A Fragment-Cofragment Model of Antibody Incidence Structures

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ABSTRACT

In the predecessor to this paper, "Uncovering Antibody Incidence Structures," Markowsky and Wohlgemuth presented a model which allowed one to calculate best possible solutions for the relation between individuals and antibodies given certain sets of tests each of which is analyzed simply for the presence or absence of a reaction. In this paper, we show that many of the concepts and theorems of the first paper generalize to the case where we actually try to compare the strengths of various reaction tests. As one might expect, the resulting model has a greater ability to detect the presence of antibodies than the model presented in the first paper. Furthermore, the additional information generated by the model described in this paper allows one to present a fairly concise definition of the best possible solution for a given amount of reaction test data.

INTRODUCTION

The fragment-cofragment model presented in this paper is an elaboration of the model considered in [1] which makes use of "fragments" to determine antibodies labeling individuals in a reaction matrix. We consider a set $\mathcal{I}$ of individuals on which tests are performed. It is the purpose of our model to determine, from available data, a set $\mathcal{A}$ of antibodies and which antibodies in the set react with antigens in the various individuals in $\mathcal{I}$. This is given formally by a binary relation $G \subseteq \mathcal{I} \times \mathcal{A}$ where $i\,G\,\alpha$ if and only if antibody α reacts with some antigen in individual i. Thus G is considered fixed but unknown, and we seek to determine G. The model in [1], referred to in this

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paper as the "Boolean model," was also directed at the problem of determining $\mathcal{A}$ and G but involved only zero-one reaction matrices as data. The present model allows us to make use of differences in reaction strength.

Reference [2] gives a brief account of the history of modeling immunogenetic factors and relates the various approaches. The reference list in [2] is complete to the best of our knowledge. The first section in [1] relates the problem we are addressing here to the more general models. Our development here parallels the development in [1], and we use much of the same notation, which we list (concisely) for convenience. Section II of [1] connects this notation with immunological terminology in more detail. The discussion section at the end of this paper also gives verbal descriptions (with some imprecison) of the definitions we make.

We use the following conventions:

(1) "iff" means "if and only if."

(2) If n is an integer, $\mathbf{n}=\{1,2,\ldots,n\}$.

(3) If X is a set and y is an element, $X+y$ denotes $X\cup\{y\}$ and $X-y$ denotes $X-\{y\}$.

(4) If S is a set, $|S|$ denotes its cardinality.

(5) If $B\subseteq X\times Y$ and $S\subseteq X$ ($T\subseteq Y$), then $SB=\{y\in Y\mid x\,B\,y$ for some $x\in X\}$ ($BT=\{x\in X\mid x\,B\,y$ for some $y\in T\}$). For $x\in X$ ($y\in Y$) we write xB (By) instead of $\{x\}B$ ($B\{y\}$).

(6) If $B\subseteq X\times Y$ and $S\subseteq X$ ($T\subseteq Y$), then $B-S$ ($B-T$) is just $B\cap[(X-S)\times Y]$ ($B\cap[X\times(Y-T)]$). For singleton sets, we drop the set braces as before.

(7) When dealing with antibodies we assume that $Ga\neq\varnothing,\mathcal{G}$ for all $a\in\mathcal{A}$. Throughout we assume $n=|\mathcal{G}|$ and $m=|\mathcal{A}|$.

(8) If $X\subseteq\mathcal{G}$ then $X'=\mathcal{G}-X$.

(9) As in [1], let $\mathcal{C}_k=\{\langle i,S\rangle\mid i\in\mathcal{G},\ |S|\leqslant k\}$.

(10) For any binary relation E with domain $\mathcal{G}$, define $M(E,k)\subseteq\mathcal{G}\times\mathcal{C}_k$ by $iM(E,k)\langle j,S\rangle$ iff $iE\cap jE\not\subseteq SE$. This gives the Boolean reaction matrices used as data in [1].

DEFINITION 1

For any binary relation E with domain $\mathcal{G}$ and $i,j\in\mathcal{G}$, $S\subseteq\mathcal{G}$, let $\Delta(E,i,j,S)$ [or just $\Delta(i,j,S)$] $=iE\cap jE-SE=iE\cap(jE-SE)$. Define the *reaction tables* $R(E,k)$ with:

rows labeled by individual $i\in\mathcal{G}$,
columns labeled by pairs $\langle j,S\rangle\in\mathcal{C}_k$, and
$\Delta(i,j,S)$ the entry in row i and column $\langle j,S\rangle$.

Thus $\Delta(G,i,j,S)$ gives all antibodies $jG-SG$ in the absorbed serum $\langle j,S\rangle$ in common with antibodies iG labeling individual i. We see that

$\Delta(G,i,j,S)\neq\varnothing$ iff $iM(G)\langle j,S\rangle$; but that $R(G,k)$ gives all distinct antibodies entering into a reaction, whereas $M(G,k)$ gives only whether or not a reaction occurs.

DEFINITION 2

For $|S|\leqslant k-1$ define

$F(G,i,j,S)=\{t\in\mathcal{G}\mid\Delta(i,j,S)\neq\varnothing,\ \Delta(i,j,S+t)=\varnothing\}$ and
$C(G,i,j,S)=\{t\in\mathcal{G}\mid\Delta(i,j,S)\neq\Delta(i,j,S+t)\}$.

Nonempty F and C are called *k-fragments* and *k-cofragments* respectively. $F(G,i,j,S)$ may be denoted by F, $F(G)$ or $F(i,j,S)$ in certain contexts, and similarly for $C(G,i,j,S)$.

RESULTS

THEOREM 3

(a) $F(i,j,S)=\bigcap_{\alpha\in\Delta(i,j,S)}G\alpha$.
(b) $C(i,j,S)=\bigcup_{\alpha\in\Delta(i,j,S)}G\alpha$.
(c) $\Delta(i,j,S)=\{\alpha\}$ *for some* α *iff* $C(i,j,S)=F(i,j,S)\neq\varnothing$ *iff* $F(i,j,S)=C(i,j,S)=G\alpha$ *for some* α.
(d) $C(j,j,S)=\{i\in\mathcal{G}\mid iM\langle j,S\rangle\}$.

Proof. (a): Theorem 6 in [1].

(b): If $tG\alpha$ for some $\alpha\in\Delta(i,j,S)$, then $\alpha\notin\Delta(i,j,S+t)$, so that $C(i,j,S)\supseteq\bigcup G\alpha$. If $t\notin\bigcup G\alpha$ for all $\alpha\in\Delta(i,j,S)$, then $\Delta(i,j,S+t)=\Delta(i,j,S)$, so $t\notin C(i,j,S)$.

(c): Follows immediately from (a) and (b).

(d): Clear. ∎

In this fragment-cofragment model the values of $F(i,j,S)$ and $C(i,j,S)$ are considered as data from which we wish to determine G. The fragments $F(i,j,S)$ are obtainable from the zero-one reaction matrices $M(G,k)$ as in the Boolean model. For a fixed i,j,S with a positive reaction $iM\langle j,S\rangle$, $F(i,j,S)$ is the set of individuals t which give a negative $\neg\,iM\langle j,S+t\rangle$ when tG is absorbed out of $\langle j,S\rangle$. Individuals t in $C(i,j,S)-F(i,j,S)$ are those that reduce the antibody content in common between row i and column $\langle j,S\rangle$ by absorption, but do not reduce it to the empty set. To put it another way, $C(i,j,S)'$ gives those individuals t that have no antibody label (in tG) in common with the set of antibodies $\Delta(i,j,S)$ accounting for a positive reaction in row i, column $\langle j,S\rangle$ of M; presumably absorption by these t would lead to no reduction of reaction strength. To provide input for the model then, an experimenter would need to decide which reactions in row i, column $\langle j,S\rangle$ are positive, and for each of these which reactions in row i, column $\langle j,S+t\rangle$ are as strong as those in row i, column $\langle j,S\rangle$.

Note that since $\Delta(i, j, S+t)$ is a subset (perhaps proper) of $\Delta(i, j, S)$, we avoid comparing reaction strengths of different antibodies. An example of a situation where this model might apply is in cell mediated lympholysis, where reactions are given in per cent lysis and cytotoxic T-lymphocytes play the role of antibodies.

Notice that in Theorem 3(d) the particular cofragments $C(j, j, S)$ are the columns of the zero-one data matrix M.

We now proceed to the idea of detectability.

LEMMA 4

For $\alpha \in \mathfrak{A}$, $C(G-\alpha, i, j, S) \subseteq C(G, i, j, S)$.

Proof. Let $t \notin C(G, i, j, S)$ and $\beta \in \Delta(G-\alpha, i, j, S)$. Then $\beta \neq \alpha$ and $\beta \in \Delta(G, i, j, S) = \Delta(G, i, j, S+t)$, so that $\neg\, t(G-\alpha)\beta$. Hence $\Delta(G-\alpha, i, j, S) = \Delta(G-\alpha, i, j, S+t)$. Therefore $t \notin C(G-\alpha, i, j, S)$. ■

DEFINITION 5

An antibody $\alpha \in \mathfrak{A}$ is called *k-fc-undetectable* (*k-fragment-cofragment undetectable*) if G and $G-\{\alpha\}$ give the same sets $F(i, j, S)$ and $C(i, j, S)$ for $|S| \leqslant k-1$. If necessary, we can designate G so as to avoid ambiguity. An antibody is called *fc-undetectable* (*fragment-cofragment undetectable*) if it is k-fc-undetectable for all k. The terms k-fc-detectable and fc-detectable have the expected meaning.

In this paper we will refer to a (k-)fc-undetectable antibody merely as (k-)undetectable. Antibodies undetectable in the Boolean model will be called "Boolean undetectable" in contradistinction to the present model.

THEOREM 6

(a) *$\alpha \in \mathfrak{A}$ is undetectable iff for every $i, j, k \in G\alpha$ there exists $\beta \in \mathfrak{A}$ such that $\{i, j, k\} \subseteq G\beta \subset G\alpha$. Thus by Theorem 3 of* [1], *if α is undetectable, then it is Boolean undetectable.*

(b) *if α is undetectable, then $|G\alpha| \geqslant 4$.*

(c) *α is detectable iff $\{\alpha\} = \Delta(i, j, S) - \Delta(i, j, S+k)$ for some i, j, k, S. Furthermore, S can be taken as $G\alpha'$.*

Proof. (a): *Sufficiency:* By Theorem 3 of [1] the condition implies that the F are not changed. Suppose $t \in C(G, i, j, S) - C(G-\alpha, i, j, S)$. Then $t\, G\, \alpha$ and $\neg\, t\, G\, \delta$ for all $\delta \in \Delta(G-\alpha, i, j, S)$. Thus there cannot exist β such that $\{i, j, t\} \subseteq G\beta \subset G\alpha$.

Necessity: Let i, j, k be given in $G\alpha$. Then $\alpha \in \Delta(G, i, j, G\alpha')_{\text{def}} = D$ and $D - \{\alpha\} \neq \varnothing$, since α is undetectable. Note that $i, j \in G\beta \subset G\alpha$ for all $\beta \in D - \{\alpha\}$. Assume that $\neg\, k\, G\beta$ for all $\beta \in D - \{\alpha\}$. Then $\Delta(G, i, j, G\alpha' + k) \cup \{\alpha\} = D$, so $k \notin C(G-\alpha, i, j, G\alpha')$, but $k \in C(G, i, j, G\alpha')$, contradicting the fact that α is undetectable. Hence $i, j, k \in G\beta \subset G\alpha$ for some β.

(b): Clear by (a).

(c): Suppose α is detectable and set $S = G\alpha'$. Then there exist $i, j, k \in G\alpha$ such that for each β with $G\beta \subset G\alpha$, $\{i, j, k\} \not\subset G\beta$. Clearly $\alpha \in \Delta(i, j, S)$. Further, if $\alpha \neq \beta \in \Delta(i, j, S)$ then $G\beta \subset G\alpha$, so that $\neg\, k\, G\beta$, whence $\beta \in \Delta(i, j, S+k)$. Thus $\{\alpha\} = \Delta(i, j, S) - \Delta(i, j, S+k)$.

Conversely, by the condition, $k \in C(G, i, j, S)$, but $k \notin C(G-\alpha, i, j, S)$, so α is detectable. ■

Theorem 6 shows that the fragment-cofragment model is somewhat sharper in its ability to detect antibodies than is the Boolean model. A fragment $F(i, j, S)$ or cofragment $C(i, j, S)$ is determined by various reaction strengths in a single row (i) of, say, per cent lysis in a reaction table. In order to use cofragments it is therefore necessary to have an experimental procedure that makes comparison of reaction strengths for various columns and the same row meaningful. It is much more natural experimentally to obtain a meaningful comparison between various rows for the same column (reagent). However, detectability in models using the latter comparisons is no sharper than in the Boolean model.

THEOREM 7

Let T be any set of G undetectable antibodies. Then:

(a) $F(G) = F(G-T)$;

(b) $C(G) = C(G-T)$;

(c) *$\alpha \notin T$ is G-detectable iff α is $G-T$-detectable*;

(d) *There is a unique set $T^* \subseteq \mathfrak{A}$ such that* (a) *and* (b) *hold for $T = T^*$ and every element of $\mathfrak{A} - T^*$ is $G-T^*$-detectable. We call $G-T^*$ the* reduction of G.

Proof. (a): If $\alpha \in T$ is undetectable, then α is Boolean undetectable, so that $M(G) = M(G-T)$ by Theorem 4 in [1]; hence $F(G) = F(G-T)$.

(b): By Lemma 4, $C(G, i, j, S) \supseteq C(G-T, i, j, S)$. Let $k \in C(G-T, i, j, S)'$. Then $\Delta(G-T, i, j, S) = \Delta(G-T, i, j, S+k)$, so that $\Delta(G, i, j, S) - \Delta(G, i, j, S+k) \subseteq T$. Suppose $\alpha \in \Delta(G, i, j, S) - \Delta(G, i, j, S+k)$ is picked so that $G\alpha$ is minimal with respect to set inclusion. Then $i, j, k \in G\alpha$, so there is some β such that $i, j, k \in G\beta \subset G\alpha$, since $\alpha \in T$ is undetectable. But then $\beta \in \Delta(G, i, j, S) - \Delta(G, i, j, S+k)$, contradicting the minimality of $G\alpha$. Consequently, $\Delta(G, i, j, S) = \Delta(G, i, j, S+k)$, whence $k \in C(G, i, j, S)'$. Therefore $C(G, i, j, S) = C(G-T, i, j, S)$.

(c): Suppose α is G-detectable. Then $\{\alpha\} = \Delta(G, i, j, S) - \Delta(G, i, j, S+k)$ for some k by Theorem 6. Since $\Delta(G-T, i, j, S) = \Delta(G, i, j, S) - T$ and

$\Delta(G-T, i, j, S+k)=\Delta(G, i, j, S+k)-T$ and $\alpha \notin T$, we have $\{\alpha\}=\Delta(G-T, i, j, S)-\Delta(G-T, i, j, S+k)$, so α is $G-T$-detectable.

Conversely, suppose $\alpha \notin T$ is G-undetectable but $G-T$-detectable. Since α is $G-T$-detectable, there exist $i, j, k \in G\alpha$ such that for all $\beta \in \mathcal{C}-T$, if $i, j, k \in G\beta$, then $G\beta \not\subset G\alpha$. Since α is G-undetectable, there exists $\beta' \in T$ with $i, j, k \in G\beta'$ and $G\beta' \subset G\alpha$. Pick β' with minimal $|G\beta'|$. Since $\beta' \in T$, β' is undetectable. Thus there exists $\beta'' \in \mathcal{C}$ with $i, j, k \in G\beta'' \subset G\beta'$. This implies that $\beta'' \in T$, which contradicts the fact that $|G\beta'|$ was minimal.

(d): By (a), (b), and (c), T^* is the set of G-undetectable antibodies. ■

DEFINITION 8

For a given $\mathbb{S} \subseteq 2^{\mathcal{G}}-\{\varnothing, \mathcal{G}\}$ define $G_{\mathbb{S}} \subseteq \mathcal{G} \times \mathbb{S}$ by $i G_{\mathbb{S}} X$ iff $i \in X$. For a given G, k define $\mathrm{Sol}(G, k)$ to be the set of all $\mathbb{S}$ such that $F(\mathbb{S})_{\mathrm{def}}=F(G_{\mathbb{S}})=F(G)$ and $C(\mathbb{S})_{\mathrm{def}}=C(G_{\mathbb{S}})=C(G)$.

$\mathrm{Sol}(G, k)$ is called the kth solution space in the fragment-cofragment model. $\mathrm{Sol}(G, \omega)=\mathrm{Sol}(G, k)$ for $k=n-1$. If every element of $G_{\mathbb{S}}$ for $\mathbb{S} \in \mathrm{Sol}(G, k)$ is detectable, we call $\mathbb{S}$ a detectable solution. We will often just use $\mathbb{S}$ rather than $G_{\mathbb{S}}$ for conciseness.

LEMMA 9

For $\mathbb{S}_1, \mathbb{S}_2 \subseteq 2^{\mathcal{G}}-\{\varnothing, \mathcal{G}\}$, $i, j \in \mathcal{G}$, $S \subseteq \mathcal{G}$, *we have* $\Delta(\mathbb{S}_2 \cup \mathbb{S}_2, i, j, S)=\Delta(\mathbb{S}_1, i, j, S) \cup \Delta(\mathbb{S}_2, i, j, S)$.

Proof. Straightforward. ■

THEOREM 10

If $\mathbb{S}_1, \mathbb{S}_2 \in \mathrm{Sol}(G, k)$, *then* $\mathbb{S}_1 \cup \mathbb{S}_2 \in \mathrm{Sol}(G, k)$.

Proof. By Lemma 16 of [1], $F(\mathbb{S}_1)=F(\mathbb{S}_2)=F(\mathbb{S}_1 \cup \mathbb{S}_2)$. That $C(\mathbb{S}_1)=C(\mathbb{S}_2)=C(\mathbb{S}_1 \cup \mathbb{S}_2)$ follows from Lemma 9 and the definitions. ■

THEOREM 11

$\mathrm{Sol}(G, \omega)$ *has a unique detectable solution.*

Proof. Since $\mathrm{Sol}(G, \omega)$ is nonempty, Theorem 7 implies that it contains a detectable solution. Let $U, V \in \mathrm{Sol}(G, \omega)$ be such that each element of U and V is U- or V-detectable respectively. Let $X \in U$. Then for some i, j, k, and $S=X'$, we have $\{X\}=\Delta(U, i, j, S)-\Delta(U, i, j, S+k)$. Then $X=C(U, i, j, S)=C(V, i, j, S)=\cup Y_l$ for $Y_l \in \Delta(V, i, j, S)$. In order to obtain a contradiction assume that each $Y_l \subset X$. Then there is some Y_p such that $k \in Y_p \subset X$, so that for $t \in X-Y_p$, we have $Y_p \in \Delta(V, i, j, S+t)-\Delta(V, i, j, S+t+k)$, that is, $k \in C(V, i, j, S+t)$. But $\Delta(U, i, j, S+t)=\Delta(U, i, j, S)-tG_U=\Delta(U, i, j, S+k)-tG_U=\Delta(U, i, j, S+t+k)$, so $k \notin C(U, i, j, S+t)$. The contradiction shows that some $Y_l=X$, that is, $X \in V$, so that $U \subseteq V$. By symmetry $V \subseteq U$. ■

The foregoing shows that there is a natural solution to the problem of determining G from sets of fragments and cofragments, namely, the reduction of the largest element in $\mathrm{Sol}(G, k)$, which we denote by $\Sigma^*(G, k)$. $\Sigma^*(G, k)$ "converges" to the unique detectable solution in $\mathrm{Sol}(G, \omega)$ as k is increased (more becomes known).

We now turn to the problem of computing $\Sigma^*(G, k)$ from the set of k-fragments and k-cofragments.

LEMMA 12

(a) *For* $t \notin F(i, j, S) \neq \varnothing$,

$$F(i, j, S) \subseteq F(i, J, S+t) \subseteq C(i, j, S+t) \subseteq C(i, j, S).$$

(b) *If* $t \notin F(i, j, S)=C(i, j, S)=G\alpha$, *then*

$$F(i, j, S+t)=C(i, j, S+t)=G\alpha.$$

Proof. Trivial. ■

Lemma 12 applies to the case where $G=\Sigma^*(G, k)$. It follows that the only elements lost when we consider k-fragments and co-fragments instead of l-fragments and cofragments for all $l \leqslant k$ are those $G\alpha$ such that $S+t$ can no longer be found disjoint from $G\alpha$, that is, those $G\alpha$ such that $|G\alpha|>|\mathcal{G}|-k$. We use the notation $G\alpha$ to refer either to $G_H X$ for $X \in H \in \mathrm{Sol}(G, k)$ or to the reaction range of some α in the original G, since G and G_H are indistinguishable by l-fragments and cofragments for $l \leqslant k$. This notation makes it somewhat easier to relate the current discussion to earlier theorems.

DEFINITION 13

For any k *let* Ω_k *be the set of* $X \subseteq \mathcal{G}$ *for which we can find* i, j, S *such that* $X=F(i, j, S)=C(i, j, S)$ *for* $|S|<k-1$ *plus the set of all* $Y \subseteq \mathcal{G}$ *such that* $F(i, j, S) \subseteq Y \subseteq C(i, j, S)$ *for* $|S|=k-1$.

LEMMA 14

$G \subseteq G_{\Omega_k}$.

Proof. Every $G\alpha$ is some X or Y in Definition 13 by Theorem 3. ■

THEOREM 15

Let

$$H=\Omega_k-\{Y \in \Omega_k \mid \text{for some } x, y, T,\ x, y \in Y,\ Y \cap T=\varnothing \text{ and } \neg F(x, y, T) \subseteq Y \subseteq C(x, y, T)\}.$$

Then $\Sigma^*(G, k) \subseteq H \in \mathrm{Sol}(G, k)$. *In particular,* $\Sigma^*(G, k)$ *is the reduction of* H.

Proof. Let $X \in \Sigma^*(G,k)$. We can call $X = G\alpha$ by assuming without loss of generality that $G = G_{\Sigma^*(G,k)}$. Since α is detectable, $\alpha \in \Delta(i,j,S)$ for some i, j, S, where $|S|$ can be taken $\leqslant k-1$. Then $F(i,j,S) \subseteq G\alpha \subseteq C(i,j,S)$ by Theorem 3, so that $G\alpha \in \Omega_k$. If $G\alpha \notin H$, then for some x, y, T, $x, y \in G\alpha$, $G\alpha \cap T = \varnothing$. Thus $\alpha \in \Delta(x,y,T)$, but then again by Theorem 3, $F(x,y,T) \subseteq G\alpha \subseteq C(x,y,T)$. The contradiction shows $G\alpha \in \Sigma(G,k)$. Hence $\Sigma^*(G,k) \subseteq H$.

In order to show $H \in \mathrm{Sol}(G,k)$ we need to show $F(G_H,i,j,S) = F(G,i,j,S)$ and $C(G_H,i,j,S) = C(G,i,j,S)$ for all i, j, S. Since we can take $G = G_{\Sigma^*(G,k)}$ and $\Sigma^*(G,k) \subseteq H$, we see that $\Delta(G,i,j,S) \subseteq \Delta(G_H,i,j,S)$. If $Y \in \Delta(G_H,i,j,S)$, then by the definition of H, $F(i,j,S) \subseteq Y \subseteq C(i,j,S)$. Hence in the case that $\Delta(G,i,j,S) = \varnothing$ we see that $C(i,j,S) = \varnothing$, so that $\Delta(G_H,i,j,S) = \varnothing$ (no such Y can exist). If $\Delta(G,i,j,S) \neq \varnothing$, then $F(G_H,i,j,S) \subseteq F(G,i,j,S) \subseteq C(G,i,j,S) \subseteq C(G_H,i,j,S)$. But if $Y \in \Delta(G_H,i,j,S)$, then $F(i,j,S) \subseteq Y \subseteq C(i,j,S)$, so that $F(G_H,i,j,S) = F(G,i,j,S) \subseteq C(G,i,j,S) = C(G_H,i,j,S)$ by Theorem 3. ■

DISCUSSION

The fragment-cofragment model uses as data the results of tests between individuals $i \in \mathcal{I}$ and reagents $\langle j, S \rangle$ where $S = \{s_1, \ldots, s_k\} \subseteq \mathcal{I}$. $\langle j, S \rangle$ can be thought of as s_1 anti-j with $s_2, \ldots, s_k$ absorbed. In order to use the fragment-cofragment model we must have $k \geqslant 2$, whereas the Boolean model applies when $k \geqslant 1$. For a fixed i, j, S where individual i and reagent $\langle j, S \rangle$ give a positive reaction, the fragment $F(i,j,S)$ is the set of all t where i and $\langle j, S+t \rangle$ give no reaction; the cofragment $C(i,j,S)$ is the set of all t where i and $\langle j, S+t \rangle$ give either no reaction or a reaction less than that with $\langle j, S \rangle$. Fragments can be calculated from a zero-one reaction matrix and are the same as in the Boolean model. In order to calculate cofragments it is necessary to have experimentally meaningful comparisons between the reaction strengths of various reagents with the same individual. The sets of fragments and cofragments for all possible i, j, S are the data from which we can compute $\mathcal{A}$, the set of antibodies, and G, the antibody incidence relation or labeling of individuals with antibodies.

The condition under which an antibody is undetectable in the fragment-cofragment model [given in Theorem 6(a)] is even more restrictive than the condition in the Boolean model and would hardly be expected to occur in practice. Except for undetectable antibodies, $\mathcal{A}$ and G are uniquely determined (Theorem 11) if k is large enough. For any fixed $k \geqslant 2$ there is a best possible solution $\Sigma^*(G,k)$. Further, the sequence $\Sigma^*(G,2), \Sigma^*(G,3), \ldots$ "converges" to the uniquely determined solution $\Sigma^*(G,\omega)$ of Theorem 11. The foregoing statements are precisely analogous to those in the Boolean model. The content of the statements is different, however, since the notion of detectability is different in the two models.

Theorem 15 provides a basis for calculating $\Sigma^*(G,k)$ for any $k \geqslant 2$, namely, deleting undetectable unions from the set H described. This algorithmic calculation has advantages and a disadvantage when compared to the algorithm in the Boolean model. An advantage is that we have a bound on the reaction ranges $G\alpha$ of those antibodies α responsible for an entry $\Delta(i,j,S)$ in the reaction table, namely $F(i,j,S) \subseteq G\alpha \subseteq C(i,j,S)$. In particular, we now have an idea of how far away the solutions $\Sigma^*(G,k)$ may be from their limit, and we know when an antibody is found (the limit is reached), namely when $F(i,j,S) = C(i,j,S)$. A disadvantage is that the computational procedure may require more time.

This paper contains the mathematical description and analysis of the fragment-cofragment model for uncovering $\mathcal{A}$ and G. A tutorial paper for experimental immunogeneticists explaining the computational use of the model is in preparation.

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