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Generalized Net Model of Osteoarthritis Diagnosing

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Abstract. Musculoskeletal disorders are the leading cause of disability among the world population. They encompass a spectrum of conditions, from those of acute onset and short duration to lifelong disorders, including osteoarthritis (OA), rheumatoid arthritis (RA), gout, osteoporosis etc. Of these conditions OA is the most common disorder and it is the major complaint prompting a patient to seek physician referral. Joint pain and reduced mobility are the first and cardinal symptoms of OA. When assessing patient with joint pain and reduced mobility it is important to build a structured, systematic and reliable diagnostics and decision making algorithm to confirm the OA is the primal diagnosis. To streamline the diagnostic process and to avoid misdiagnosis, mathematical modeling methods can be applied. In this paper we propose a mathematical model, which represents the diagnostic plan for patients with OA symptoms. The present study represents a successful example of Generalized Nets application in orthopedics.
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1. Introduction: Definition and Diagnosis of Osteoarthritis

Osteoarthritis (OA) is the most common chronic condition of the synovial joints. Sometimes called degenerative joint disease or degenerative arthritis, OA has a greater impact on mobility than any other medical condition in ageing population. Approximately 80% of the population is likely to show radiographic evidence of bone degradation in the joints by the age of 65. The prevalence of osteoarthritis is expected to double by 2020[6]. Literature is limited on the incidence and prevalence of OA because of the problems of defining it and determining its onset. Worldwide estimates indicate that 9.6% of men and 18% of women ≥ 60 years have symptomatic OA [7]. OA can affect any joint, but it occurs most often in knees, hips, lower back and neck, small joints of the fingers and the bases of the thumb and big toe. The incidence of hand, hip and knee OA increases with age, and women have higher rates than men,

especially after the age of 50 years. The prevalence of radiographic hand OA varies greatly and has been reported to range from 27% to over 80% [8] About 10% of people aged over 55 years have painful disabling knee OA of whom one quarter are severely disabled / [9] Hip OA is less common then either hand or knee OA [10] but it has been identified as one of the most common causes of debilitating pain in the general population / [11]

OA is a debilitating joint disease characterized by degenerative changes to the bones, cartilage, menisci, ligaments, and synovial tissue. Characterized by these degenerative changes the OA has evolved to be considered a disease of the whole joint. OA is a heterogeneous disorder for which the exact cause is unknown. The word *osteoarthritis* is derived from the Greek words: *"osteo"* which means "of the bone", "*arthro"* which means "joint" and "*itis"* which means "inflammation". Despite the name of the condition, the inflammation associated with the bones and joints is not an evident feature. Although it can result from the physical damage associated with osteoarthritis, it is not believed to cause the condition. This is a distinguishing factor between osteoarthritis and rheumatoid arthritis, which is more strongly linked to inflammation. There is no universally accepted definition for osteoarthritis. The condition is thought to consist of a group of overlapping distinct diseases which may occur in response to a variety of different biological and mechanical factors including metabolic, genetic or hereditary predisposition, age, physical factors such as obesity, and environmental factors [12]. An alternative definition is provided by Eyre (2004) who defines osteoarthritis as a process which 'occurs when the dynamic equilibrium between the breakdown and repair of joint tissues become unbalanced' [13]. Typically the condition is characterized by unbalanced degeneration and regeneration of articular cartilage and bone where the intrinsic repair mechanisms are insufficient. The pathological changes can be focal or more generalized and these changes often correlate poorly at one time point with clinical signs and symptoms but correlate longitudinally. OA has a multifactorial etiology, and can be considered the product of interplay between systemic and local factors, and can be categorized in two major categories: Idiopathic (Primary) OA and Secondary OA. Idiopathic OA is considered to be a normal part of the ageing process, results in many factors and can be localized or generalized. Secondary OA has more specific underlying causes, 10 to 15% of OA patients develop the disease due to hormone imbalance, genetic defects, the environment, crystals, or prolonged sustained trauma. Although the etiology of OA is incompletely understood, the accompanying biochemical, structural and metabolic changes in the joint cartilage has been well documented. It is now known that cytokines, mechanical trauma and altered genetics are involved in pathogenesis and that these factors can initiate a degenerative cascade that results in many characteristic alterations in the articular cartilage in OA [14]. Symptoms of osteoarthritis vary, depending on which joints are affected and how severely they are affected. However, the most common symptoms are pain and stiffness. Affected joints may get swollen, especially after extended activity. These symptoms tend to build over time rather than show up suddenly. Never the less, the pain, reduced mobility, side effects from medication and other factors associated with OA can lead to negative health effects not directly related to the joint disease. The diagnosis of OA is largely based on obtaining a detailed history and conducting a complete physical examination. The initial diagnostic goal is

to differentiate osteoarthritis from other joint pathologies. In the present study a reduced GN-model of OA diagnosing will be constructed. The history and physical examination findings are usually sufficient to diagnose osteoarthritis but the radiographic findings confirm the initial impression. Key risk factors include age >50 years, female gender, family history of OA, and a physical/manual occupation. Both active and passive range of joint movement is reduced in moderate to advanced OA, and this is usually associated with pain. Arthrocentesis and laboratory testing may help identify an underlying cause of secondary OA. For example: synovial fluid analysis may help confirm OA is non-inflammatory. In advanced disease, radiologic and other signs of OA include asymmetrical narrowing of the joint space indicating loss of cartilage and/or the presence of osteophytes or bony overgrowth.

2. Material and methods: The Apparatus of Generalized Nets

The presented model is based on the Generalized Nets (GNs) [1, 2], because of the contrast of the dynamic and parallel processes of GNs, with the static and linear processes of traditional modeling. Generalized nets represent a significant extension and generalization of the concept of Petri nets, as well as of other Petri nets extensions and modifications. GNs nets constitute a discrete tool for universal description of adaptable, flexible, structured and reusable models of complex systems with many different and interacting components, not necessarily of the homogeneous structure and origin, usually involved in parallel, simultaneous activities.

A generalized net consists of: static and dynamic components, temporal components, and memory components. In general the GNs may or may not have some of the components in their definition. GNs which do not have some of the components form special classes called reduced GNs [2]. The presented reduced GN-model has similar features with previous models for medical diagnosing [14, 18, 19], but this is the first one GN-model highlighting the diagnostic algorithm for OA and thus representing an application of GNs in orthopedics.

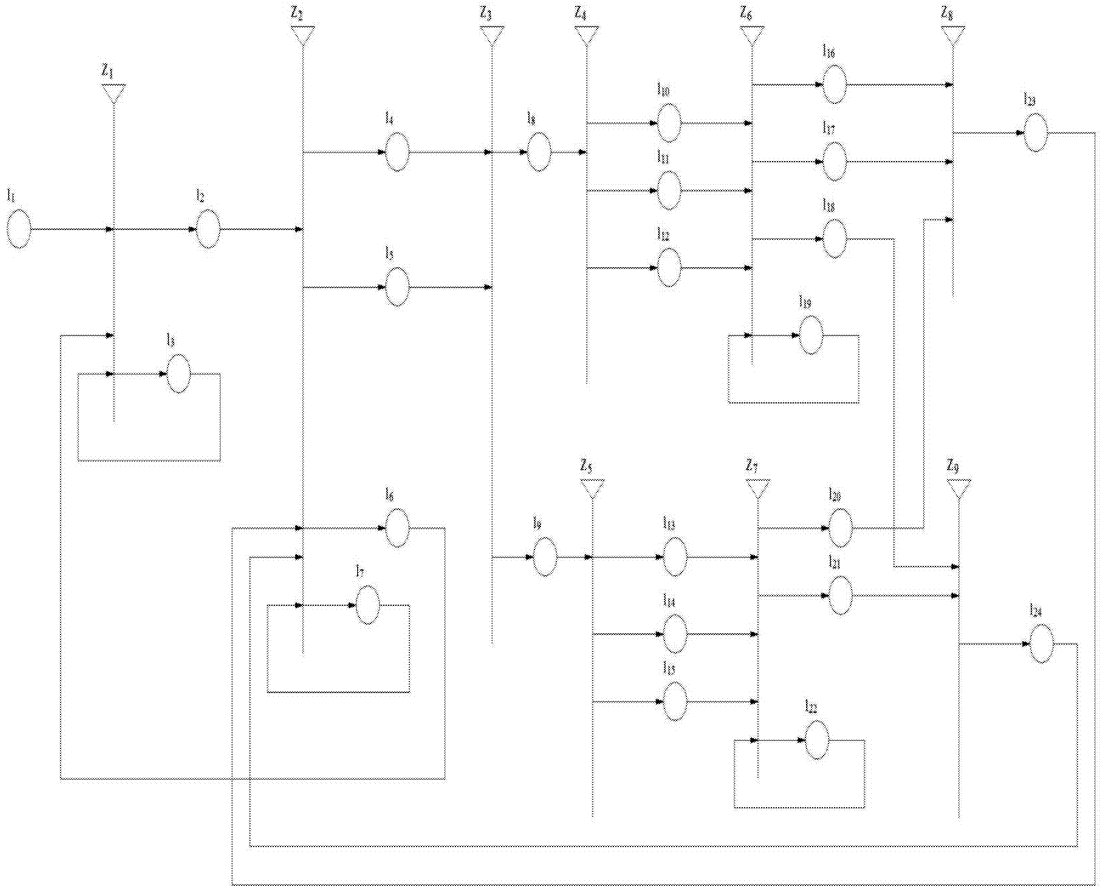
3. Results: The Generalized Net model of osteoarthritis diagnosing

Here we represent a reduced GN-model of OA diagnosing. The GN model (fig.1) has 9 transitions and 24 places with the following meaning.

- Transition Z_1 represents the personal data of the patient.
- Transition Z_2 represents the current functional status of the patient.
- Transition Z_3 represents the diagnostic plan for testing.
- Transition Z_4 represents the set of initial diagnostic tests.
- Transition Z_5 represents the set of subsequent diagnostics tests.
- Transition Z_6 represents the results from the initial diagnostic tests.

- Transition Z_7 represents the results from the subsequent diagnostics tests.
- Transition Z_8 represents the primal diagnosis.
- Transition Z_9 represents the possible differential diagnosis.

Figure 1. GN model of Osteoarthritis diagnosing



The net contains 5 types of tokens: α, β, μ, η and ε. Some of the model transitions contain a so called "special place" where a token stays and collect information about the specific parts of the diagnosing process which it represents as follows:

- In place l_3, token β stays permanently and collects the overall information obtained from the diagnostics steps in the personal record (personal data).
- In place l_7, token μ stays permanently and collects information about the current functional status of the patient obtained from the history, physical examination and clinical tests.
- In place l_{19}, token η stays permanently and collects information about the results from the initial diagnostics tests.

- In place l_{22}, token ε stays permanently and collects information about the results from the subsequent diagnostics tests.

At the time of duration of the GN-functioning, some of these tokens can split, generating new tokens, that will transfer in the net obtaining respective characteristics, and also in some moments they will unite with some of tokens β, μ and η.
Token α enters the net with additional characteristics "*patient with joint pain and reduced mobility*" in place l_1

$$Z_1 = < \{l_1, l_3, l_6\}, \{l_2, l_3\}, r_1 >,$$

$r_1 =$

	l_2	l_3
l_1	*false*	*true*
l_3	*true*	*true*
l_6	*false*	*true*

where:

The tokens from the tree input places enter place l_3 and unite with token β that obtains the above mentioned characteristics. On the other hand, token β splits to two tokens, the same token β and α_1 that enters place l_2. In place l_2, token α_1 obtains characteristics *"detailed history, physical examination and diagnosing tests are necessary"*

$$Z_2 = < \{l_2, l_7, l_{23}, l_{24}\}, \{l_4, l_5, l_6, l_7\}, r_2 >,$$

where :

$r_2 =$

	l_4	l_5	l_6	l_7
l_2	*false*	*false*	*false*	*true*
l_7	$W_{7,4}$	$W_{7,5}$	*true*	*true*
l_{23}	*false*	*false*	*false*	*true*
l_{24}	*false*	*false*	*false*	*true*

and,

- $W_{7,4}$ = *"the history of the patient and physical examination shows: age>50, the joint pain is not present at rest or at night, morning stiffness less than 30 minutes, some of the affected joints are the knees, hips, small hand joints (PIP and DIP joints), lumbar or cervical spine, limited range of motion with crepitus, small effusions, and joint line tenderness"*.
- $W_{7,5}$= *"there are inflammatory signs and symptoms"*

The tokens from all input places enter place l_7 and unite with token μ that obtains the above mentioned characteristic. On the other hand, token μ splits to four tokens, the same token μ that stays permanently in the place l_7 and tokens α_1, α_2 and α_3. Token α_3 enters place l_6 with characteristics*"*

"results from physical examination and diagnostic tests"

When predicate $W_{7,4}$ has truth value "true", token α_1 enters place l_4 and there it obtains characteristics:

"*there are key diagnostic factors for OA, consider further testing*"

When predicate $W_{7,5}$ has truth value "true", token α_2 enters place l_5 and there it obtains characteristics:

"*consider the possibility if inflammatory arthritis, such as rheumatoid arthritis, is a differential diagnosis"*

$$Z_3 = < \{l_4, l_5\}, \{l_8, l_9\}, r_3>,$$

where :

$$r_3 = \begin{array}{c|cc} & l_8 & l_9 \\ \hline l_4 & true & false \\ l_5 & false & true \end{array}$$

In place l_8 token α_1 obtains characteristics: "*first diagnostics tests to order*" while in place l_9 token α_2 obtains characteristics: "*consider subsequent diagnostic tests".*

$$Z_4 = < \{l_8\}, \{l_{10}, l_{11}, l_{12}\}, r_4>,$$

where :

$$r_4 = \begin{array}{c|ccc} & l_{10} & l_{11} & l_{12} \\ \hline l_8 & true & true & true \end{array}$$

The tokens take on the characteristics: "*x-ray of the affected joints*" in place l_{10}, "*serum CRP test*" in place l_{11} and "*serum ESR test*" in place l_{12}.

$$Z_5 = < \{l_9\}, \{l_{13}, l_{14}, l_{15}\}, r_5>,$$

where :

$$r_5 = \begin{array}{c|ccc} & l_{13} & l_{14} & l_{15} \\ \hline l_9 & true & true & W_{9,15} \end{array}$$

and,

- $W_{9,15}$ = *"the patient is febrile and the affected joint are red, hot, and acutely tender."*

Token that enters in place l_{13} obtains characteristics:

"*rheumatoid factor (RF) test*"

Token in place l_{14} obtains characteristics:

"*Anti–citrullinated protein antibody (anti-CCP) test"*

When predicate $W_{9,15}$ has truth value "true", token enters place l_{15} and there it obtains characteristics:

"*consider Arthrocentesis and joint fluid analysis"*

$$Z_6 = < \{l_{10}, l_{11}, l_{12}, l_{19}\}, \{l_{16}, l_{17}, l_{18}, l_{19}\}, r_6 >,$$

where :

$$r_6 = \begin{array}{c|cccc} & l_{16} & l_{17} & l_{18} & l_{19} \\ \hline l_{10} & false & false & false & true \\ l_{11} & false & false & false & true \\ l_{12} & false & false & false & true \\ l_{19} & W_{19,16} & W_{19,17} & W_{19,18} & true \end{array}$$

and,

- $W_{19,16}$ = *"x-ray shows: osteophytes, joint space narrowing, and subchondral sclerosis and cysts".*
- $W_{19,17}$ = *"serum CRP and serum ESR levels are in normal values ".*
- $W_{19,18}$ = *"serum CRP and serum ESR levels are abnormal".*

The tokens from all input places enter place l_{19} and unite with token η that obtains the above mentioned characteristic. On the other hand token η splits to four tokens, the same token η and tokens α_1, α_2 and α_3 that enter respectively in places l_{16}, l_{17} and place l_{18}. When predicate $W_{19,n}$ has truth value "true", token η_1 obtains characteristics: " the result from the x-ray is typical for OA" in place l_{16}, token α_2 obtains characteristics: " exclude inflammatory arthritis" in place l_{17} and token α_3 that enters in place l_{18} obtains characteristics : " consider both OA and RA or other inflammatory joint diseases"

$$Z_7 = < \{l_{13}, l_{14}, l_{15}, l_{22}\}, \{l_{20}, l_{21}, l_{22}\}, r_7 >,$$

where :

$$r_7 = \begin{array}{c|ccc} & l_{20} & l_{21} & l_{22} \\ \hline l_{13} & false & false & true \\ l_{14} & false & false & true \\ l_{15} & false & false & true \\ l_{22} & W_{22,20} & W_{22,21} & true \end{array}$$

and,

- $W_{22,20}$ = *"RF test and anti-CCP tests are negative".*
- $W_{22,21}$ = *"RF test and anti-CCP tests are positive, arthrocentesis and joint fluid analysis shows: leukocytes >2000 cells/mm^3, and the presence of sodium monourate crystals".*

The tokens from all input places enter place l_{19} and unite with token ε that obtains the above mentioned characteristic. On the other hand token ε splits to four tokens, the same token ε and tokens α_1 and α_2 that enter respectively in places l_{20} and l_{21}. When predicate $W_{22,n}$ has truth value *"true"*, token α_1 obtains characteristics: " *consider OA as a diagnosis* " in place l_{20} and token α_2 obtains characteristics: " *consider Gout, Pseudogout and RA"* in place l_{21}.

$$Z_8 = < \{l_{16}, l_{17}, l_{20}\}, \{l_{23}\}, r_8>$$

where :

$$r_8 = \begin{array}{c|c} & l_{23} \\ \hline l_{16} & true \\ l_{17} & true \\ l_{20} & true \end{array}$$

The tokens obtain the characteristics "*the diagnosis of the patient is OA*" in place $l_{23.}$

$$Z_9 = < \{l_{18}, l_{21}\}, \{l_{24}\}, r_9>,$$

where :

$$r_9 = \begin{array}{c|c} & l_{24} \\ \hline l_{18} & true \\ l_{21} & true \end{array}$$

The tokens obtain the characteristics "*inflammatory arthritis, gout or pseudogout are possible diagnoses*" in place $l_{24.}$

4. Discussion

The so described GN-model may provide a framework that can be used by primary care practitioners to guide diagnostic processes for OA, enabling more accurate and efficient identification of that condition and would assist in optimizing patient outcomes and more effective treatment. The presented model in our paper is the first step in a system for diagnosis through GN-modeling assistance and can be improved in multiple ways to yield improvements in results. The model can be complicated and detailed, with including of more detailed physical examination. The future models will include the presents of a complete physical examination / inspection, palpation, range of motion

testing, provocative testing, instability testing etc./ which will significantly improve the accuracy of the primary diagnosis and the reliability of the proposed algorithm. Our method will accurately identify the various steps during the diagnosing processes and significantly improve the health care level. The so obtained results could be used for assisting the process of decision making in the diagnostic processes.

5. Conclusion

Osteoarthritis is a common and important musculoskeletal disorder affecting the quality of life and proper functioning not only of the affected joint but also on the entire body. Effective and successful treatment of the disease is closely linked to an accurate diagnosis. To streamline the diagnostic process and to avoid misdiagnosis, mathematical modeling methods can be applied. The present study represents a successful example of Generalized Nets application in orthopedics.

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