differently with respect to different levels of granularity. Were there artificially produced lipid molecules, we see no reason why these should not become part of, say, a membrane that is part of a living cell. We will now look at the remaining criteria, discussing in turn (i) genetic identity, (ii) functionality and (iii) spatiotemporal origin. First, we can check whether includer and includee have the same genetic identity. For criminalistic purposes, the 'genetic fingerprint' is normally a reliable guide to decide whether detached organic materials derive from a certain individual organism. This criterion can, however, not be generalised: On the one hand, the cells of monozygotic twins have exactly the same genetic identity. On the other hand, mosaic organisms occur where different organs can have cells of different genetic identity. Further problem cases for genetic criteria are colonial organisms (e.g. microorganisms in a biofilm or the zooids constituting the jellyfish-like *Portuguese man o' war*), composed of a multitude of single organisms which cannot survive when separated. The boundary between a colony and a single organism is vague. Slime moulds normally live as colonies

Table 8.2 Decision algorithm proposed in Schulz et al. (2005)

```
If located-in (c, d, t) then
  If Artifact (c) then
    contained-in (c, d, t)
  Else
    If function-integrity-relevant (c, d, t) then
      part-of (c, d, t)
    Else
      If (not same-genetic-origin (c, d, t)) or
        (instance-of (c, MaterialObject) and instance-of (d, ImmaterialObject)) then
          contained-in (c, d, t)
      Else
       If hitherto-located-in (c, d, t) or (hitherto-located-in (c, m, t) and part-of (m, d, t)) then
          part-of (c, d, t)
        Else
          contained-in (c, d, t)
        End If
      End If
    End If
  End If
End if
```

of single cells, but can aggregate to form a single body-like whole. Composite organisms like lichens aggregate fungal and prokaryotic cells. Talking about genetic identity or similarity is, therefore, not trivial. These problem cases notwithstanding, the following cases are typically distinguished:

- Two entities are **autogenic** if and only if they share the genetic identity of the same individual. Example: a saphenous vein autograft used in coronary artery bypass surgery.
- Two entities are **allogenic** if and only if they share the genetic identity of the same species, but not of the same individual. Example: typical organ transplants (kidney, liver, heart) from one human to another.
- Two entities are **xenogenic** if and only if they do not share the genetic identity of the same species. Example: a baboon heart transplanted to a human baby.

All three predicates can only be applied in a meaningful way if both includer (I) and includee (i) carry genetic information, and they are difficult to apply in the case of chimeras that contain body parts of different genetic identity. On first sight, we have reason to assert parthood for autogenic includees and to assert containment for allogenic and xenogenic includees. But it is difficult to derive clear-cut criteria for parthood or containment from this. If, for example, xenogenic entities play a vital role in the organism, it could be justified to consider them as parts of the organism.

This points us to the next feature that could be used in parthood criteria, i.e. the *functionality* of the includee for the includer:

- We have reason to assume that the includee i is part of the includer I if i is **part-for** a certain type I_{TYPE}, of which I is an instance. The relation **part-for** holds between an individual includee i and a type, if and only if i has a (token) function f, which can only be realized in case i is included in some instance of I_{TYPE}. A typical example is an ion channel protein which is synthesised in a ribosome, but becomes functional only once it is included in a cell membrane. Similarly, despite having its own independent genome, a mitochondrion can be considered to be part of some eukaryotic cell because mitochondria completely depend upon their host cell for survival and functioning, viz. ATP supply. This contrasts with an intestinal *E. coli* bacterium (or any other cell from a human organism's microbiome), which is able to live and function outside its host.
- In contradistinction, we have reason to assume that the includee i is only contained in the includer I if i has a function that cannot be realised while it is included in some instance of I. Examples: the ion channel as long as it is still within the cytoplasm; a surgically removed heart valve in a cooling container. The heart valve is only functional when included in some biological heart, i.e. it is a **part-for** the type heart. It cannot be functional when isolated from a heart in the cooling container.

Conversely, the function of the includer depends on an includee. In this case, we can say that the includer is a "whole for" the includee, i.e. the part is necessary for the functioning of the whole. This allows us to formulate two additional criteria:

- We have reason to assume that the includee i is *part of* the includer I if I has a function that can only be realised if some instance of a certain type i_{TYPE} is included in it. Examples: My digestive tract requires a stomach for its complete functioning, or a cell cannot live without mitochondria.
- We have reason to assume that the includee i is *contained* in the includer I if the latter has a function that cannot be realised if some instance of a certain type i_{TYPE} is included. An example is the complex of a receptor and an antagonist molecule. In such a complex, a small molecule a of a certain type is bound to a receptor and blocks its function. In this situation, we have reason to deny that a is a part of the receptor.

Functional criteria can, however, be in conflict with criteria referring to the *spatiotemporal origin* of the includee in the includer and the *physical connection* (Schulz and Johansson 2007) of includer and includee.

- We have reason to assume that the includee is part of the includer if the includee originated within the includer. Example: The heart and the brain of a human originate within that human.
- We have reason to assume that the includee is contained in the includer if the includee originated outside the includer. Example: A brain metastasis of a breast cancer is included within the brain, but it originated in the breast tissue.
- We have reason to assume that the includee is part of the includer if the includee is physically connected to the includer (it cannot be severed from the

includer without physical damage). This criterion would allow the rejection of the parthood hypotheses for containees like urine or faeces, which are not tightly connected to the surrounding body structures. In contrast, a metastasis is tightly connected to the surrounding tissue (blood supply), whereas a sequestrum (piece of dead bone) is much less connected.

These criteria can be combined with additional conditions, such as:

- We have reason to assume that the includee is part of the includer if the includee originated together with the includer. Example: The endothelium of my aorta originated together with my aorta.
- We have reason to assume that the includee is part of the includer if the spatiotemporal inclusion is permanent. Examples: all the organs in the development of an embryo, a primary tumour of the brain.

Criteria that draw on the origin of the includee could be disputed because they draw on (causally irrelevant) historical properties of the includee. This problem is especially pressing because within one and the same includer, instances of the same type may fulfil different spatiotemporal criteria. Consider, for example, a cell in a thyroid gland containing several molecules of the hormone L-thyroxin. Some of these molecules may have been synthesised within this cell and never left it, others were synthesised within the cell, left it and returned, others were synthesised in a neighbour cell, whereas still others could have been synthesised in a lab and entered the body as a drug. The problem is here, that within a snapshot view of the cell, there is no difference between these molecules. If the fact that a certain molecule never left the cell were a sufficient criterion to consider it a part of it, why should we withhold this status to the other L-thyroxin molecules just because of their deviant history? The criterion of connection (for the discussion of several strengths of connection, see Schulz and Johansson 2007), however, would make a difference also in a snapshot view. If i originated within I and is tightly connected to it (and cannot just go in and out like many molecules in cells), then this seems to be a good criterion for granting parthood.

These criteria capture some of the intuitions underlying our judgements about biological parthood (cf. Table 8.1). At times, however, their results are unsatisfactory and can also contradict each other. Artificial heart valves are, by all means, necessary for the functioning of the including organism, but they do not originate from this body, nor do they have a genetic identity. Similarly, medically indicated allografts and xenografts are normally necessary for the functioning of the receiving organism, but they do not originate in these organisms, nor do they share the same genetic identity. The bacteria on the mucous membranes of a human body are canonical contributors to its proper functioning, they may have originated within this body, but they do not share its genetic identity. As they allow for exceptions, these criteria can only be considered ‘soft criteria’; they are more or less reliable rules of thumb.

8.3 Hard Criteria: Containers, Grains and Components

8.3.1 Topological Descriptions of Material and Immaterial Objects

Our question was: how and when can we infer parthood from spatial inclusion? This question is only meaningful if we can characterise spatial inclusion in a non-circular way, i.e. if we can describe the makeup of physical objects in terms of their spatial arrangement without any reference to parthood. The following example illustrates the challenges of such an approach.

Imagine a simple toy object o, consisting of a wooden box b and a dice d (Fig. 8.2 i, ii), which is located inside b, i.e. it fills the hollow space h (Fig. 8.2 iii) enclosed by b. A standard mereological approach would describe o as a mereological sum of its two component parts b and d, like in Fig. 8.2 iv. Note that b *contains* d, which is, therefore, not a part of b, but both would then form the sum o.

How can we describe this scenario without any reference to parthood and mereological sums? Let us assume that we can find out for each point in space whether it is occupied by some material entity. This allows us to define the toy object o as all physical matter that exactly coincides with the points that make up the regions of the box and the dice. We can generalise on this by defining what we may call a "topological sum", or "t-sum" for short, which is solely based on point-set theoretical considerations. By this, we avoid the use of the mereological part-of relation.

Definition 1. Let $s_1, \ldots, s_n$ be material or immaterial objects. S is the t-sum of the summands $s_1, \ldots, s_n$ if and only if S is the (self-connected or scattered) object that comprises any spatial region occupied by some summand and the totality of matter that is located at any point in space occupied by some of its summands.

According to this definition, the complete toy object o would then be constituted by the totality of material entities in the joint region occupied by b and d (Fig. 8.2 iv). Objects like b in our example may act as a container, i.e. as material entities that host a hollow space like h (Fig. 8.2 iii) which, in turn, can be filled by another object which is not itself part of the host. Hollow spaces exist, whether they are empty or not, i.e. whether they contain material objects such as d, a marble or a bug. Using Definition 1 we could try to define the container c as everything that is within the regions occupied by the material object b and the hollow space h (Fig. 8.2 vi). But then we have the problem of how to distinguish between c in case it is filled by d on the one hand and the whole object o on the other hand, for the dice d included in h is located within the region of c and, according to our definition, it will inevitably be included in the t-sum, as it lies inside its spatial region. A filled container would, therefore, always be a different kind of thing than an empty container. Moreover, we were not able to distinguish between the container and the container plus its content. That is, according to our example (as d is inside h) the following holds:

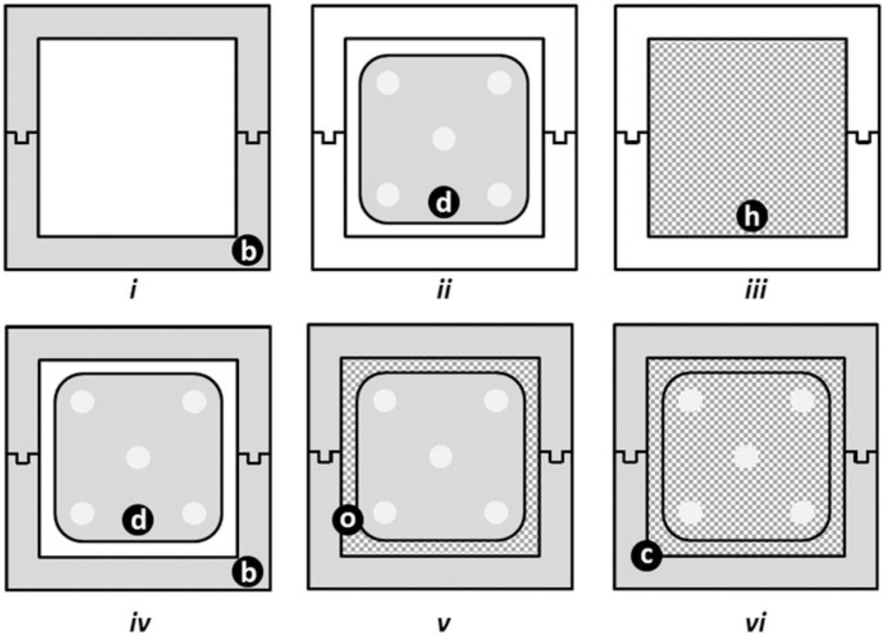

Fig. 8.2 The figure shows different (partly overlapping) objects that can be composed out of a box b (**i**) and a dice d (**ii**). The immaterial hollow h (**iii**) is the space enclosed in b. These three elements can be combined in different ways: (**iv**) shows the t-sum of the material parts b and d; (**v**) shows the t-sum of the material parts b and d and the immaterial h; (**vi**) shows the container c as the ti-sum of b and h that excludes d even if it is included in b. The *grey mark* signifies that both the spatial region and the matter situated in it belong to the object in question, while the chequered area signifies that only the spatial region belongs to the object, but not the matter contained in this region

$$\textbf{t-sum}(b, h) = \textbf{t-sum}(b, h, d) \tag{8.7}$$

This shows that the t-sum does not satisfy our purpose because it always adds the included entity to the container. We can avoid this by defining a sum that excludes the material includees of immaterial includers (ti-sum):

Definition 2. Let $s_1, \ldots, s_n$ be material or immaterial objects. S is the ti-sum of the summands $s_1, \ldots, s_n$ if and only if S comprises any space occupied by some of the summands and the totality of matter that is located at this space except the matter located inside of immaterial summands.

In contrast to proposition 8.7 above that holds for the t-sum, the following hold for the ti-sum:

$$\textbf{ti-sum}(b, h) \neq \textbf{ti-sum}(b, h, d) \tag{8.8}$$

$$c = \textbf{ti-sum}(b, h) \tag{8.9}$$

This means that the ti-sum allows to adequately describe containers. We are now able to distinguish between aggregations of material objects, containers as aggregations of material objects with spaces, regardless of whether the spaces are occupied, and aggregations between material objects, their spaces and the fillers of the spaces.

These distinctions are hugely important for describing material biological entities from cell components to organisms. What, for example, is a skull? Just as the box *b* encloses *h* (Fig. 8.2), the cranial bones and tissues enclose the cranial cavity. And just as the container *c*, cranial bones and cranial cavity (together with other immaterial parts) make up the skull. Like *c* as a container for *d*, the skull is, thus, a container for the brain, and just *c* and *d* constitute *o*, the skull and the brain (together with other material and immaterial entities) constitute the head.

As mentioned before, it is typical for biological objects that they contain hollow spaces. In fact, the invention of a membrane that encloses a hollow, thus allowing the distinction between an inside and an outside, seems to be one of the crucial innovations in the evolution of life. Every cell has a cell lumen, and there are plenty of vescicles with an inside in the cell. In multicellular organisms, hollows are part and parcel of the anatomy, like the inside of the bladder, the lumen of the aorta, the heart chambers and so on. These spaces are inside containers, and most of these spaces are in fact filled with material entities. These material entities are, however, not part of the container in question: what is inside the skull is not part the skull, the content of the bladder is not part of the bladder, and the content of the aorta is not part of the aorta. To generalise, things included in a container are not part of the container but contained in it.

There are many more examples that suggest themselves as clear cases of mere containment as opposed to parthood:

- If Mary swallows a glass marble, this marble does not become a part of her stomach, but is only contained in it because the marble existed before swallowed, it is expected to be expelled, it is not a biological object, it is not physically connected to her stomach and it does not have any function in her stomach. Even if it remains jammed in some body structure, it is not part of it. Also, if a milk tooth were swallowed instead of the marble, it would not be considered to be a part of the stomach either, although the tooth would be an object of biological origin, originating even in the same body.
- Similarly, a cotton wool pad in my mouth during a dental treatment is contained in my head, but not part of it because the pad existed before, the pad remains only for a short time in the head, it is not physically connected to my head and although it has a specific function while located in my oral cavity during the treatment, this is not a physiological function.
- My oral cavity does now contain a certain amount of saliva, which is not a part of it. This is because a cavity is an immaterial object, whereas saliva is a material object and an immaterial object cannot possibly have a material part.

We have thus identified inclusion in the immaterial hollow of a container as a sufficient condition for containment. To be sure, this is a very local criterion. But as a

Table 8.3 Types of complex entities

	mono-sortal	**multi-sortal**
flexible re. number	"flexible collectives" (e.g., a portion of water)	"flexible compounds" (e.g., a hand)
strict re. number	"strict collectives" (e.g., a pair of kidneys)	"strict compounds" (e.g., a water molecule)

sufficient condition for containment it is also a sufficient condition against parthood. It should, however, be noted that we can only somewhat tautologically infer non-parthood with respect to the container itself. It is possible that the container is both a body part and containing other body parts. It is only excluded that the container contains container parts, i.e. parts of itself. The blood included in the aorta, for example, is not part of the aorta. It is, however, part of the body of which the aorta is also a part.

8.3.2 Collections and Compounds

More parthood relations can be drawn from subrelations of **part-of**. In Jansen and Schulz (2011), we distinguished different kinds of complex entities based on the parthood relation (Table 8.3). A collective is the sum of one or more grains that are all instances of the same type, while a compound is the sum of one or more components that may be of different types. A portion of water can be regarded as a collection of grains of the same type, namely H_2O molecules, while a H_2O molecule is a compound of two hydrogen atoms and one oxygen atom. A complex is strict if numbers of parts matter; it is flexible if they do not. E.g., adding an oxygen atom to a water molecule would turn it into a hydrogen peroxide molecule; the molecule would cease to be a water molecule. On the other hand, a portion of water would remain a portion of water if more H_2O molecules were added, and a flock of sheep would remain a flock of sheep if more sheeps joined. Both collectives and compounds are given by the summation of non-overlapping material components. We introduce the relation **has-grain** for relating collectives with their elements and **has-component** to connect compounds with their components. As exemplified in the toy example, the region covered by a component may include immaterial entities, but whether what is contained by this space is ignored or not will depend on our definition, just as we can decide whether the dice d or only the space h belongs to the box in Fig. 8.2. As pointed out in Jansen and Schulz (2011), the classification depends on the specificity of the sortal distinctions: If the right and the left kidney are considered as two different sorts, then a pair of kidneys would be a strict compound instead of a strict collective. The cardinality criterion (i.e. strict vs. flexible in number) allows the inference that, if we take away one component of a numerically strictly defined entity, it becomes an entity of a slightly different sort, often a defective entity. For instance, if a pawn has been taken away from a complete set of chess pieces, the remainder will no longer be of the type "complete chess set". Similar examples would be the extraction of a tooth, a fingernail, the tonsils or an eye lens.

There are also compounds of collectives, such as mixtures or solutions. A mixture of water and ethanol is a compound of exactly two components, i.e. the water fraction and the ethanol fraction. Either fraction is a collection of H_2O or C_2H_5OH molecules, respectively. In biology, more complex compounds of collectives are tissues and body substances. Now compounds are generally expected to have their components clearly delimited from each other, whereas in biological systems, especially in larger anatomical structures, the exact boundaries of an object have to be drawn by fiat. The kidneys, for example, are connected to other body structures by tubular structures (vein, artery, ureter) which do not display any discontinuity that would demarcate the boundary of the kidney. In principle, it would be possible to extend the application of the term "compound" to objects that are structured by fiat divisions, such as the brain that is anatomically divided into the right and the left hemisphere. However, as this is in tension with the intuitive idea of composition, we prefer to introduce the relation **has-fiat-division** for these cases.

All of the three newly introduced relations are specialisations of inclusion, therefore:

$$\textbf{has-grain}(I, i, t) \rightarrow \textbf{includes}(I, i, t) \quad (8.10)$$

$$\textbf{has-component}(I, i, t, p) \rightarrow \textbf{includes}(I, i, t) \quad (8.11)$$

$$\textbf{has-fiat-division}(I, i, t, p) \rightarrow \textbf{includes}(I, i, t) \quad (8.12)$$

As there are many possible fiat divisions and often several ways to decompose a compound, we add the partition scheme p as a fourth argument of the relations **has-component** and **has-fiat-division**. For instance, we can consider all atoms of a small organic molecule as its components, but also its carbon chain and its functional groups. In any of these two partitions, the typical characteristics of a compound are preserved: the components do not overlap and the whole is of a different type if one of its components is missing. The relation **has-grain** is, by definition, intransitive, as are **has-component** and **has-fiat-division**, once the partition scheme p is hold fixed. With the help of these three subrelations of **has-part**, we can expose some non-contentious parthood and containment cases:

- First, if a certain H_2O molecule is a grain of a certain amount of H_2O, it is obviously one of its parts. This is an instance of the general **has-grain** relationship between a collection and its grains, as introduced above. The argument that all grains are parts of the collection derives from the fact that a collection is grounded in its elements, i.e. it ontologically depends on them. Although the removal of just one grain generally does not affect the identity and sortality of the collection (mind the looming Sorites paradox!), there is nothing on which the collection depends and which constitutes the collection apart from its grains.

- The relation between my right femur and my skeleton is an example for the relation between a component and a compound. The sortality of the compound depends on the completeness of its components. This would support the claim to axiomatically state that all component-compound relations are parthood relations.
- The relation between the lower third of my oesophagus and the oesophagus is an example for the relation between a fiat part and its whole. By definition, fiat divisions are parts of their wholes. With fiat parts, the whole is, in a way, prior to the parts.
- The relation between my brain and my body is another case of the relation between an anatomic component and the human body as a compound. Here, an even stronger case can be made for parthood: My brain is now part of my body because (i) both are physically connected, (ii) my body does not function without my brain, (iii) my brain does not function without my body, and (iv) my brain's function cannot be substituted by any other object. (It can, however, be spatially separated from my body and it could also outlive my body, but given the present state of art in medicine, it will no longer be functional in this case.) Another argument would be that a brainless body would be an entity of a different sort. Whether the brain is a component of the body in the above sense depends on how it is divided into different, non-overlapping components.

8.4 Some Possible Axioms

In effect, the hard criteria we found are either categorial criteria or derive from the logical properties of specific subrelations of **has-part**. Such criteria refer, among other things, to the ontological categories of includer and includee. We will now formulate some axioms for biological parthood based on such categorial distinctions. In these axioms, we refer to the following categories as top-level types of entities using the three-letter type names given here:

- *MAT*: material object, e.g. a cell, a molecule, an organ, the intestinal mucosa.
- *CPD*: compound, i.e. it implies a well-defined number, type, and arrangement of elements. If one part is missing, the compound is incomplete. For instance: my lens is a component of my eye.
- *CON*: container. A container has a 3-D immaterial part, the possible contents of which are not part of the container. An example is the cranium, which has the cranial cavity as an immaterial part.
- *COL*: collection of grains of the same type, the exact number of which is irrelevant, e.g. the cells in an early embryo before differentiation, or the water molecules in a litre of water. Collections are typically homomereous, i.e. they have proper parts of the same type.
- *MFI*: material fiat object, i.e. an object that is divided by a fiat (arbitrary) boundary from a larger includer. An example is the lower third of the oesophagus.

- *ART*: non-biological artefact. It means that it is the output of a manufacturing process and does not engage in metabolic exchange with biological objects.
- *SEL*: self-connected object. I.e. an uninterrupted line can be drawn between any two points within the region of the object. Abutting of subunits of the object is sufficient; there is no requirement for strong chemical bonds.
- *IMT*: immaterial object. Example: three-dimensional hollow space. As illustrated in Fig. 8.2, hollow spaces necessarily have a "host". Holes are part of their hosts (Smith et al. 2013, 2005). Immaterial objects can also have fiat boundaries. Example: the lumen of the lower third of the oesophagus.
- *SPR*: spatial region, i.e. a three-dimensional portion of space.

We will now formulate some axioms for biological parthood based on such categorial distinctions.

For a start, immaterial (*IMT*) includers do not have material (*MAT*) parts. Hence, if an instance of *MAT* is included in an instance of *IMT*, it must be contained therein. If, e.g., the cavity of my stomach includes a portion of food, it contains that food. The lumen of my aorta includes a portion of blood; therefore it contains it. In general:

$$(\textbf{includes}(I, i, t) \wedge \textbf{instance-of}(I, IMT, t) \wedge \textbf{instance-of}(i, MAT, t)) \rightarrow \textbf{contains}(I, i, t) \tag{8.13}$$

$$\textbf{has-part}(I, i, t) \wedge \textbf{instance-of}(i, MAT, t) \rightarrow \textbf{instance-of}(I, MAT, t) \tag{8.14}$$

Following these patterns, we can formalize the following restrictions:

- A material object can only be part of material objects; it cannot be part of an immaterial object or a spatial region.
- An immaterial object can be part of a material or an immaterial object, but it cannot be part of a spatial region.
- A spatial region can only be part of spatial regions; it cannot be part of a material or immaterial object.

Containers are material entities and have at least one immaterial part. An aorta, for example, is such a container; it has an immaterial part, i.e. its lumen. Hence, the existence of a container implies the existence of an immaterial part:

$$\textbf{instance-of}(I, CON, t) \rightarrow \exists i\, (\textbf{has-part}(I, i, t) \wedge \textbf{instance-of}(i, IMT, t)) \tag{8.15}$$

Conversely, not every material entity that has immaterial parts is a container and not every includer of a container contains what is in the container. For instance, my aorta is a body part that is a container for some portion of blood. This portion of blood is, therefore, not part of my aorta. However, the blood is part of my body, as well as the aorta and its lumen.

Further restrictions follow from the properties of the relations **has-grain**, **has-component** and **has-fiat-division**, which are specific subrelations of **has-part**. Because of this subrelation property we can state:

$$\textbf{has-grain}(I, i, t) \rightarrow \textbf{has-part}(I, i, t) \tag{8.16}$$

$$\textbf{has-component}(I, i, t, p) \rightarrow \textbf{has-part}(I, i, t) \tag{8.17}$$

$$\textbf{has-fiat-division}(I, i, t, p) \rightarrow \textbf{has-part}(I, i, t) \tag{8.18}$$

Of these, **has-grain** holds between a collective and its grains, **has-component** between a compound and its components and **has-fiat-division** holds between a thing and its fiat parts (i.e. parts existing due to human fiat). In contrast to **has-part**, each of these relations is asymmetric and none of them is reflexive or transitive.

As a consequence of formulae (8.16), (8.17) and the transitivity of **has-part**, a grain of a component of a compound is also a part of this compound. For instance, a water molecule of a water/ethanol mixture is a part of this mixture. Also, if we regard the totality of water molecules as a component of the cytoplasm of a cell, then each individual water molecule is also part of it (and of the cell if we regard the cytoplasm as a component of the cell).

Collections and compounds may comprise sub-collections and sub-compounds. Although these are not grains or components of their includer, they can be considered parts of it. For this it is, however, necessary that all grains of the sub-collection or all components of the sub-compound are also grains or components of the original includer. For example, the collection of all mitochondria in my liver is a part of the collection of mitochondria in my body.

$$\begin{aligned} &(\textbf{instance-of}(I, COL, t) \wedge \textbf{instance-of}(i, COL, t) \\ &\wedge \forall x (\textbf{has-grain}(i, x, t) \rightarrow \textbf{has-grain}(I, x, t))) \\ &\rightarrow \textbf{has-part}(I, i, t) \end{aligned} \tag{8.19}$$

$$\begin{aligned} &(\textbf{instance-of}(I, CPD, t) \wedge \textbf{instance-of}(i, CPD, t) \\ &\wedge \neg \exists p (\textbf{has-component}(i, x, t, p) \rightarrow \textbf{has-component}(I, x, t, p))) \\ &\rightarrow \textbf{has-part}(I, i, t) \end{aligned} \tag{8.20}$$

We can also try to formalise the functional intuitions connected with the **part-for** relation: If an entity i only realises its function when included in an instance of I_{TYPE} and if it is presently included in I, which is actually an instance of I_{TYPE}, then i is a part of I. As we said, an ion channel protein is a **part-for** a cell membrane and if such a protein is actually included in a certain cell membrane, it is a part of it. However, a cardiac pace maker is also a part-for a human body and similar arguments could be brought forward for xenografts (e.g. a baboon heart to be transplanted to a human child). As these cases are more contentious, we exclude from this criterion all artefacts and xenogeneic material, i.e. material from different species:

$$(\textbf{part-for}(i, I_{TYPE}) \wedge \textbf{instance-of}(I, I_{TYPE}, t) \wedge \textbf{includes}(I, i, t) \\ \wedge \neg\textbf{instance-of}(i, ART, t) \wedge \neg\textbf{xenogeneic}(I, i, t)) \rightarrow \textbf{has-part}(I, i, t) \tag{8.21}$$

In a similar way we can now formalise the intuitions connected with the **whole-for** relation. According to this intuition, i is part of I if i is included in I and if i is an instance of i_{TYPE} and if I needs some instance of type i_{TYPE} in order to realise its function. For instance, the cell membrane needs ion channel proteins in order to realise its function. Hence, this intuition says, the ion channel proteins are part of the membrane. We need, however, to be careful to not overgeneralise this criterion, for a car does not only rely on its motor and wheels (which are all among its parts), but also on petrol (which is not one of its parts). Similarly, the stomach cannot realise its function without food and the lungs not without air to breathe. Petrol, food and breathing air are all taken into their includer by way of containers: The petrol tank is a container for petrol as the stomach is a container for food. Hence, we should not extend the criterion to things that are included in a container that is part of the includer. However, we must not exclude all such things, for the aorta is a container for blood, but the blood contained in the aorta is, nevertheless, a part of the body.

Again, we exclude artefacts from the criterion. Otherwise, we would be forced to admit that a drug that keeps alives a biological entity is also part of that entity:

$$(\textbf{whole-for}(I, i_{TYPE}) \wedge \textbf{instance-of}(i, i_{TYPE}, t) \wedge \textbf{includes}(I, i, t) \\ \wedge \neg\exists c(\textbf{instance-of}(c, CON, t) \wedge \textbf{part-of}(c, I, t) \wedge \textbf{includes}(c, i, t)) \\ \wedge \neg\textbf{instance-of}(i, ART, t)) \rightarrow \textbf{has-part}(I, i, t) \tag{8.22}$$

8.5 Discussion

8.5.1 Relevant Inferences

It is mostly the combination of compounds and collections which helps to clarify important issues: For instance, a single calcium channel is part of a cell membrane because the whole collection of calcium channels of which it is a grain is necessary for the functioning of the membrane (cf. (8.16)), and is, therefore, part of the membrane. The parthood condition of the single molecule then derives from the transitivity of the part-of relation. We do not assert that the portion of urine that is included in the bladder is a part of the body because neither the urine has any function in the bladder nor does the body's functioning depend on the urine. To the contrary: The urine has to be discarded regularly. This is different for the portion of blood in the body because it has clearly described functions in the body and the body could not function without it. Even a small amount of blood would be part of the body because it constitutes a fiat division of the entire blood and is therefore part of the latter.

Our axioms also solve the puzzle of the virus that is gradually digested by a cell as depicted in Fig. 8.1. As long as the virus is dismantled to viral protein molecules or fragments, these are contained but not parts. However, if these macromolecules are split into small molecules such as amino acids or nucleic acid monomers, these are no longer distinguishable from, e.g., the collection of alanine or cytosine molecules that were already included in the cell before. The collections of these molecules are functionally relevant for the cell's functioning; therefore, a given monomer becomes part of the cell as soon as it is no longer part of any of the viral molecules.

With regard to drugs, it is, therefore, also decisive for parthood whether a single drug molecule is identical to any member of any molecule collection that forms a component of a biological entity such as a cell, an organ or an organism. For example, the collection of all insulin molecules in an organism constitutes a functionally important component of the organism. In the case where a diabetic receives injections of biosynthetic human insulin, these molecules – as they are indistinguishable from the organism's own insulin molecules – become parts of the body. In contradistinction, porcine insulin molecules in a human's body would be merely located in it. A clear fiat division was introduced regarding xenogeneic material, whereas allogeneic and autogeneic materials are allowed to be parts. Examples are venous autografts, such as coronary bypasses, which fulfil an important function for the heart and are, therefore, parts of it, as well as blood transfusions.

8.5.2 Trade Offs and Boundary Issues

For those cases not resolved by the above criteria, several trade-offs and boundary issues can be identified. For example, the function of a tooth is restored by an inlay artefact. According to formula (8.21), it would not be part of the tooth. This is quite intuitive for clearly identifiable materials which do not naturally occur in biological systems, like gold or amalgam. However, it would be less clear for certain composites that do not just fill a hole, but result in an aesthetically nearly complete restoration; such a material could be composed, in large part, of mineral components very similar to those contained in dentin and enamel. Another case is given with allogeneic and xenogeneic material included within a biological entity. The more this material contributes to the overall function the more it should be accepted as a part. Note that we stay content here to present this situation as a graduality of reasons for parthood. Some authors, like Buddensiek (2006) and van Inwagen (1990), infer that the parthood relation itself is a gradual affair.

A "soft" criterion is physical connection, which is not used in any of the above rules. The more an object is connected to its surrounding structure, the more it would be considered a part, even if other criteria could be used to argue against it. The encapsulated bone splinter in a muscle would be less a part of the muscle than the invasive brain metastasis, which is tightly connected by blood vessels and tissue fibres to the surrounding brain tissue. The function criterion could also be reformulated in the following way: If the malfunction of an includee does not impact the function of the includer, this would be suggestive of containment. However, this criterion will not hold if levels of granularity are crossed: Even in a healthy organism there are always dysfunctional cells and molecules.

8.5.3 The Importance of the Components of a Compound

Many entailments change if the whole, e.g. a complete organism, is defined in a different way. For instance, if we look at the human body as a 'holobiont', i.e. as the sum of all genetically human parts plus the microbiome, i.e. the genetically alien intestinal bacteria, then the latter would be part of the body, even independently of their function, just by virtue of our definition. Whereas the foetus requires the mother's organism to function, this not true the other way round; therefore, formula (8.22) applies and parthood is not asserted because the foetus is allogeneic. Examples include molecules, which are compounds of atoms with a certain structure. These atoms and nothing else belongs to the molecule. Similarly, a cell might be seen as a compound of their organelles and a body consists of a given set of parts. Considering the depiction of a canonical organism, these parts, and nothing else, are the anatomic entities of a canonical body.

8.5.4 Is the Inclusion Condition Empty?

In this paper, our fundamental assumption was that parthood implies inclusion. All parts, that is, are of necessity located within the whole. Then we asked how we could possibly distinguish between includees that are parts and those that are not, i.e. mere containees. Our result was that this is a very difficult endeavour. Hence it could be asked whether it might have been a cul-de-sac from the beginning. Here is a reason that could be given for that kind of skepticism: A standard assumption of standard mereology is universalism, according to which for any two arbitrary entities that co-exist at a certain time there exists an entity, their so-called mereological sum, which contains both of them as its parts (Rea 2008). Hence, for any water molecule and any cell, say, there is a mereological sum cell + molecule and, trivially, that water molecule is part of this sum. Such a sum exists for any arbitrary molecule; any such molecule can be regarded to be part of such a sum that is roughly the same as the cell in question. But this does not answer the question whether a certain molecule is part of a certain cell. Somewhat trivially, according to universalism there is always an entity that comprises the cell and the molecule such that the molecule is part of this whole, namely the mereological sum of the cell and this molecule. In contrast, van Inwagen (1990) posits that there are only material simples and organisms; nothing else really exists. Hence neither molecules nor organs are part of the body, as neither molecules nor organs really exist. This position is far too radical to capture adequately the biomedical domain, as most commonly purported biological parts seem to vanish into ontological irrelevance.

Even if we reject van Inwagen's position and embrace mereological universalism, the basic assumption of this paper could, nevertheless, seem to be wanting. It might be true, or so it could be objected, that parthood implies spatial inclusion, but this does not rule out the parthood of anything.

If, say, the island Helgoland is a part of Germany, then Germany simply extends as far as Helgoland. If it were not, Germany would simply not extend thus far. The implication of spatial inclusion might be valid, that is, but uninformative. Nevertheless, this is only part of the story, for in many cases we have independent evidence of the spatial borders of certain biological entities: Atoms and molecules are bounded by electron shells, cells and organelles are bounded by membranes and organisms are bounded by their epidermis (their skin). However, these (three dimensionally extended) borders are not without difficulties:

- Not everything within these borders is necessarily a part of the includer in question: If we shoot alpha particles through a cluster of atoms, this particle does not become part of any of these atoms. If a child swallows a marble, the marble does not become part of the child.
- There might even be cases where different entities co-exist within the same border. Atoms in a crystal structure, for example, share their electron shell at least partially. Siamese twins live within the same epidermis.
- The borders are fuzzy. To start with, electrons do not have a crisp location. While the skin is a clear border on the macro-level, it becomes an unequal surface with many holes when seen at the cellular or sub-cellular level.

However, if borders are set this way, another question arises: Is the basic assumption of this paper really true? That is, is the inclusion criterion necessary for biological parthood? If we take the location criterion in a strict sense, it implies that anything ceases to be part of a body once it leaves the boundary of the epidermis. E.g., a portion of blood flowing through a dialysis machine would cease to be part of the body while flowing through the pipes and tubes of the machine and, eventually, upon re-entering the body, become part of it again. This might be counterintuitive. Whoever wants to discard the necessity of inclusion for parthood may nevertheless benefit from the results of this paper, for it still answers the question: In which cases, if any, can we ascertain biological parthood given that something is included in a biological entity?

8.6 Conclusions

In this paper, we have studied parthood and containment in biology. The objective was to find criteria for inferring from a given spatial inclusion relation that holds between two biological objects i and I, whether i is part of I or whether i is merely contained in I. Our approach is built on a precursor study (Schulz et al. 2005), which, however, has not proved practicable, as it is based on difficult primitives like function, integrity and genetic sameness, and on criteria that have not been sufficiently introduced so as to constitute a solid basis for empirical investigations as the authors suggest. In our paper, we have attempted to work out more refined criteria and submit them to a more rigorous scrutiny. The most notable difference is that (Schulz et al. 2005) regards continuous historic inclusion as a criterion for parthood of genetically identical material, even in case it is functionally not relevant. According to that proposal, urine and other body substances would be part of the body wherever they are located within the body, as well as misplaced pieces of body matter in uncommon body locations, e.g. as a result of traumatic changes of structure. On the other hand, only artefacts are a priori rejected as parts, whereas xenogeneic entities are allowed as long as they are functionally relevant. In contrast, we propose that there is an, admittedly, arbitrary line between allogeneic and xenogeneic materials. There is also a fuzzy distinction regarding the criterion of "entities of the same sort", which is crucial for regarding something as a collection: If "collection of insulin molecules" is regarded as a component of a body, then a non-human insulin molecule is a body part, in contrast to a refined "collection of human insulin molecules". We also admit that the functionality criterion may exhibit borderline cases.

There are unexplored waters between the islands of parthood and containment. They will remain even if we artificially enlarge the islands. There are soft criteria that may conduce that a certain scenario tends to parthood or to containment. Any delimitation that improves ontological purity may seem problematic if we want to align ontology with human language and cognition. One could argue, of course, that ontology has nothing to do with human language or cognition. However, if ontological divisions appear cognitively plausible, this will improve the usability and acceptance of ontologies and will probably also reduce the errors that may be committed. It would therefore be useful to submit the axioms proposed in this paper as a plausibility check, i.e. a user rating based on real-world examples.

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