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A Scenario Development on Hepatitis B and C

Yukio Ohawa† Naoaki Okazaki‡ Naohiro Matsumura‡
†Graduate School of Business Sciences, University of Tsukuba: Tokyo 112-0012, Japan
‡ Faculty of Engineering, The University of Tokyo: : Tokyo 113-8656, Japan
Email: †osawa@gssm.otsuka.tsukuba.ac.jp ‡{okazaki,matumura}@miv.t.u-tokyo.ac.jp

Abstract: Obtaining scenarios has been a major approach for decisions in domains where a sequence of events and actions in the future is significant. Chance discovery, in which events with significance for making a decision, can be regarded as the emergence of a scenario, with extracting chances i.e. essential events in the turning points of valuable scenarios by means of the interaction with the environment. In this paper, we apply a method of chance discovery to the data of diagnosis of hepatitis patients, for obtaining scenarios of how the most essential symptoms appear in the patients of hepatitis of type B and C. In the process of discovery, the results are evaluated to be novel and potentially useful, under the mixture of objective facts and the subjective widening and narrowing of the surgeon's concerns.
Keywords: Scenario emergence, Hepatitis B and C, Chance discovery

Ｂ型・Ｃ型肝炎症状変化のシナリオ生成

大澤幸生† 岡崎直観‡, 松村真宏‡
†筑波大学ビジネス科学研究科 112-0012, Japan
‡ 東京大学工学系研究科：113-8656, Japan
Email: †osawa@gssm.otsuka.tsukuba.ac.jp ‡{okazaki,matumura}@miv.t.u-tokyo.ac.jp

意思決定において事象と行動の時系列すなわちシナリオが重要となることが多く、シナリオ開発が様々なアプローチから試みられてきた。筆者らが研究してきたチャンス発見手法も、環境との相互作用の中でシナリオの分岐点となる事象とその価値を見出しながらシナリオを創発的に開発するチャレンジであった。本論文では、チャンス発見のプロセスをＢ型・Ｃ型肝炎の検査データと外科医師の臨床経験との相互作用に適用して肝炎進行・治癒についてのシナリオを開発し、インターフェロンの効果など様々の医療上重要な示唆を得た。客観的な事実との相互作用から医師の主観的関心を発散・収束した効果と考えられる。
キーワード：シナリオ創発, Ｂ型・Ｃ型肝炎, チャンス発見

1. Introduction: Scenarios as the basis of Chance Discovery for Critical Decisions

Scenarios have been a significant basis of decisions, in domains where a sequence of events in the future becomes significant. Let us stand on the position of a surgeon, for example, looking at the time series of symptoms during the progress of an individual patient's disease. The surgeon should make an appropriate action for curing this patient, at an appropriate time. If he does the patient's disease may be cured efficiently, but otherwise the patient's health condition might turn radically into a worse state. The situation of this surgeon can be described as a choice from two sequences, for example,

Sequence 1) state 1 -> state 2 -> state 3 -> state 4
Sequence 2) state 1 -> state 2 -> state 5 (1)

Suppose that state 4 and 5 mean two opposite situations, i.e., one where the disease is cured and a fatal situation. The surgeon should choose a effective action at the time state 2 appears, for this patient to shift to state 4. This kind of state, which is essential for decision has been called a chance [1].

On the other hand, the event-sequence in (1) has been called a *scenario* in cases where considering a sequence is essential for decision. All in all, the discovery of a chance is quite relevant to obtaining valuable scenarios. Thus scenarios are tools for chance discovery, and also the purpose of chance discovery. That is, detecting the branching events between multiple scenarios between the two scenarios, as state 2 in (1), means the chance discovery for the surgeon. This chance is regarded as valuable, only if the purpose is achievable, i.e. if the scenario including state 2 is valuable, because a scenario is easier to understand than an event shown alone. Suppose you are the patient and told just that you have a polyp in the stomach, it would be hard to decide to cut it or to do nothing to leave it in the current position. On the other hand, suppose the doctor tells that you are in the branch of two scenarios – in one, it will turn larger and worse. In the other, the polyp is cut away, you will be cured. Normally, you will prefer the latter choice.

2. Scenario "Emergence" in the Mind of Experts

In the term "scenario development", a scenario sounds like

something to be "developed" by human(s) who consciously rules the process of making a scenario. However, scenario really "emerges" by partially unconscious interaction of human(s) and the environment. For example, a *scenario workshop* starts from scenarios preset by writers, then experts in the corresponding domain discusses to improve the scenarios [2]. It is usual that the discussants write down their opinions during the workshop, but rarely they notice why those opinions came out and the why the workshop selected the scenarios obtained finally. In the very origin of aiding creation, the KJ method begins from cards on which the initial ideas are written and arranged in the 2D-space by co-working discussants. The new combination of proposed scenarios may help the emergence of a new valuable scenario. In the design process, ambiguous information can trigger creations [3].

The common points among "experts" in scenario workshops, "combination" of ideas in KJ method, and the "ambiguity" in the information to a designer is that multiple scenarios in the interaction of subjects with their own environments are bridged via the links between the contexts in the mental world they attend. From these bridges, they unconsciously introduce some situations or events which may work as "chances" to import others' scenarios. In the example of (1), a surgeon who almost gave up because he imagined scenario 2, may obtain a new hope in scenario 1 proposed by his colleague, by noticing that state 2 is shared by the two scenarios.

In this paper, we show a method of aiding scenario emergence, by means of visual interaction with real data using two tools KeyGraph and Text Drop. KeyGraph, with an additional function to show causal directions in the relations between events (let us call this *scenario map*), visualizes the complex relations among values of variables in diagnosis data of hepatitis, and Text Drop helps in extracting the part of data corresponding to the interest of an expert, a surgeon here.

These tools help in picking essential scenarios of specific types of patience from the complex diagram of their mixture, i.e. KeyGraph These results are evaluated by the surgeon as useful in the decision of curing hepatitis B and C. This evaluation is subjective in the sense that too small number of patients were observed to follow the entire scenarios obtained, to evaluate the scenarios quantitatively. Further more, we should say the evaluation is made in the process of discovery, merging the subjective interest of the expert and the objective within the process of chance discovery. Rather than calling data-mining, this is a self-mining of the subject, where the quality of the self's experience affects much on the result.

3. A Chance Discovery Method for Explaining the Scenarios of Hepatitis Patients

3.1 The Double Helical Process of Chance Discovery

In the most recent state of art, the process of chance discovery is supposed to follow the Double Helix (DH) model [1], in figure 1.

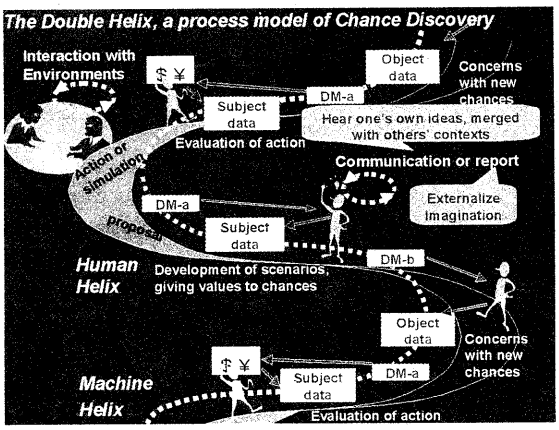

Fig.1 The DH Model: A process model of chance discovery.

It starts from a state of mind concerned with winning a new chance, and this *concern* (ambiguous interest) is reflected to acquiring data to be analyzed by a data-mining tool, specifically designed for chance discovery, for making a new decision. Looking at the result of this analysis, possible scenarios and their values may become clarified in the user' mind. If multiple users co-works sharing the same data-mining result, the effect of scenario emergence might help in mining valuable scenarios by bridging the various experience of participants to form a novel scenario. Based on the chances discovered here, the user(s) make actions or simulate actions in a virtual (imagined /computed) environment, and obtains renewed concerns with chances – the helical process returns to the initial step as in Fig.1. Fig.1 is embodied in this paper, in the application to hepatitis diagnosis. The user sees and manipulates KeyGraph, thinking and talking about the scenarios the diagram may imply. Here, "manipulate" means to cut, move, and unify nodes/links in KeyGraph - it enforces the bridges between multiple experiences to be combined in scenario emergence. In other words, manipulation urges user to ask "why is this node here?" and to virtually experience alternative scenarios s/he did not think of.

3.2 KeyGraph and Text Drop for Accelerating DH

In the case of marketing for textile products, Nittobo Inc. made a success in selling a new product with adding a new value represented by a scenario in the life of people who may buy the product. They visualized the map of the market by means of KeyGraph [1,4], shown as a diagram of co-occurrences between products in the basket data of buyers of textiles. In this map, their marketing researchers found a valuable new scenario in the life people who may go buying textiles across a wide range in the market. They successfully found essential new products in valuable scenarios they found. This realized a sales hit of the new textile.

However, it was not efficient to follow the process in figure 1, using KeyGraph solely. A critical defect of this method was that

user could not extract the interesting part of the data easily, when s/he has got a new concern with chances. For example, they may become interested in a customer who buys product A or product B, who also buys product C, but does never touch product D. Then, the user desires to look *easily* into such customers deeply to take advantage of chances in the submarket formed by such kind of customers they came to be interested in. Text Drop is a simple tool for Boolean-selection of the part of data corresponding to users' interest which can be described in a Boolean formula, e.g.

"(product A | product B) & product C & !product D". (2)

Then Text Drop obtains a new data, made of baskets including product A or product B, and product C, but not including product D. Its simple interface is useful in the case where the user can express his/her own interest in Boolean formula as in (2). The interest of user might be more ambiguous, especially in the beginning of the process of chance discovery. In such a case, the user is supposed to enter the formula "as much as precisely" reflecting one's own interest. Having KeyGraph, Text Drop, and the freedom to use these on necessity, the user can follow the procedure below to realize a DH process.

[DH Process supported by KeyGraph and Text Drop]

1) Obtain a data of baskets, reflecting user's interest
2) Apply KeyGraph to the data to visualize the map representing the relations, or the causal order of occurrences if possible, among items in the baskets.
3) Manipulate KeyGraph as follows:
   3-1) Move nodes and links to the positions in the 2D output of KeyGraph, or remove nodes and links which are apparently meaningless in the target domain.
   3-2) Write down scenarios, imaginable on KeyGraph
4) Read or visualize the comments of experts in 3-2), and become aware of interesting items in the data for user him/herself.
5) Enter interesting items or their combination in Boolean formula, into Text Drop. The data of baskets, reflecting user's new interest is obtained. Return to Step 1).

4. Results for the Diagnosis Data of Hepatitis

4.1 The Hepatitis Data

The following shows the style of data in the case of the diagnosis of hepatitis. Each item represents the pair, of a variable and its observed value. That is, an item put as "a_b" means a piece of data where the value of variable a is b. For example, T-CHO_high (T-CHO_low) means T-CHO (total cholesterol) is higher (lower) than a predetermined threshold. Each line in the data represents the sequence of diagnosis results for one patient. See description (3).

Patient 1) item1, item2, ….., item m1.
Patient 2) item 2, item 3, ….., item m2.
Patient 3) item 1, item 5, …, item m3. (3)

As in (3), we can regard one patient as a unit of co-occurrence of items. That is, there are various cases of patients and the sequence of one patient's diagnosis items means his/her scenario of wandering in the map of the various symptoms. By applying KeyGraph to the data in (3), we can obtain the following components:

- *Islands of items*: A group of items co-occurring frequently, i.e. occurred to many same patients or many same lines in (3). The doctor can be expected to know what kind of patient each island corresponds to.
- *Bridges across islands*: A patient may switch from one island to another, in the progress of the disease or its cure.

Figure 2 is the KeyGraph obtained first, for cases of hepatitis B. The arrows, which did not appear in the original KeyGraph, depict approximate causation, i.e., X -> Y means that if X is true, then the patient's data tended to include Y also. That is, each line in (3) is a set of observations of a certain patient from his/her certain situation in the disease progress or cure. On this specific feature of diagnosis data, the relative strength of the statement "if item X is in a patient's data, then item Y occurred also for the same patient" in comparison with its inverse, say "if item Y is in a patient's data, then item X occurred also for the same patient" means X is likely to be a cause of Y. Thus, even if there are relations where the order of causality and time are opposite (i.e. if X is the cause of Y but was observed after Y), we can obtain approximate scenarios by connecting X->Y relations in sequence, just with comparing the two results of KeyGraph - for data including X and for one including Y. In a case the order of causality and time are opposite, we may interpret that Y appeared before X only because the threshold of Y was set easy to exceed, e.g., the upper threshold of T-CHO may be set low and easy to exceed than that of F-CHO, which makes T-CHO_high appear before F-CHO_high even if T-CHO is a result of F-CHO. Let us call a KeyGraph with these arrows a *scenario map*.

4.2 Results for Hepatitis B

Figure 2 was shown to a surgeon (see acknowledgement) in Step 2), and was manipulated in step 3). In the manipulation, he grouped the nodes in the circles in Figure 2, got rid of unessential nodes from the figure, and unified redundant nodes as "jaundice" and "T-BIL_high" (high total bilirubin). Figure 3 was the result of this manipulation. Simultaneously, we wrote down what the doctor has been teaching us about hepatitis looking at the KeyGraph, and we applied KeyGraph to the memo. According to its result, two of the most significant terms were "mixture" and "jaundice". An important lesson here was that KeyGraph depicted a mixture of various scenarios. Some of the scenarios were common sense for the surgeon, about the progress of hepatitis B, e.g.,

(Scenario B1) Transition from CPH (chronic persistent hepatitis) to CAH (chronic active hepatitis).

(Scenario B2) Decrease in blood platelets (PT) and hemoglobin (HDB), leading to jaundice i.e., increase in the T-BIL. Considering D-BIL increases more keenly than I-BIL, this is from the activation of lien, due to the critical illness of liver.

(Scenario B3) Biliary blocks accelerate jaundice

Although scenarios for the cure of hepatitis B were not observed apparently, we could see that a quick sub-process from LDH_high to LDH_low (LDH: lactate dehydrogenase) is a significant bridge from a light hepatitis to a critical state of liver as the high value of T-BIL.

According to the surgeon, a sudden change in the value of LDH is quite often observed in the introductory steps of hepatitis B, in the real treatment, but the quick change has been regarded as an ambiguous information for treatment. However, the result of KeyGraph for the sub-data extracted from various aspects showed LDH plays a significant role in the scenario of progress of hepatitis, e.g., Fig.4. Figure 4 shows the scenario map, for cases including "IG-M_high", considering that IG-M (immunoglobulin M) is activated in the beginning of infection with virus. For the reason that the data of symptoms is taken from a certain time to the termination of the individual patient's data, the data including IG-M_high was regarded as a summary of the overall scenario of infectious disease.

Note that Fig.4 is still a simple summary of scenarios, just showing 30 nodes where 50 to 60 is the typical range. Having obtained the new concern, what the scenario can be like if it includes the change in the value of LDH, i.e. decrease shortly after increase, we obtained the result in Figure 5 for data of hepatitis B including "LDH_high" and "LDH_low". This figure shows the change in the value of LDH triggers a shift from the initial state stared by biliary-relevant enzymes as G-GTP and ALP, to a critical state in the large circle where T-BIL, I-BIL, and D-BIL are high and CHE (choline esterase) decreases.

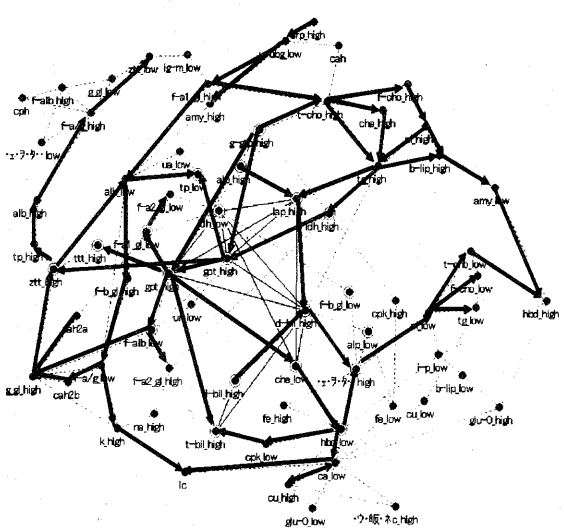

Fig.2 The scenario map (KeyGraph with arrows) for hepatitis B.

According to the surgeon, he has been tacitly aware of this position of the change in LDH, in the real experiences. This was a useful, but not published piece of knowledge for detecting a sign of critical changes in the liver.

4.3 Results for Hepatitis C

In cases of hepatitis C, as Fig.6 shows, we easily find a mixture of a number of scenarios, e.g.,

(Scenario C1) Transition from CPH to CAH,

(Scenario C2) Transition to critical states, e.g. cancer, jaundice.

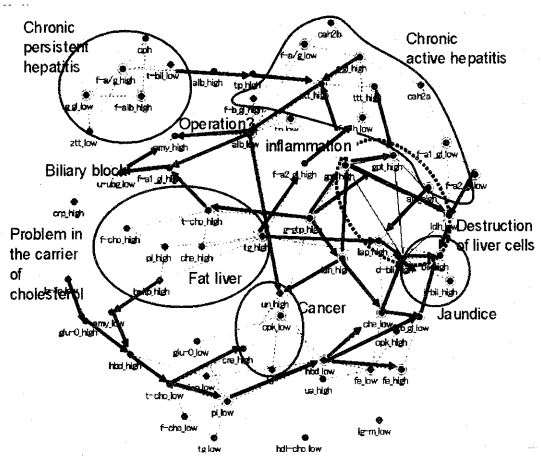

Fig.3 The scenario map, after manipulation on Fig.2. The surgeon acquired concerns with biliary relevant enzymes, G_GTP, LDH etc., especially LDH he has been feeling important in his own experiences. *Note: in all figures hereafter, the arrows were drawn reflecting the causations as in 4.1, and round frames and their interpretations were drawn manually.*

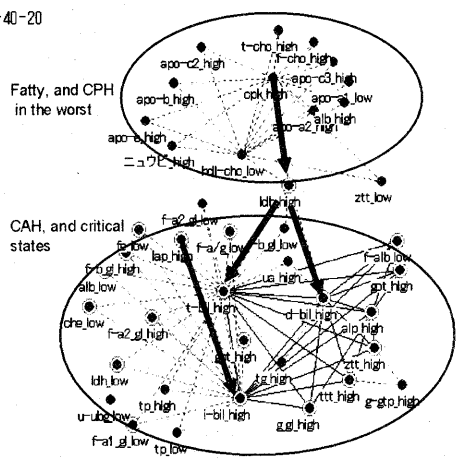

Fig.4 The scenario map or hepatitis B with IG-M_high, to see scenarios in the early of disease where biliary enzymes as LDH are affected. A temporary increase in LDH is found to be a bridge from a persistent to an active states. This deepened the concern with LDH, and embodied the concern to an interest in entering "LDH_high & LDH_low" to Text Drop.

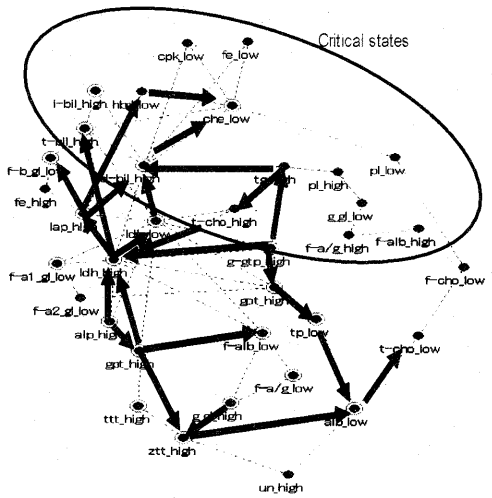

Fig. 5 The scenario map for hepatitis B, with LDH_high and LDH_low. This figure "tacitly matches with experiences and potentially useful, although not published ever" according to the surgeon.

These common-sense scenarios are quite similar to the scenarios in the cases of hepatitis B, but we also find "interferon" and an ambiguous region in the top (in the dotted circle) of figure 6. That is, GOT and GPT can be low both after the fatal progress of heavy hepatitis and if the disease is cured. The latter case is rare because GOT and GPT are expected to normally take "normal" value, i.e., between the lower and the upper threshold, rather than being "low" i.e. lower than the lower threshold.

Thus we saw the results of renewed scenario map for cases including both GOT_low and GPT_low. We still find a complex mixture of scenarios, and find some events looking like a better state in the region without arrows in figure 7.

Fig.7 seems to be separated roughly into good and bad liver states. We assumed this represents the shift from a bad liver to a mixture of good and bad states due to the treatment by interferon. This suggested that the data with "GOT_low & GPT_low & !interferon" (i.e. GOT and GOT both became low at least once, and interferon has never been used) may separate the two areas, one of critical scenario and the other not so severe. In the result of Fig.8, we find two clusters:

(Upper cluster) The scenario of fat liver, to be cured, *not requiring interferon*. This cluster does not mean to turn to a critical state. The item F-B_G1_high and F-A1_Gl_high are the turning points from bad to a better state.

(Lower cluster) Critical scenario *beyond the effect of interferon*, i.e., of high bilirubins. F-A1_Gl_low and F-A1_Gl_gl_low are on the switch to the critical states.

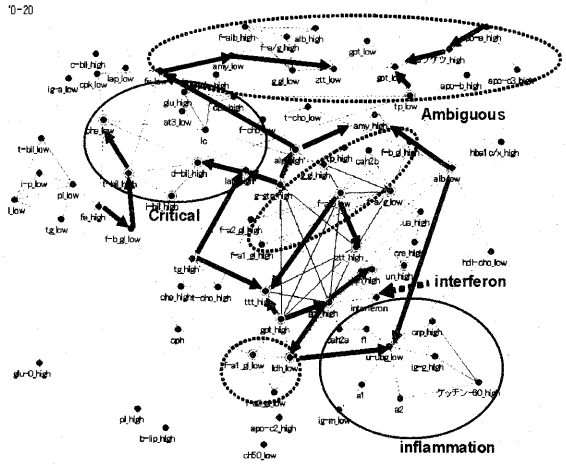

Fig.6. For cases of hepatitis C. The ambiguity in interpreting GOT_low and GPT_low in the dotted frame at the top caused a new concern.

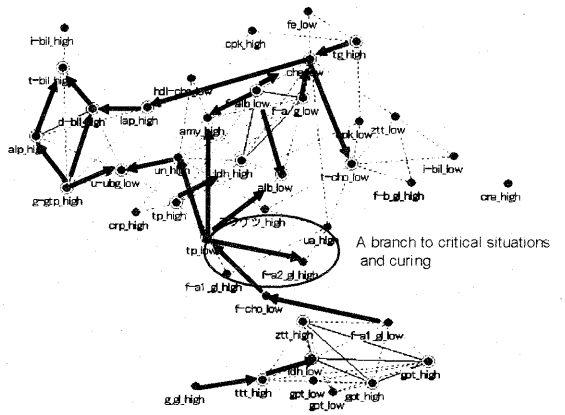

Fig.7 Scenarios for cases including GOT_low and GPT_low

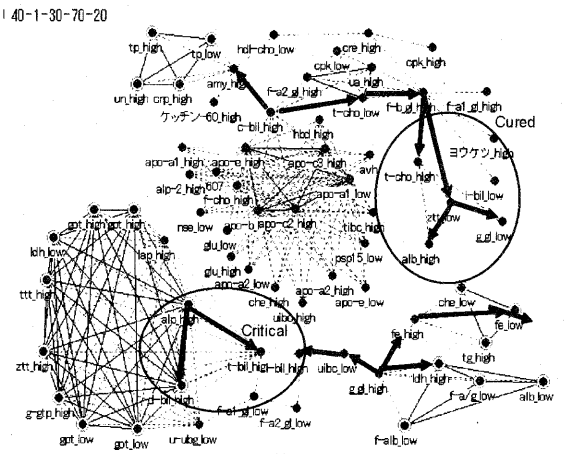

Fig.8 Hepatitis C without interferon, with GOT_low & GPT_low. Making scenario maps including GOT_low, GPT_low, and additional conditions, we clarified the significance of proteins, e.g. F_B_GL.

We can suppose that globulins as F-A1_Gl, F-A12_Gl, and F-B_GL are relevant to the role of interferon, in curing hepatitis C, and this hypothesis also matches with Fig. 6 where interferon is linked in the branch of F-A1_Gl _high/low and F-A1_Gl _high/low. Finally, under this new concern with globulins, we obtained the scenario map as in Fig.9, showing that a case treated with interferon and had a switch from F-A1_GL_high to F-A1_GL_low had a significant turning point to be cured on the recovery of TP (total protein) quantity, matching with the result in Fig.7 where TP_low, TP_high, and globulins are in the intersection of critical and easier scenarios. The decrease in GOT and GPT, and then in ZTT followed this, matching with the results in [5]. HCV (virus of hepatitis C) also decreased.

5. Discussion: Subjective but Trustworthy

We obtained some qualitative new findings. That is, HDL is relevant to the turning point for hepatitis B, to shift to a critical situation of the liver. And, the effect of interferon is relevant to the change in the quantity of protein (e.g. F-A1_GL and F-B_GL), and this effect appears beginning with the recovery of TP. The latter result is apparently significant from Fig.9, but it is still an open problem how interferon affects such proteins as a globulins. All in all, "reasonable, and sometimes novel and useful" scenarios of state-transitions were obtained according to the surgeon.

Although not covered above, we also found other scenarios approaching to significant situations. For example, reader can find the increase in AMY (amylase) at the arrow terminals in Fig.3, Fig.6, Fig.7, and Fig.8, which seems to be relevant to surgical operations. This corresponds to reference [6]. Also, the decrease in GOT because of the exhaustion of liver cells, "bridge" effect of F-B_GL in the cure by interferon, etc. were visualized, not shown in this paper. These are the effects of the double helix process we developed, which can be summarized very shortly as a concern-based focusing of target data.

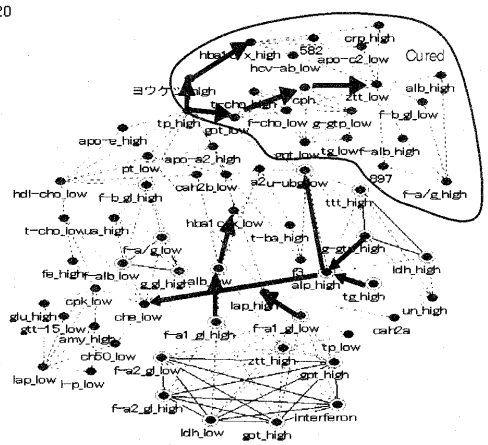

Fig.9 Cases with F-A2_GL_high & F_A2_GL_low, and interferon. The effect of interferon is clearly extracted at the top of the map.

Apparently, subjective interests of the surgeon influences the results to be obtained in this manner, but the results are objectively trustworthy because they just show the summary of facts, i.e. objective facts selected on the surgeon's subjective experiences. As a positive face of this combination of subjectivity and objectivity we discovered a broad range of decision-oriented knowledge, i.e. scenarios, because subjectivity has both effects of widening and narrowing the target environment. Here, widening was aided by the projection of the scenario maps to one's own experiences in various real-world contexts. The narrowing, i.e. data-focusing, was aided by Text Drop. Like a human wandering in an unknown island, a doctor wondering which way the patient can go will be helped by scenario map, a map with directed landmarks especially if the symptom is ambiguous or novel.

6. Conclusions

Scenario emergence and chance discovery are useful concepts for decisions in the real world, where events occur dynamically and one is required to make a decision promptly at the time a chance, i.e. significant event occurred. Here we showed an introductory application of scenario emergence with discovering the triggering events of essential scenarios, in the area of hepatitis treatment. Some interesting results were obtained according to the surgeon, but it is meaningless to say "interesting" – the next step we are to work on clarifying what a human means by "interesting" via the further runs on the DH process, which can be regarded as a process of human's self-discovery.

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