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ESTUDIO DE MODELOS DISCRETOS: ESTRUCTURA Y DINÁMICA

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Resumen

En esta tesis hemos estudiado dos problemas: el primero consiste en encontrar condiciones mínimas para obtener una cierta clase de recubrimientos del plano discreto mediante cuadrados y el segundo corresponde al estudio de redes Booleanas.

El problema de recubrimiento por cuadrados nace como una variante del problema de embaldosado. El problema de embaldosado consiste en cubrir el plano discreto, o una parte de éste, sin dejar hoyos y sin superponer baldosas con un número finito de formas distintas. El caso estudiado consiste en cubrir completamente el plano discreto usando sólo cuadrados que pueden superponerse, pero no pueden compartir bordes ni vértices (recubrimiento fuerte). Además, se estudia el caso donde se permite dejar zonas de tamaño acotado sin cubrir y donde todos los cuadrados en el recubrimiento deben estar conectados (recubrimiento débil). Hemos probado que, en el caso donde todos los cuadrados tienen el mismo tamaño e intersectan el mismo número de cuadrados, los recubrimientos fuertes y débiles presentan cotas inferiores para el tamaño y número de cuadrados que los intersectan. Además, para un tamaño de cuadrado dado, mostramos una cota superior de orden lineal para el número de cuadrados que lo intersectan en un recubrimiento sea fuerte o débil,

El segundo problema trata de redes Booleanas, las que fueron introducidas por S. Kauffman (1969) con el objeto de modelar las redes de regulación génica. El primer aspecto estudiado son las redes Booleanas cuyo grafo asociado es por capas. Probamos que el comportamiento límite de este tipo de redes queda completamente determinado por el estado inicial de los nodos en la primera capa, y que los atractores de estas redes son de largo potencia de dos. Más aún, en el caso que todas las bucles sean monótonas crecientes todos los atractores son puntos fijos. El segundo aspecto estudiado es la robustez de la dinámica y del comportamiento límite de una red Booleana frente a distintos esquemas de actualización (paralelo, secuencial por bloques o secuencial). Cada esquema de actualización permite definir un grafo con signo, los resultados obtenidos prueban que si dos esquemas de actualización generan el mismo grafo con signo, estas redes tienen exactamente el mismo comportamiento dinámico. Por otro lado, dado que los puntos fijos son invariantes frente a los distintos esquemas de actualización, nos concentramos en estudiar cómo pequeños cambios en el esquema de actualización producen diferencias en el conjunto de ciclos dinámicos asociados a una red Booleana. Uno de los principales resultados es el que muestra que, dado un esquema de actualización es posible encontrar otro con el cual no comparte ciclos dinámicos. Por último, presentamos un algoritmo que opera como un filtro de ciclos dinámicos para redes Booleanas donde todos los circuitos son positivos. Dada una red Booleana, que tiene sólo circuitos positivos, este filtro permite encontrar en tiempo polinomial una nueva red Booleana que tiene exactamente los mismos puntos fijos, pero no tiene ningún ciclo dinámico. Este algoritmo permite, además, encontrar un punto fijo de la red Booleana en tiempo polinomial.

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CHAPTER 1

Introducción

1.1 Versión en español

El trabajo que se presenta consta básicamente de dos partes. La primera desarrolla un problema relacionado con el problema de embaldosado que da origen al primer capítulo de esta tesis. Y el segundo, estudia las dinámica de las redes Booleanas y da origen a los siguientes tres capítulos donde se estudia distintos aspectos de las redes Booleanas.

1.1.1 Recubrimiento con cuadrados

El problema de embaldosado del plano es un problema ampliamente estudiado desde su introducción en 1961 por Hao Wang [5]. Este problema consiste básicamente en cubrir el plano, o una parte de éste, usando baldosas con un número finito de formas distintas, sin superponer baldosas y sin dejar espacios sin cubrir. Este problema ha sido estudiado de muchas maneras distintas, por ejemplo: el embaldosado con poliominoes [4], el embaldosado permitiendo la rotación de las baldosas [2, 3], etc. Una noción importante en el problema de embaldosado es la adyacencia entre dos baldosas, esto es, dos baldosas son adyacentes si comparten un borde.

En este nuevo problema, la noción de adyacencia está ligada a la superposición de los cuadrados, es decir, decimos que dos cuadrados (o baldosas) son adyacentes si ellos se superponen cumpliendo una condición que en este caso corresponde a no compartir bordes ni vértices y, más aún, no pueden existir cuadrados que compartan bordes o

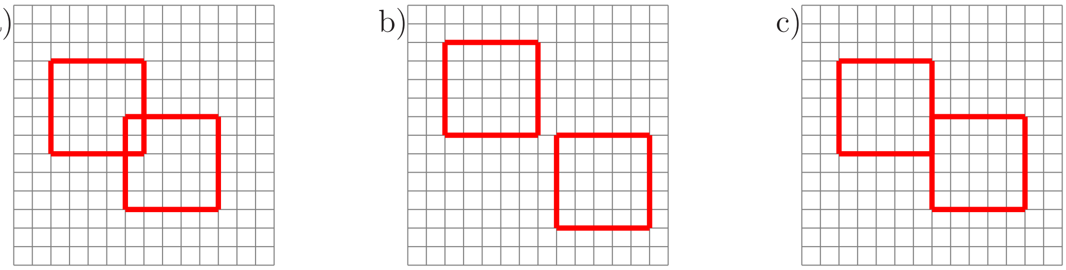


FIGURA 1.1. a) Cuadrados adyacentes, b) Cuadrados no adyacentes, c) Configuración prohibida.

vértices como se observa en la Figura 1.1.

En efecto, podemos observar que un embaldosado es un recubrimiento del plano que mantiene ciertas reglas de adyacencia entre sus baldosas. En esta tesis proponemos un problema similar al problema de embaldosado, que consiste en cubrir el plano discreto mediante baldosas cuadradas, pero a diferencia del problema estudiamos los recubrimientos fuertes y los recubrimientos débiles.

Un *recubrimiento fuerte* es un conjunto de cuadrados $\mathcal{C}$ en el plano discreto, tal que:

1. $\forall S, S' \in \mathcal{C}, S \not\subseteq S'$.
2. $\forall S, S' \in \mathcal{C}, S$ y S' no comparten bordes ni vértices.
3. $\forall \binom{i}{j} \in \mathbb{Z}^2, \exists S \in \mathcal{C}$, tal que $\binom{i}{j} \in \mathrm{Int}(S)$.

donde:

$$S = \begin{bmatrix} i \\ j \end{bmatrix}_n = \left\{ \binom{i+l}{j+m} \in \mathbb{Z}^2 : l, m = 0, \ldots, n \right\}$$
$$\mathrm{Int}(S) = \left\{ \binom{i+l}{j+m} \in \mathbb{Z}^2 : l, m = 1, \ldots, n-1 \right\}$$

Un *recubrimiento k-débil* es un conjunto de cuadrados $\mathcal{C}$ en el plano discreto, tal que:

1. $\forall S, S' \in \mathcal{C}^*, S \not\subseteq S'$.
2. $\forall S, S' \in \mathcal{C}^*, S$ y S' no comparten bordes ni vértices.
3. $\forall \binom{i}{j} \in \mathbb{Z}^2, \exists S \in \mathcal{C}^*$ tal que $\begin{bmatrix} i \\ j \end{bmatrix}_{2k} \cap \mathrm{Int}(S) \neq \emptyset$.
4. Todos los cuadrados en el recubrimiento están conectados, es decir, $\forall S_0, S_m \in \mathcal{C}^*$, $\exists S_1 \ldots S_{m-1} \in \mathcal{C}^*$, tal que $S_l \cap S_{l-1} \neq \emptyset$, $\forall l = 1, \ldots, m$.

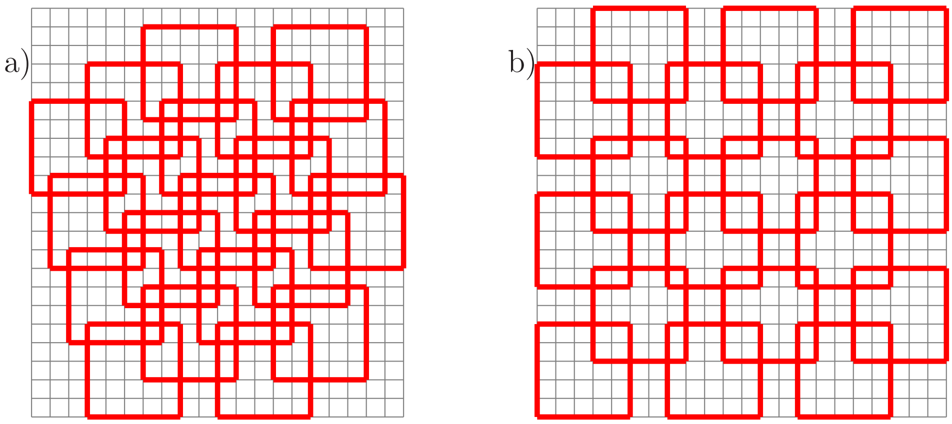


FIGURA 1.2. a) Ejemplo de recubrimiento fuerte b) Ejemplo de recubrimiento débil.

Dado el problema planteado, estudiamos lo que llamamos recubrimientos regulares, éstos corresponden a recubrimientos donde todas las baldosas tienen el mismo tamaño y mismo número de baldosas adyacentes.

En primer lugar estudiamos el problema: dado un tamaño de baldosa cuál es el máximo número de baldosas adyacentes que puede tener esta baldosa en un recubrimiento regular. En este caso obtenemos un resultado que muestra que el máximo número de baldosas adyacentes que puede tener una baldosa de tamaño n en un recubrimiento regular es $2(n-1)$ si n es impar y $2(n-1)-1$ si n es par. En ambos casos se muestran ejemplos de los recubrimientos con máximo número de cuadrados adyacentes y se muestra la imposibilidad de tener un número mayor de cuadrados adyacentes.

En segundo lugar, obtenemos las condiciones mínimas para tener un recubrimiento ya sea débil o fuerte. En efecto, se observa que para tener un recubrimiento regular fuerte del plano discreto se necesita que el número de baldosas adyacentes a un cuadrado sea al menos seis, lo que induce que el tamaño de los cuadrados debe ser al menos cinco, para probar este resultado se muestra la imposibilidad de construir un recubrimiento con un número de cuadrados adyacentes menor y la necesidad de que el tamaño del cuadrado sea el adecuado para soportar el número de cuadrados adyacentes requerido, y para mostrar que efectivamente existe un recubrimiento regular fuerte con seis cuadrados adyacentes se muestra un recubrimiento que cumple con las propiedades requeridas. En el caso de recubrimientos débiles, se observa que las restricciones son mucho menores y mediante un ejemplo se muestra que es posible construir un recubrimiento débil con sólo dos baldosas adyacentes y cuadrados de tamaño tres.

Los resultados de este trabajo fueron publicados en:

- Salinas L., Goles E., Covering by squares, Theoretical Computer Science 396, 10-27, 2008.

1.1.2 Redes Booleanas

Notación

La segunda parte de esta tesis está dedicada al estudio de las redes Booleanas, estas redes fueron introducidas por Kauffman [23] con el objeto de modelar de manera discreta las redes de regulación génica, si bien es cierto existen otras aplicaciones para estas redes, por ejemplo teoría de circuitos, Ciencias de la Computación [15, 35], etc. su principal aplicación sigue siendo el estudio de redes de regulación génica. Un ejemplo de aplicación de las redes Booleanas es el trabajo realizado por Mendoza el al. [27]; en este trabajo se estudia una red Booleana, que modela la interacción de 11 genes que regulan la morfogénesis de la Arabidopsis Thaliana. Los atractores de esta red se identifican con las distintas etapas de la floración, un estado que impide el desarrollo de la flor y un último estado que, si bien no aparece naturalmente, podría inducirse experimentalmente.

En esta tesis nos interesamos en estudiar los atractores de una red Booleana, es decir, su comportamiento límite. En biología, los atractores de una red Booleana pueden representar un estado de un patrón de actividad motora nerviosa, una red inmune, un tipo de célula, etc. Por ejemplo, en redes de regulación génica los atractores están asociados a distintos tipos de células definidos por patrones de actividad génica. En particular, los puntos fijos están asociados a fenómenos de proliferación celular y apoptosis [21]. Los ciclos dinámicos se asocian a ciclos celulares, división, etc. De esta forma conocer los atractores de una red Booleana resulta ser muy importante.

Una red Booleana es un par $N = (F, s)$ definido por:

1) Un conjunto finito de *variables de estado* $\{x_1, \dots, x_n\}$, donde $x_i \in \{0, 1\}$,

2) Una *función de activación global* $F : \{0, 1\}^n \to \{0, 1\}^n$, tal que:

$$F(x) = (f_1(x), \dots, f_n(x)) \text{ y } x = (x_1, \dots, x_n),\ x_i \in \{0, 1\}$$

3) Un *esquema de actualización* definido por una función de actualización que denotamos $s : \{1, \dots, n\} \to \{1, \dots, n\}$.

De este modo una red Booleana con función de activación global F y función de actualización s se actualiza de la siguiente forma:

$$x_i^{r+1} = f_i(x_1^{l_1}, \dots, x_n^{l_n}),$$

donde $l_j = r$ si $s(i) \leq s(j)$ y $l_j = r + 1$ si $s(i) > s(j)$.

Esto es equivalente a aplicar la función $F^s : \{0,1\}^n \to \{0,1\}^n$ de manera paralela, con $F^s(x) = (f_1^s(x), \ldots, f_n^s(x))$ definida por:

$$f_i^s(x) = f_i(g_{i,1}^s(x), \ldots, g_{i,n}^s(x)),$$

donde la función $g_{i,j}^s$ se define como $g_{i,j}^s(x) = x_j$ si $s(i) \leq s(j)$ y $g_{i,j}^s(x) = f_j^s(x)$ si $s(i) > s(j)$. Por lo tanto, la función F^s corresponde al comportamiento dinámico de $N = (F, s)$.

Como $\{0,1\}^n$ es un conjunto finito, podemos encontrar dos tipos de comportamiento límite en una red Booleana:

- *Punto Fijo*: un punto fijo es un elemento $x \in \{0,1\}^n$ tal que $F^s(x) = x$.
- *Ciclo*: un ciclo de largo p es una secuencia $[x^0, \ldots, x^{p-1}, x^0]$ tal que $x^j \in \{0,1\}^n, p > 1$, x^j son todos distintos y $F^s(x^j) = x^{j+1}$, para todo $j = 0, \ldots, p-2$ y $F^s(x^{p-1}) = x^0$.

Los puntos fijos y los ciclos son llamados *atractores* de la red Booleana.

El *grafo asociado* a $N = (F, s)$ es el grafo dirigido $G^F = (V, A)$, donde:

- $V = \{1 \ldots, n\}$
- $(i, j) \in A$ si y sólo si f_j depende de x_i, es decir, si existe $x \in \{0,1\}^n$ tal que:

$$f_j(x_1, \ldots, x_{i-1}, 0, x_{i+1}, \ldots, x_n) \neq f_j(x_1, \ldots, x_{i-1}, 1, x_{i+1}, \ldots, x_n).$$

Un *circuito* de $G^F = (V, A)$ es una secuencia de nodos distintos (excepto por los extremos) $i_1, i_2, \ldots, i_k, i_1$ de V donde $(i_l, i_{l+1}) \in A$ para todo $l = 1, \ldots, k-1$ y $(i_k, i_1) \in A$. k es el largo del circuito. Una *bucle* es un circuito de largo uno.

Además se define el *grafo con signo* asociado a una red Booleana $N = (F, s)$ como: $G_s^F = (G^F, \text{sign}_s)$, donde cada arco tiene asignada una función signo dada por la función $\text{sign}_s : A(G^F) \to \{-1, +1\}$ en el digrafo definido por:

$$\text{sign}_s(i, j) = \begin{cases} +1 & \text{si } s(i) \geq s(j) \\ -1 & \text{si } s(i) < s(j) \end{cases}$$

Un *grafo por capas* es un grafo sin circuitos de largo $k \geq 2$.

Una función Booleana $f : \{0,1\}^n \to \{0,1\}$ es monótona creciente con respecto a la i–ésima variable si:

$$\forall x \in \{0,1\}^n, \ f(x_1, \ldots, x_{i-1}, 0, x_{i+1}, \ldots, x_n) \leq f(x_1, \ldots, x_{i-1}, 1, x_{i+1}, \ldots, x_n),$$

y, monótona decreciente con respecto a la i–ésima variable si:

$$\forall x \in \{0,1\}^n, , \ (x_1,\ldots,x_{i-1},0,x_{i+1},\ldots,x_n) \geq f(x_1,\ldots,x_{i-1},1,x_{i+1},\ldots,x_n).$$

Una función Booleana $f : \{0,1\}^n \to \{0,1\}$ es definida por signo, si para todo $i = 1,\ldots,n$, es monótona creciente o monótona decreciente con respecto a la variable x_i.

Luego, para cualquier red Booleana con funciones definidas por signo $N = (F,s)$ podemos definir una función de peso $w_F : A(G^F) \to \{-1,1\}$ como:

$$w_F(i,j) = \begin{cases} -1 & \text{si } i \in I^-(f_j) \\ +1 & \text{si } i \in I^+(f_j) \end{cases}$$

Diremos que un arco $(i,j) \in A(G^F)$ es positivo si $w_F(i,j) = 1$ y negativo en caso contrario. Diremos que un camino es positivo si el número de arcos negativos en el camino es par, y negativo si es impar. Así, llamaremos grafo signado de N a: (G^F, w_F).

Resultados

En primer lugar estudiamos las redes Booleanas con grafos por capas (ver Figura 1.3), estas redes tienen una dinámica muy simple, debido a que su estructura permite que el comportamiento límite de la red quede completamente definido por los valores iniciales de las variables en la primera capa. La importancia de estudiar este caso radica en que este comportamiento parece replicarse de alguna manera en otras redes Booleanas más complejas y que cumplen propiedades muy interesantes.

En el capítulo 3 probamos que los atractores de estas redes son de largo potencia de dos. Además, si todas las bucles son monótonas creciente, entonces los atractores son sólo puntos fijos que se alcanzan en a lo más k actualizaciones, donde k es el número de capas de la red. Como el número de capas de la red está acotado por el número de nodos, obtenemos que el transiente para alcanzar un punto fijo en este tipo de redes es a lo más el número de nodos del grafo asociado.

Por otro lado, estudiamos el comportamiento de redes por capas con función de actualización tal que para todo $(i,j) \in A$, $\text{sign}_s(i,j) = +1$. Estas redes, cumplen la propiedad de tener una dinámica paralela y secuencial idénticas (Tchuente [34]), debido a esto nos preguntamos si la recíproca de esta proposición es cierta, y encontramos que en ausencia de bucles efectivamente es así. Sin embargo, tal como veremos en el capítulo 5, es posible encontrar redes Booleanas con dinámicas secuencial y paralela idénticas que no tinene asociado un grafo por capas. Este tipo de redes aparecen al aplicar el algoritmo "Filter" sobre redes Booleanas cuyo grafo tiene sólo circuitos positivos.

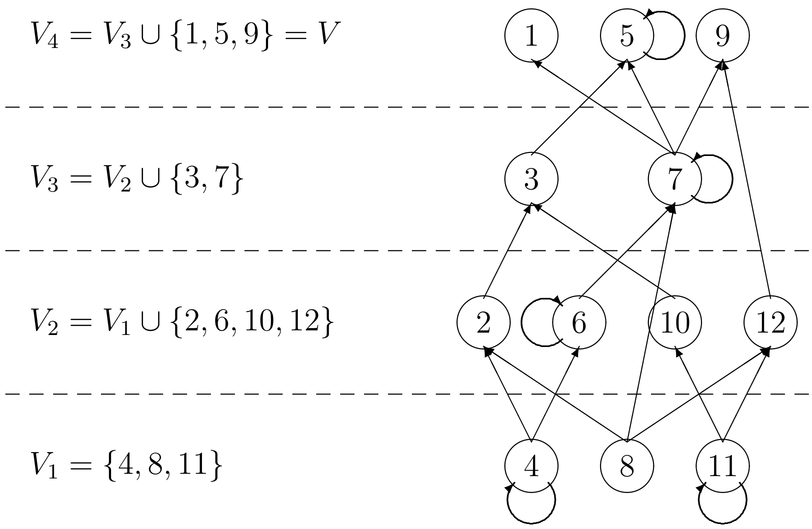


Figura 1.3. Ejemplo de grafo por capas.

En segundo lugar, estudiamos la robustez de un red Booleana respecto de sus esquema de actualización, en este trabajo sólo se consideran esquemas de actualización deterministas (paralelo, secuencial por bloque, secuencial) y definimos clases de equivalencia del comportamiento dinámico de una red Booleana en base a su grafo asociado y sus esquemas de actualización. Además, definimos el concepto de arco crítico, que nos permite estudiar como un pequeño cambio en el esquema de actualización de una red Booleana nos permite destruir ciclos dinámicos, y como mediante un cambio mayor podemos encontrar redes Booleanas que no comparten ningún ciclo. Como corolario, además, se obtiene que para redes que no contienen bucles negativas, la dinámica paralela no comparte ningún ciclo con las dinámicas secuenciales asociadas a esta misma red.

Por último estudiamos un procedimiento iterativo aplicado a redes Booleanas con actualización paralela. Dada un red Booleana con actualización paralela $N = (F, s_p)$ se define su red secuencial como $\mathcal{S}(N) = (F^{(1)}, s_p)$ donde $F^{(1)}(x) = (f_1^{(1)}(x), \ldots, f_n^{(1)}(x))$:

$$f_1^{(1)}(x) = f_1(x)$$
$$f_i^{(1)}(x) = f_i(f_1^{(1)}(x), \ldots, f_{i-1}^{(1)}(x), x - i, \ldots, x_n) \qquad \forall i = 2, \ldots, n.$$

No es dificil verificar que el comportamiento dinámico de $(F^{(1)}, s_p)$ es idéntico al comportamiento dinámico de (F, π_0) donde $\pi_0(i) = i, \forall i = 1, \ldots, n.$. Es por esto que llamamos a $\mathcal{S}(N)$ la red secuencial de N, además ambas redes, N y $\mathcal{S}(N)$, tienen los mismos puntos fijos y los cyclos dinámicos pueden ser diferentes.

En el capítulo 5 se prueba que si N es una red Booleana tal que todos sus circuitos son positivos, entonces $\mathcal{S}^n(N) = \mathcal{S}^{n-1}(N)$, Además los atractores de $\mathcal{S}^n(N)$ son sólo puntos fijos que se alcanzan en a lo más n actualizaciones. Es decir, hemos definido un algoritmo de orden polinomial que "filtra" los ciclos dinámicos de una red Booleana. Cabe notar que las redes cuyo grafo asociado tiene sólo circuitos positivos siempre tienen al menos un punto fijo [8].

Los resultados respecto de redes booleanas dieron origen a tres artículos:

1. Goles E. Salinas L, Comparison between parallel and serial dynamics of Boolean networks, Theoretical Computer Science 396, 247-253, 2008.
2. Aracena J., Goles E., Salinas L., On the robustness of up date schedules in Boolean networks, enviado a BioSystems.
3. Salinas L., Goles E., Sequential Operator for Filtering Cycles in Boolean Networks, en preparación.

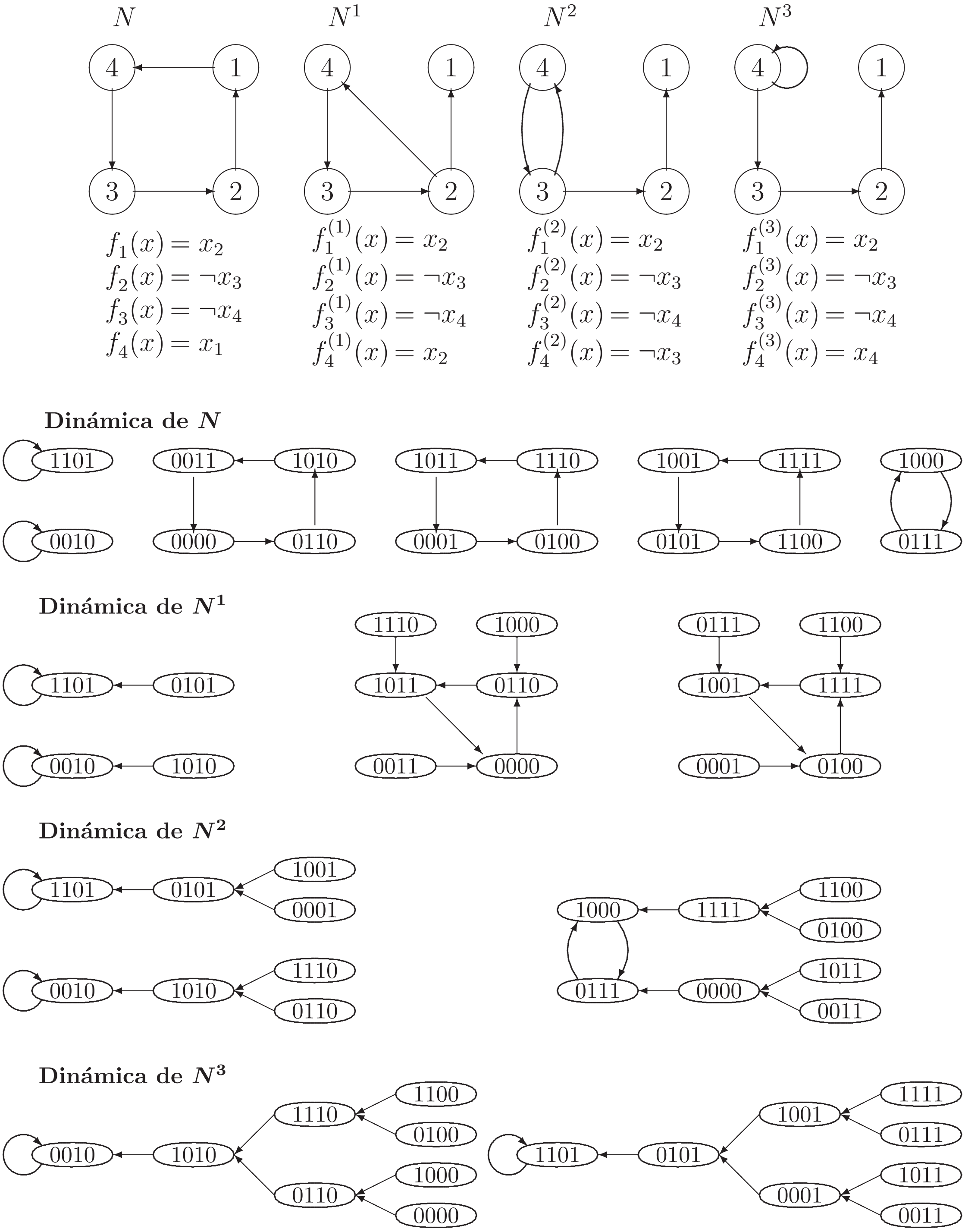


FIGURA 1.4. Ejemplo de la aplicación del algoritmo sobre una red Booleana.

1.2 Version Française

Le travail que nous présentons ici se compose essentiellement de deux parties. La première, qui développe un problème relatif au problème de pavage, est décrite dans le premier chapitre de cette thèse. La deuxième étudie la dynamique des réseaux Booléens et différents aspects de ces réseaux. Elle est exposée dans les trois chapitres suivantes.

1.2.1 Recouvrement par carrés

Le problème du pavage du plan est un problème amplement étudié depuis son introduction en 1961 par Hao Wang [5]. Ce problème consiste à couvrir le plan, ou une partie de celui-ci, en utilisant des tuiles dont le nombre de formes distinctes est fini. Ces tuiles ne peuvent ni être superposées ni être disposées de façon à ce qu'il reste des espaces du plan ne soient pas recouverts. De nombreuses versions du problème du pavage ont été étudiées, par exemple : le pavage par des poliominoes [4], ou encore le pavage avec rotation possible des tuiles [2, 3], etc. Une notion importante dans le problème de pavage est celle de l'adjacence de deux tuiles. Au sens habituel, deux tuiles sont dites adjacentes si elles partagent un bord.

Pour le problème du pavage auquel nous nous intéressons ici, la définition d'adjacence que nous utilisons est quelque peu différente. Comme l'illustre la Figure 1.5 nous dirons que deux tuiles sont adjacentes si elles se superposent sans partager de bords ni de sommets.

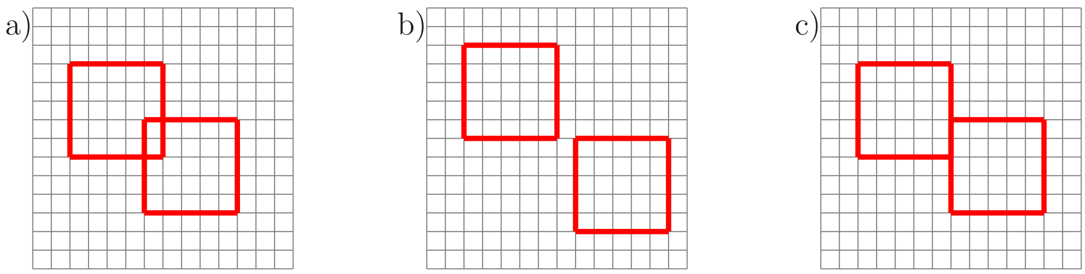


FIGURE 1.5. a) Carrés adjacents, b) Carrés non adjacents, c) Configuration interdit.

Ainsi, nous pouvons noter que le pavage du plan est un recouvrement de celui-ci qui respecte certaines règles d'adjacence des tuiles. Dans cette thèse, nous proposons un problème semblable à celui du pavage qui consiste à recouvrir le plan discret par des tuiles carrées. Mais, contrairement au problème du pavage, nous étudisons les recouvrements forts et les recouvrements faibles.

Un *recouvrement fort* est un ensemble de carrés $\mathcal{C}$ dans le plan discret, tel que :

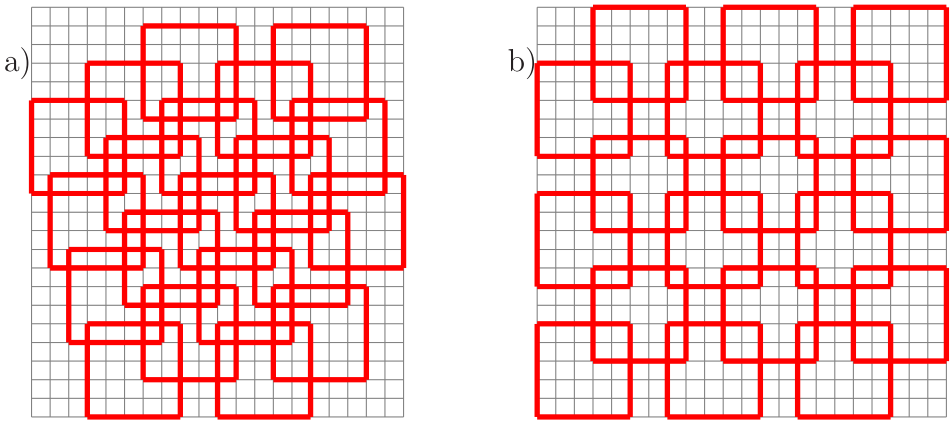


FIGURE 1.6. a) Un exemple de recouvrement fort b) Un exemple de recouvrement faible.

1. $\forall S, S' \in \mathcal{C}, S \not\subseteq S'$.
2. $\forall S, S' \in \mathcal{C}, S$ et S' ne partage pas de bords ni de sommets.
3. $\forall \binom{i}{j} \in \mathbb{Z}^2, \exists S \in \mathcal{C}$, tel que $\binom{i}{j} \in \text{Int}(S)$.

où:

$$S = \begin{bmatrix} i \\ j \end{bmatrix}_n = \left\{ \binom{i+l}{j+m} \in \mathbb{Z}^2 : l, m = 0, \dots, n \right\}$$
$$\text{Int}(S) = \left\{ \binom{i+l}{j+m} \in \mathbb{Z}^2 : l, m = 1, \dots, n-1 \right\}$$

Un *recouvrements k-faibles* est un ensemble de carrés $\mathcal{C}$ dans le plan discret, tel que :

1. $\forall S, S' \in \mathcal{C}^*, S \not\subseteq S'$.
2. $\forall S, S' \in \mathcal{C}^*, S$ et S' ne partage pas de bords ni de sommets.
3. $\forall \binom{i}{j} \in \mathbb{Z}^2, \exists S \in \mathcal{C}^*$ tel que $\begin{bmatrix} i \\ j \end{bmatrix}_{2k} \cap \text{Int}(S) \neq \emptyset$.
4. Tous les carrés du recouvrement sont connectés, c'est-à-dire, $\forall S_0, S_m \in \mathcal{C}^*$, $\exists S_1 \dots S_{m-1} \in \mathcal{C}^*$, tel que $S_l \cap S_{l-1} \neq \emptyset$, $\forall l = 1, \dots, m$.

Une fois le problème posé, nous étudions les recouvrements réguliers, c'est-à-dire les recouvrements où toutes les tuiles ont la même taille et le même nombre de tuiles qui leur sont adjacentes.

Tout d'abord, nous étudions le problème suivant : étant donné une tuile d'une certaine taille quel est le nombre maximal de tuiles qui peuvent lui être adjacents dans un recouvrement régulier? Nous obtenons que le nombre maximal de tuiles pouvant être adjacents à une tuile de taille n dans un recouvrement régulier est $2(n-1)$ si n est impair et $2(n-1)-1$ si n est pair. Dans les deux cas, on peut trouver des exemples de recouvrement avec un nombre maximal de tuiles adjacentes et on peut prouver qu'il est impossible d'obtenir un plus grand nombre de tuiles adjacentes.

Ensuite, nous obtenons les conditions minimales pour avoir un recouvrement faible ou fort. En effet, pour avoir un recouvrement régulier fort du plan discret, on observe que chaque tuile doit être adjacente à au moins six autres tuiles, ce qui implique que la taille des carrés doit être d'au moins cinq. Pour prouver ce résultat nous montrons d'une part qu'il est impossible de construire un recouvrement avec moins de six tuiles adjacentes et d'autre part que la taille d'une tuile doit être suffisament grande pour pouvoir être adjacente au nombre requis de tuiles.

Pour montrer qu'il existe effectivement un recouvrement fort régulier avec six carrés adjacents, nous exhibons un recouvrement qui vérifie les propriétés requises. Dans le cas des recouvrements faibles, on observe que les restrictions sont beaucoup moins importantes. Au moyen d'un exemple, on montre qu'il est possible de construire un recouvrement faible avec seulement deux tuiles adjacentes et des tuiles de taille trois.

Les résultats de ce travail ont été publiés dans :

- Salinas L., Goles E., Covering by squares, Theoretical Computer Science 396, 10-27, 2008.

1.2.2 Réseaux Booléens

Notation

La deuxième partie de cette thèse est consacrée à l'étude des réseaux Booléens introduits par Kauffman [23] afin de modeliser de manière discrète les réseaux de régulation génétique. Bien que ces réseaux aient d'autres applications, par exemple à la théorie des circuits, ou aux Sciences du Calcul [15, 35], etc., leur application principale demeure l'étude de réseaux de régulation génétique. Un exemple d'application des réseaux Booléens est le travail effectué par Mendoza et al. [27]; dans ce travail, les auteurs étudient un réseau Booléen modélisant l'interaction de 11 gènes qui régulent la morphogénèse de l'Arabidopsis Thaliana. Les attracteurs de ce réseau sont identifiés avec les différentes étapes de la floraison, un état qui empêche le développement de la fleur et un dernier état qui, bien qu'il n'apparaisse pas naturellement, pourrait être induit expérimentalement.

Dans cette thèse nous nous intéressons à l'étude des attracteurs d'un réseau Booléen, autrement dit, à son comportement limite. En biologie, les attracteurs d'un réseau Booléen peuvent représenter un schéma d'activité motrice nerveuse, un réseau immunitaire, un type de cellule, etc. Par exemple, dans des réseaux de régulation génétique les attracteurs sont associés aux différents types de cellules determinés par les différents schémas d'activité génétique. En particulier, les points fixes sont associés à des phénomènes de prolifération cellulaire et d'apoptose [21]. Les cycles dynamiques correspondent aux cycles cellulaires, division, etc. Par conséquent, la connaissance des attracteurs d'un réseau Booléen est très importante.

Un réseau Booléen est une couple $N = (F, s)$ défini par :

1) Un ensemble fini de *variables d'état* $\{x_1, \ldots, x_n\}$, $x_i \in \{0, 1\}$,

2) Une *fonction d'activation* $F : \{0, 1\}^n \to \{0, 1\}^n$, telle que:

$$F(x) = (f_1(x), \ldots, f_n(x)) \text{ et } x = (x_1, \ldots, x_n),\ x_i \in \{0, 1\}$$

3) Une *actualisation* definie par une fonction d'actualisation, notée $s : \{1, \ldots, n\} \to \{1, \ldots, n\}$.

Ainsi, un réseau Booléen avec une fonction d'activation globale F et une fonction d'actualisation s s'actualise de la manière suivante :

$$x_i^{r+1} = f_i(x_1^{l_1}, \ldots, x_n^{l_n}),$$

où $l_j = r$ si $s(i) \leq s(j)$ et $l_j = r + 1$ si $s(i) > s(j)$.

Ceci est équivalent à l'application de la fonction $F^s : \{0, 1\}^n \to \{0, 1\}^n$ de manière parallèle, avec $F^s(x) = (f_1^s(x), \ldots, f_n^s(x))$ défini par :

$$f_i^s(x) = f_i(g_{i,1}^s(x), \ldots, g_{i,n}^s(x)),$$

où la fonction $g_{i,j}^s$ est définie par $g_{i,j}^s(x) = x_j$ si $s(i) \leq s(j)$ et $g_{i,j}^s(x) = f_j^s(x)$ si $s(i) > s(j)$. Par conséquent, la fonction F^s a le même comportement dynamique que $N = (F, s)$.

Comme l'ensemble des états $\{0, 1\}^n$ est fini, nous pouvons trouver deux types de comportements limite dans un réseau Booléen :

- *Point fixe*: un point fixe est un point $x \in \{0, 1\}^n$ tel que $F^s(x) = x$.
- *Cycle*: un cycle de longueur p est une suite $[x^0, \ldots, x^{p-1}, x^0]$ telle que $x^j \in \{0, 1\}^n, p > 1$, les x^j étant tous distincts, et $F^s(x^j) = x^{j+1}$, pour tout $j = 0, \ldots, p - 2$ et $F^s(x^{p-1}) = x^0$.

Les points fixes et les cycles sont appelés les *attracteurs* du réseau Booléen.

Le *graphe associé* à $N = (F, s)$ est le graphe dirigé $G^F = (V, A)$, où :

- $V = \{1 \ldots, n\}$
- $(i, j) \in A$ si et seulement si f_j dépend de x_i, c'est-à-dire, s'il existe $x \in \{0,1\}^n$ tel que

$$f_j(x_1, \ldots, x_{i-1}, 0, x_{i+1}, \ldots, x_n) \neq f_j(x_1, \ldots, x_{i-1}, 1, x_{i+1}, \ldots, x_n).$$

Un *circuit* de $G^F = (V, A)$ est une suite de sommets distincts (sauf les extrémités) $i_1, i_2, \ldots, i_k, i_1$ de V où $(i_l, i_{l+1}) \in A$ pour tout $l = 1, \ldots, k-1$ et $(i_k, i_1) \in A$. k est la longueur du circuit. En particulier, une *boucle* est un circuit de longueur un.

On définit également le *graphe signé* associé à un réseau Booléen $N = (F, s)$ par : $G^F_s = (G^F, \text{sign}_s)$, où à chaque arc du digraphe est associé un signe determiné par la fonction $\text{sign}_s : A(G^F) \to \{-1, +1\}$ telle que :

$$\text{sign}_s(i,j) = \begin{cases} +1 & \text{si } s(i) \geq s(j) \\ -1 & \text{si } s(i) < s(j) \end{cases}$$

Un *graphe en couches* est un graphe sans circuits de longueur $k \geq 2$.

Une fonction Booléenne $f\ : \{0,1\}^n \to \{0,1\}$ est dite monotone croissante par rapport à la i-ème variable si :

$$\forall x \in \{0,1\}^n\,,\ f(x_1, \ldots, x_{i-1}, 0, x_{i+1}, \ldots, x_n) \leq f(x_1, \ldots, x_{i-1}, 1, x_{i+1}, \ldots, x_n),$$

et, elle est dite monotone décroissante par rapport à la i-ème variable si :

$$\forall x \in \{0,1\}^n,\ ,\ (x_1, \ldots, x_{i-1}, 0, x_{i+1}, \ldots, x_n) \geq f(x_1, \ldots, x_{i-1}, 1, x_{i+1}, \ldots, x_n).$$

On dit qu'une fonction Booléenne $f : \{0,1\}^n \to \{0,1\}$ est définie *par signe*, si pour tout $i = 1, \ldots, n$, elle est monotone croissante ou monotone décroissante par rapport à x_i.

Dès lors, pour tout réseau Booléen $N = (F, s)$ avec des fonctions définies par signe, nous pouvons définir une fonction de signe $w_F : A(G^F) \to \{-1, 1\}$ comme suit :

$$w_F(i,j) = \begin{cases} -1 & \text{si } i \in I^-(f_j) \\ +1 & \text{si } i \in I^+(f_j) \end{cases}$$

On dit qu'un arc $(i, j) \in A(G^F)$ est positif si $w_F(i, j) = 1$ et négatif sinon. On dit qu'un chemin est positif si le nombre d'arcs négatifs dans le chemin est pair, et qu'il est négatif si le nombre d'arcs négatifs dans le chemin est impair. Ainsi, on appelle graphe signé de N le couple (G^F, w_F).

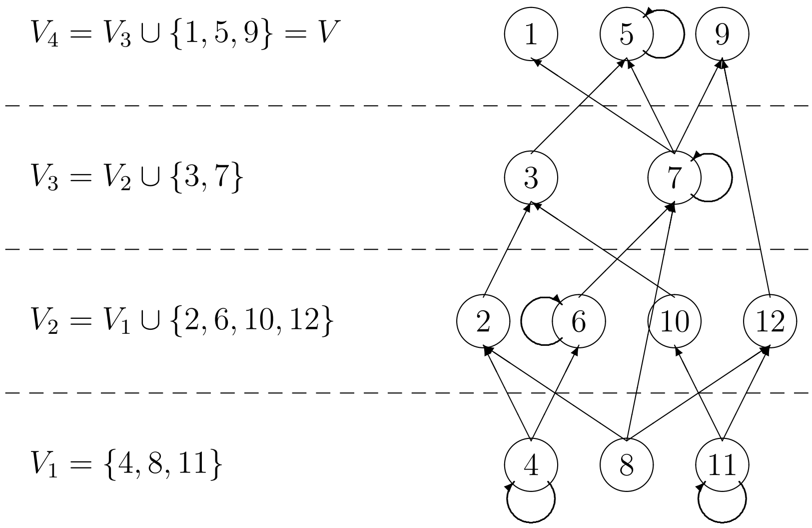


FIGURE 1.7. Exemple de graphe en couches.

1.2.3 Résultats.

Dans un premier temps, nous étudions les réseaux Booléens dont les graphes associés sont des graphes en couches (voir Figure 1.7). Parce que leur structure permet un comportement limite entièrement défini par les valeurs initiales des variables de la première couche, ces réseaux ont une dynamique très simple. Leur importance s'explique d'une part par le fait que d'autres réseaux Booléens plus complexes semblent exhiber le même comportement et d'autre part parce qu'ils vérifient des propriétés très intéressantes.

Dans le chapitre 3, nous prouvons que la taille des attracteurs de ces réseaux est une puissance de deux. De plus, si toutes les boucles sont monotones croissante, alors les seuls attracteurs existants sont des points fixes qui s'atteignent en au plus k actualisations, où k c'est le nombre de couches du réseau. Comme le nombre de couches du réseau est borné par le nombre de sommets, le nombre d'états transitoires menant à un point fixe dans ce type de réseau est au plus le nombre de sommets du graphe associé.

Aussi, nous étudions le comportement des réseaux en couches dont la fonction d'actualisation est telle que pour tout $(i, j) \in A$, $\text{sign}_s(i, j) = +1$. Ces réseaux ont la propriété notable d'avoir des dynamiques parallèle et séquentielle identiques [34]. Nous nous sommes donc demandé si la réciproque de cette proposition est aussi vérifiée. Nous avons trouvé qu'en l'absence de boucles, elle l'est effectivement. Cependant, comme nous le verrons dans le chapitre 5, il est possible de trouver des réseaux Booléens avec des dynamiques séquentielle et parallèle identiques mais dont le graphe associé n'est pas un graphe en couches. Ce type de réseaux apparait après avoir appliqué l'algorithme "Filter" sur des réseaux Booléens dont le graphe associé a seulement des circuits positifs.

Dans un deuxième temps, nous étudions la robustesse d'un réseau Booléen par rapport à son schéma d'actualisation. Pour ce travail, nous ne considérons que des schémas d'actualisation déterministes (parallèle, bloc-séquentiel, séquentiel) et nous définissons des classes d'équivalence du comportement dynamique d'un réseau Booléen en fonction de son graphe associé et de ses schémas d'actualisation. Nous définissons également le concept d'arc critique qui nous permet de détruire des cycles dynamiques grâce à une petite modification du schéma d'actualisation d'un réseau Booléen. De même, nous montrons comment, à l'aide d'une modification plus importante nous pouvons trouver des réseaux Booléens qui ne partagent aucun cycle. De plus, en guise de corollaire, nous obtenons que pour les réseaux sans boucles négatives, la dynamique parallèle ne partage aucun cycle avec la dynamique séquentielle associée au même réseau.

Nous étudions finalement un processus iteratif qui s'applique aux réseaux Booléens avec une actualisation parallèle. Étant donné un réseau Booléen avec actualisation parallèle, nous définissons son réseau séquentiel comme $\mathcal{S}(N) = (F^{(1)}, s_p)$ où $F^{(1)}(x) = (f_1^{(1)}(x), \dots, f_n^{(1)}(x))$:

$$\begin{aligned} f_1^{(1)}(x) &= f_1(x) \\ f_i^{(1)}(x) &= f_i(f_1^{(1)}(x), \dots, f_{i-1}^{(1)}(x), x - i, \dots, x_n) \qquad \forall i = 2, \dots, n. \end{aligned}$$

Il n'est pas difficile de vérifier que le comportement dynamique de $(F^{(1)}, s_p)$ est identique au comportement dynamique de (F, π_0), où $\pi_0(i) = i, \forall i = 1, \dots, n.$. C'est pourquoi nous appelons $\mathcal{S}(N)$ le réseau séquentiel de N. De plus, les deux réseaux, N et $\mathcal{S}(N)$, ont les mêmes points fixes et les cycles dynamiques peuvent être différentes.

Dans le chapitre 5 on éprouve que si N c'est un réseau Booléen tel que tous ses circuits sont positifs, donc $\mathcal{S}^n(N) = \mathcal{S}^{n-1}(N)$. De plus les attracteures de $\mathcal{S}^n(N)$ sont seulement des points fixes qui s'atteignent en au plus n actualisations. C'est-à-dire, nous avons défini un algorithme d'ordre polynomial qui "filtre" les cycles dynamiques d'un réseau Booléen. Il faut remarquer que les réseaux dont le graphe associé a seulement des circuits positifs, ont toujours au moins un point fixe [8].

Les résultats sur de réseaux Booléens ont donné naissance à trois articles :

1. Goles E. Salinas L, Comparison between parallel and serial dynamics of Boolean networks, Theoretical Computer Science 396,247-253, 2008.

2. Aracena J., Goles E., Salinas L., On the robustness of update schedules in Boolean networks, soumis a Bio Systems.

3. Salinas L., Goles E., Sequential Operator for Filtering Cycles in Boolean Networks, pre-print.

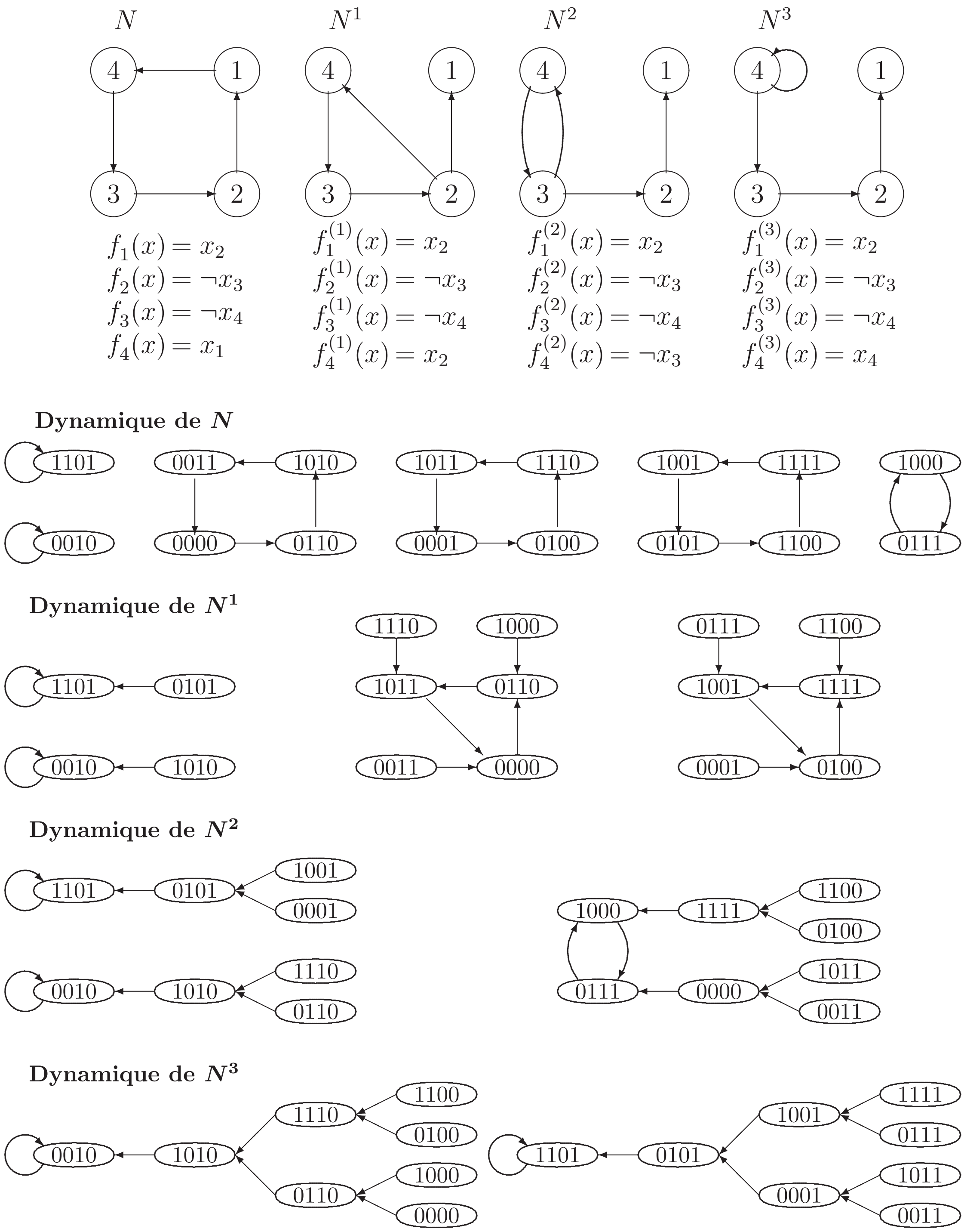


Figure 1.8. Un exemple de l'application de l'algorithme sur un réseau Booléen.

CHAPTER 2

Covering by squares

The tiling problem was introduced by Hao Wang in [5] and since then, many different versions of it have been studied (Tiling with poliominoes [4], rotation tiling[2, 3]). In tiling problem the basic idea is to cover the plane or a part of the plane without any overlap or gap, using tiles that can have different forms, also two tiles in a tiling are adjacent if they share and edge. In this work we are interested in a related problem, in this case, the tiles are squares and the overlap of tiles is allowed, in fact we say two squares are adjacent in the covering if they overlap and do not share any vertex or segment of edge. Also we study "weak coverings", this is an infinite set of squares, where all the squares are connected and every point in the plane is "near" of a square, i.e., in this type of covering we allow overlaps and gaps, but the size of the gap is bounded.

In section two, we introduce the "do not touch" condition and set up notation. In the third section, we discuss the cardinality of a finite set of squares that we call overlap, where the squares do not touch between them and the intersection is pairwise not empty. We prove the cardinality of an overlap depends on the size of the smallest square in the overlap, also we prove this dependence is $O(n)$ (where n is the size of the smallest square), but if we do not use the "do not touch" condition this dependence is $O(n^2)$.

Section four is devoted to the study of coverings of the discrete plane. We give minimal conditions to have a strong covering and a weak covering, this conditions are related with the size of squares and the number of adjacent squares. Also, we establish the

[1] work published in: Salinas L., Goles E, "Covering by squares", Theoretical Computer Science, Volume 396, Number 1–3, 10 May 2008.

maximum intersection number for a regular covering with respect to the size of the squares.

2.1 Notation and Definitions

We denote by $S = \left[\begin{smallmatrix} i \\ j \end{smallmatrix}\right]_n$, the square $S \subseteq \mathbb{Z}^2$ with lower left vertex in $\binom{i}{j}$ and width n.

$$S = \left[\begin{smallmatrix} i \\ j \end{smallmatrix}\right]_n = \left\{ \binom{i+l}{j+m} \in \mathbb{Z}^2 : l, m = 0, \ldots, n \right\}$$

For a given square $S = \left[\begin{smallmatrix} i \\ j \end{smallmatrix}\right]_n$, we call:

- Interior points of S the elements of $\mathrm{Int}(S) = \left\{ \binom{i+l}{j+m} : l, m = 1, \ldots, n-1 \right\}$,
- Frontier points of S the elements of $\mathrm{Fr}(S) = S \setminus \mathrm{Int}(S)$,
- Vertices of S the elements of $\mathrm{Ver}(S) = \left\{ \binom{i}{j}, \binom{i+n}{j}, \binom{i}{j+n}, \binom{i+n}{j+n} \right\}$,
- $\mathrm{Fr}_*(S) = \mathrm{Fr}(S) \setminus \mathrm{Ver}(S)$

Definition 2.1 *Let be S and S' two squares in $\mathbb{Z}^2$, S* touches *S' if either $\mathrm{Ver}(S) \cap \mathrm{Fr}(S') \neq \emptyset$ or $\mathrm{Ver}(S') \cap \mathrm{Fr}(S) \neq \emptyset$, i.e. there is a square that has a vertex in the frontier of the other square.*

As seen in Figure 2.1 two squares touch if they share any vertex or segment of edge. Also, Fig 2.2 shows two squares with horizontal edges in an upper plane than vertical edges, we observe that if these two squares do not touch between them, the represented squares hold the "do not touch" condition that we have introduced in this article.

Definition 2.2 *An* overlap of squares *$\mathcal{O}$ is a set of squares in the discrete plane satisfaying:*

1. $\forall S, S' \in \mathcal{O}, S \not\subseteq S'$.
2. $\forall S, S' \in \mathcal{O}$, *$S$ does not touch S'.*
3. $\forall S, S' \in \mathcal{O}, S \cap S' \neq \emptyset$.

Definition 2.3 *We call* strong covering *a set of squares $\mathcal{C}$, such that:*

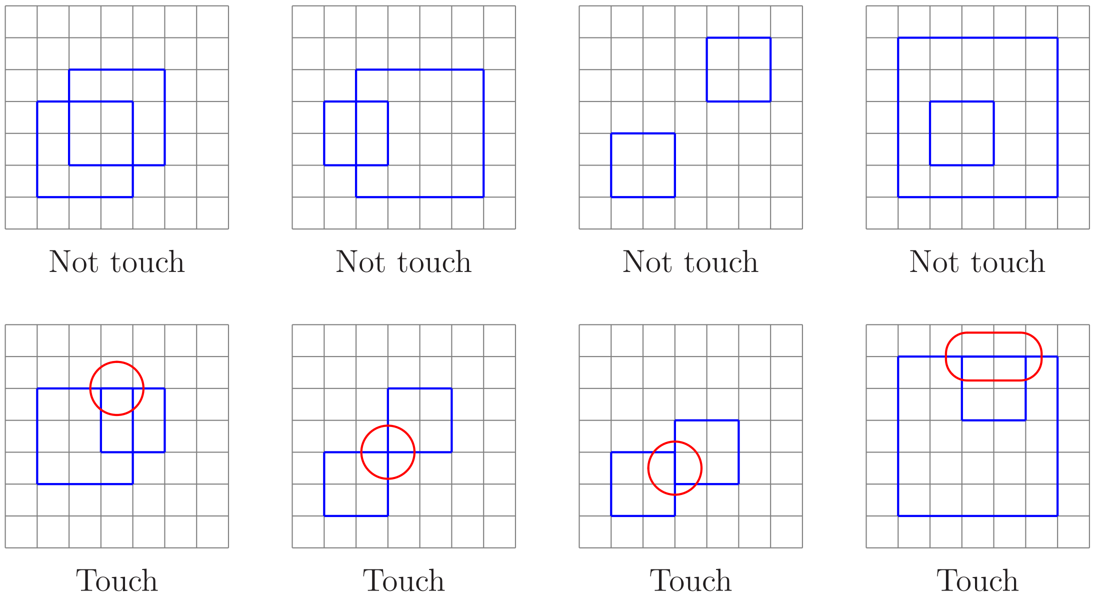


FIGURE 2.1. Examples of squares touching and not touching another square.

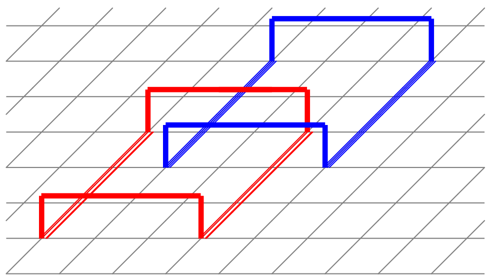


FIGURE 2.2. Representation of a square with horizontal edges in an upper plane.

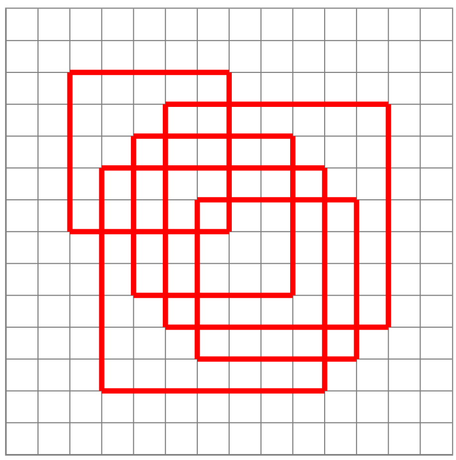


FIGURE 2.3. Example of Overlap.

1. $\forall S, S' \in \mathcal{C}, S \not\subseteq S'$.

2. $\forall S, S' \in \mathcal{C}, S$ *does not touch* S'.

3. $\forall \binom{i}{j} \in \mathbb{Z}^2, \exists S \in \mathcal{C}$, *such that* $\binom{i}{j} \in \mathrm{Int}(S)$.

Definition 2.4 *We call* k–weak covering ($k \in \mathbb{N}$) *a set of squares* $\mathcal{C}^*$, *such that:*

1. $\forall S, S' \in \mathcal{C}^*, S \not\subseteq S'$.

2. $\forall S, S' \in \mathcal{C}^*, S$ *does not touch* S'.

3. $\forall \binom{i}{j} \in \mathbb{Z}^2, \exists S \in \mathcal{C}^*$ *such that* $\left[\begin{smallmatrix} i \\ j \end{smallmatrix}\right]_{2k} \cap \mathrm{Int}(S) \neq \emptyset$.

4. *All squares are connected, i.e.* $\forall S_0, S_m \in \mathcal{C}^*, \exists S_1 \ldots S_{m-1} \in \mathcal{C}^*$, *such that* $S_l \cap S_{l-1} \neq \emptyset$, $\forall l = 1, \ldots, m$.

Notice that the squares in a strong covering are connected, and hence, a strong covering is a weak covering too. In fact a strong covering is a 0-weak covering. Also, for $k > k'$ if $\mathcal{C}$ is a k'-weak covering then $\mathcal{C}$ is a k-weak covering.

Definition 2.5 *The* intersection number *of a square* S *in a covering (strong or weak) is the number of squares in the covering that intersect* S.

Definition 2.6 *The* intersection number of a covering *(strong or weak) is the maximum intersection number of the squares in the covering. If the maximum does not exist, we say the intersection number of the covering is infinity.*

Definition 2.7 *A* regular strong covering *(*regular weak covering *respec.) is a strong covering (weak covering respec.) where every square has the same width and the same intersection number.*

Notice that a periodic set of squares in the plane can be described by two vectors $\binom{x_1}{y_1}, \binom{x_2}{y_2} \in \mathbb{Z}^2$ and a finite set of squares $S_l, l = 1, \ldots, k$ such that $S_l \cap P\left(\binom{x_1}{y_1}, \binom{x_2}{y_2}\right) \neq \emptyset$, where $P\left(\binom{x_1}{y_1}, \binom{x_2}{y_2}\right)$ is a parallelogram generated by the vectors $\binom{x_1}{y_1}$ and $\binom{x_2}{y_2}$. This representation is not unique.

We say $\Pi_{\binom{x_1}{y_1},\binom{x_2}{y_2}}\binom{a}{b}$ is the projection of $\binom{a}{b}$ on $P\left(\binom{x_1}{y_1}, \binom{x_2}{y_2}\right)$, if:

$$\Pi_{\binom{x_1}{y_1},\binom{x_2}{y_2}}\binom{a}{b} = \binom{a}{b} - \left(\lfloor\alpha\rfloor\binom{x_1}{y_1} + \lfloor\beta\rfloor\binom{x_2}{y_2}\right)$$

where $\binom{a}{b} = \alpha\binom{x_1}{y_1} + \beta\binom{x_2}{y_2}$.

The sides of the squares S_l in the paralellogramm are the sides of S_l and their projections.

We define a set $A \subseteq \mathbb{Z}^2$, such that $\forall \binom{i}{j} \in A, \begin{bmatrix} i \\ j \end{bmatrix}_n \cap P\left(\binom{x_1}{y_1}, \binom{x_2}{y_2}\right) \neq \emptyset$,

$$\left[A; \binom{x_1}{y_1}, \binom{x_2}{y_2}\right]_n = \left\{ \begin{bmatrix} i_* \\ j_* \end{bmatrix}_n : \exists \binom{i}{j} \in A, \Pi_{\binom{x_1}{y_1},\binom{x_2}{y_2}} \binom{i_*}{j_*} = \Pi_{\binom{x_1}{y_1},\binom{x_2}{y_2}} \binom{i}{j} \right\}$$

The set A is called the generator set of the covering.

2.2 Cardinality of an overlap

In this section we prove that the maximum cardinality of an overlap is lineal with respect to the size of the smallest square. It is easy to see that if we do not consider the "do not touch" condition this cardinality is $(n+1)^2$ where n is the size of the smallest square. An example is the set $\left\{ \begin{bmatrix} i \\ j \end{bmatrix}_n : i, j = 0, \ldots, n \right\}$.

FACT 2.1 *Given S and S' two squares in $\mathbb{Z}^2$ such that $S \cap S' \neq \emptyset$ and S does not touch S' then $|\operatorname{Fr}_*(S) \cap \operatorname{Fr}_*(S')| = 2$.*

PROOF. Without loss of generality, let $S = \begin{bmatrix} 0 \\ 0 \end{bmatrix}_n$ and $S' = \begin{bmatrix} i \\ j \end{bmatrix}_{n'}$ where $0 < i < n$. Thus, we consider two possibilities:

1. $\binom{i}{j} \in \operatorname{Int}(S) \Longrightarrow 0 < i, j < n$ and $n' > \max\{n - i, n - j\}$. Hence
$$\operatorname{Fr}_*(S) \cap \operatorname{Fr}_*(S') = \left\{ \binom{i}{n}, \binom{n}{j} \right\}$$
2. $\binom{i}{j} \notin \operatorname{Int}(S) \Longrightarrow 0 < i < n$ and $-n' < j < 0$. Hence,
$$\operatorname{Fr}(S)_* \cap \operatorname{Fr}_*(S') = \begin{cases} \left\{ \binom{i}{0}, \binom{i}{n} \right\} & \text{if } j + n' > n \\ \left\{ \binom{i}{0}, \binom{n}{j+n'} \right\} & \text{otherwise} \end{cases}$$

□

The main result of this section is Proposition 2.1, to prove this proposition we use Fact 2.1 which gives a bound for the cardinality of the overlap.

PROPOSITION 2.1 *The maximum cardinality of an overlap of squares $\mathcal{O}$ containing a given square S_0 of width n is $2n - 1$.*

PROOF. If S and S_0 are two squares in the same overlap, then by Fact 2.1, the intersection between their frontiers has two points. These points do not belong to the frontier of another square S' because, in this case, S' touches either S or S_0. Since $|\operatorname{Fr}_*(S_0)| = 4(n-1)$, there exists a maximum of $2(n-1)$ squares intersecting S_0. Now we show a construction which reaches this bound.

Without loss of generality we consider $S_0 = \left[\begin{smallmatrix}0\\0\end{smallmatrix}\right]_n$, and the other elements of $\mathcal{O}$ are:

$$S_i = \left[\begin{smallmatrix}-i\\i\end{smallmatrix}\right]_{n_i}, \quad S'_i = \left[\begin{smallmatrix}i\\-i\end{smallmatrix}\right]_{n_i}, \qquad i = 1, \ldots, n-1.$$

where $n_1 = n + 2$ and,

$$n_i = \min\{n_* > n_{i-1} : S_i \text{ do not touch the squares } S_j \text{ or } S'_j, j = 1, \ldots, i-1\}$$

It is easy to verify that the squares so defined satisfy the constraints of an overlap of squares. □

Examples of overlaps of maximum cardinality are shown in Figure 2.4.

2.3 Strong and weak coverings

As seen in the previous section, the cardinality of an overlap is finite, then it covers only a limited part of the discrete plane. Now, we treat some aspects of strong and weak coverings of the discrete plane. We will restrict our attention to regular coverings, but we will give a few comments about the non regular case.

2.3.1 Maximum intersection number in a covering

The main result of this section is Theorem 2.1, this theorem provides a bound for the intersection number of a regular covering with respect to the size of squares in the covering. In the non regular case this bound does not exist because the size of squares in the covering is not bounded, and if we bound the size of squares, the maximum intersection number will be the maximum intersection number for the largest square in the covering. In first place, we give some previous results that we will use in the proof of the main result of this section.

LEMMA 2.1 *Given a square S of width $n > 2$. Let R_S a set of squares of width n such that:*

1. *$\forall S' \in R_S, S \cap S' \neq \emptyset$,*

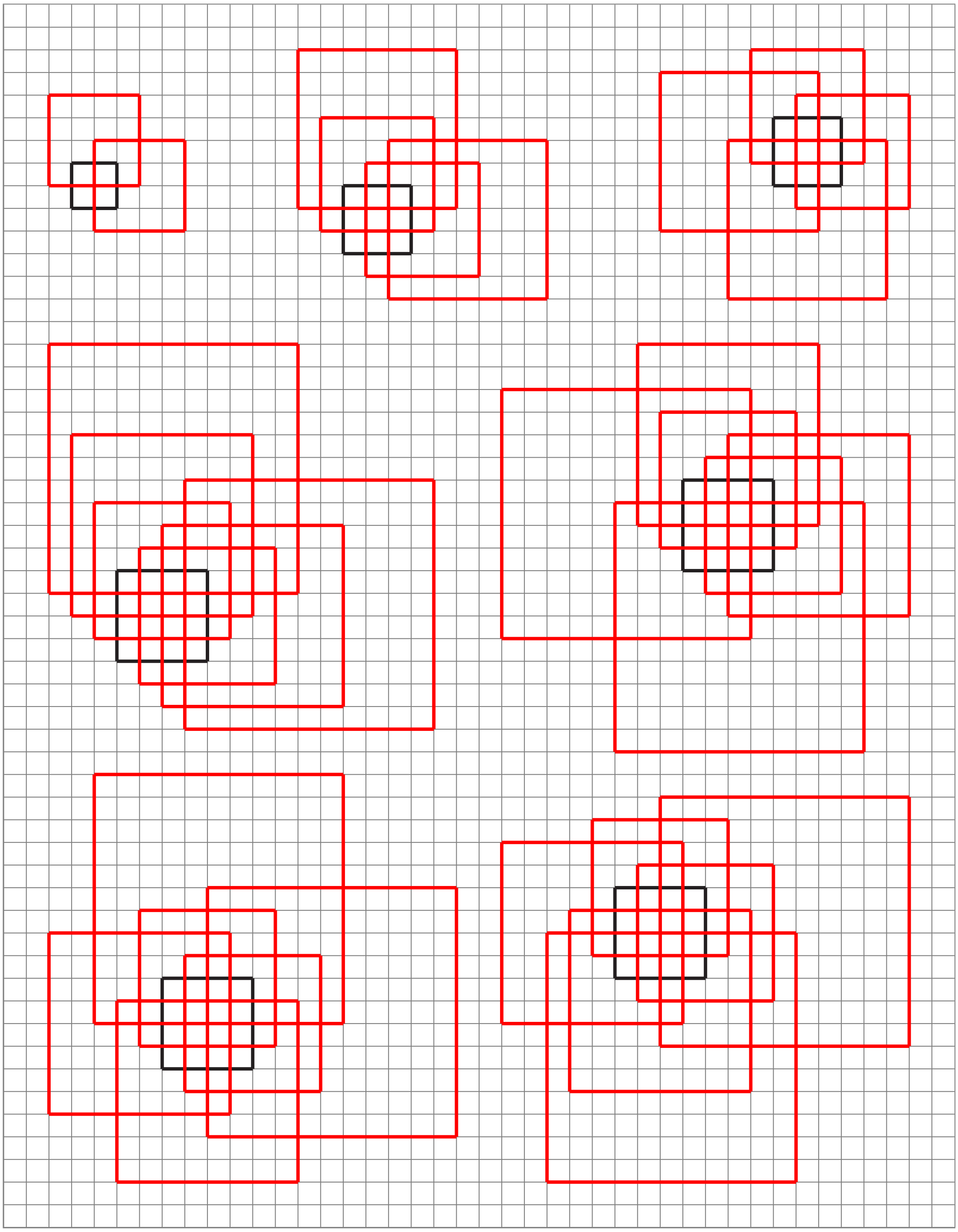


Figure 2.4. Examples of overlaps of maximum cardinality.

2. $\forall S' \in R_S, S'$ *does not touch* S,

3. $\forall S', S'' \in R_S, S'$ *does not touch* S''.

Then the maximum cardinality of R_S *is* $2(n-1)$.

PROOF. Notice that R_S is not an overlap because the squares in R_S do not intersect between them necessarily.

By Fact 2.1 every square in R_S intersects S in two points belonging to $\mathrm{Fr}_*(S)$, and $|\mathrm{Fr}_*(S)| = 4(n-1)$ then there is a maximum of $2(n-1)$ squares. If $S = \left[\begin{smallmatrix}0\\0\end{smallmatrix}\right]_n$, an example of R_S reaching the maximum cardinality is the set: $\left[\begin{smallmatrix}n-1\\n-1\end{smallmatrix}\right]_n$, $\left[\begin{smallmatrix}-(n-1)\\-(n-1)\end{smallmatrix}\right]_n$, $\left[\begin{smallmatrix}-n+k\\1+k\end{smallmatrix}\right]_n$, $k = 1, \ldots, n-2$ and $\left[\begin{smallmatrix}n-k\\-(1+k)\end{smallmatrix}\right]_n$, $k = 1, \ldots, n-2$ (see Figure 2.5). □

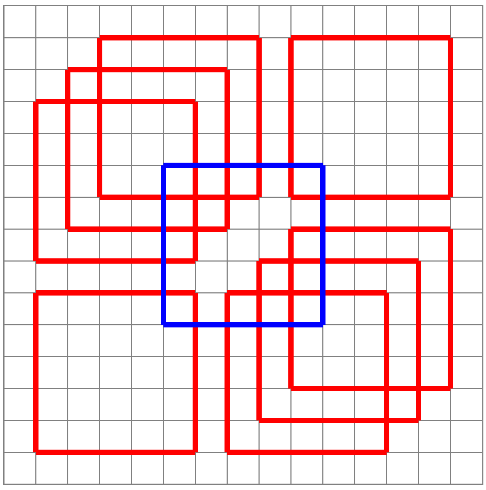


FIGURE 2.5. R_S of maximun cardinality.

FACT 2.2 *Let* $S = \left[\begin{smallmatrix}i\\j\end{smallmatrix}\right]_n$ *be a square in a regular covering intersected by* $S_* = \left[\begin{smallmatrix}i_*\\j_*\end{smallmatrix}\right]_n$, *such that either* $|i - i_*| = 1$ *or* $|j - j_*| = 1$ *then the intersection number of* $\left[\begin{smallmatrix}i\\j\end{smallmatrix}\right]_n$ *is lesser than* $2(n-1)$.

PROOF. To have the maximum intersection number for all every line and every column must have two squares with a vertex on it. If either $|i - i_*| = 1$ or $|j - j_*| = 1$ there will be either a line or a column which can be used only by one square. □

FACT 2.3 *There does not exist a regular covering of width even n with an intersection number* $2(n-1)$.

PROOF. If we have a regular covering every square in the covering must intersect the same number of squares, then if the intersection number of the covering is $2(n-1)$ we cannot have two squares with the condition $|i - i_*| = 1$ or $|j - j_*| = 1$, then for every square in the covering the odd lines must contain upper vertices of the squares intersecting it and even lines have to contain lower vertices. Since n is even the line $n-1$ must have upper vertices, then this square holds the condition $|i - i_*| = 1$ or $|j - j_*| = 1$ and it is not possible to have an intersection number $2(n-1)$. □

THEOREM 2.1 *Let n be the size of the squares in a regular covering (strong or weak), then intersection number of the covering is lesser or equal than: $2(n-1)$ if n is odd and $2(n-1)-1$ if n is even.*

PROOF.

IF n IS ODD. We will prove that the covering $R_{n,2(n-1)}$ is a regular covering with the intersection number $2(n-1)$. In the case $n = 3$, it is a 1-weak covering and for $n \geq 5$, it is a strong covering.

$$R_{n,2(n-1)} = \left[\left\{\binom{0}{0}\right\}; \binom{n+1}{0}, \binom{2}{2}\right]_n$$

For the case $n = 3$ it is enough to see the Figure 2.6 to prove that is a 1-weak covering with an intersection number four.

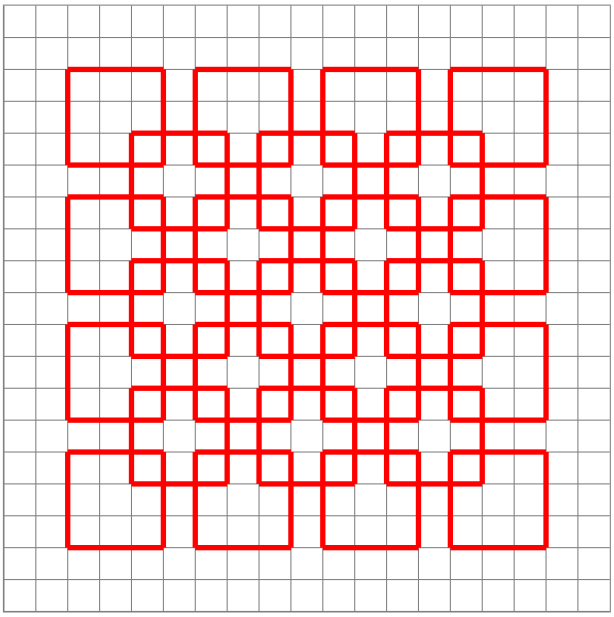


FIGURE 2.6. 1-weak covering of width 3 and intersection number 4.

For the case $n \geq 5$, we see that every point in the plane is in the interior of a square. It is enough to see that it is true for the points in $P\left(\binom{n+1}{0}, \binom{2}{2}\right) =$

$\left\{\binom{i}{j}/j = 0, 1 \text{ and } i = j, \ldots, j+n\right\}$.

- If $j = 0$ and $0 \leq i \leq n-3 \Longrightarrow \binom{i}{j} \in \text{Int}\begin{bmatrix}-2\\-2\end{bmatrix}_n$
- If $j = 0$ and $n-2 \leq i \leq n \Longrightarrow \binom{i}{j} \in \text{Int}\begin{bmatrix}n-3\\-4\end{bmatrix}_n$
- if $j = 1$ and $1 \leq i \leq n-1 \Longrightarrow \binom{i}{j} \in \text{Int}\begin{bmatrix}0\\0\end{bmatrix}_n$
- if $j = 1$ and $n \leq i \leq n+1 \Longrightarrow \binom{i}{j} \in \text{Int}\begin{bmatrix}n-1\\-2\end{bmatrix}_n$

To prove that the intersection number of every square is $2(n-1)$ it is enough to prove that $\begin{bmatrix}0\\0\end{bmatrix}_n$ intersect $2(n-1)$ squares. If we consider the generator squares it is easy to see that the squares intersecting $\begin{bmatrix}0\\0\end{bmatrix}_n$ are:

$$\begin{bmatrix}2i-a\\2i-b\end{bmatrix}_n, \quad a, b \in \{0, n+1\} \text{ and } i = 1, \ldots, \tfrac{n-1}{2}$$

The vertices of squares intersecting $\begin{bmatrix}0\\0\end{bmatrix}_n$ are in the points:

$$\binom{2i-a}{2i-b}, \quad a, b \in \{0, 1\} \text{ and } i = 1, \ldots, \tfrac{n-1}{2}$$

Which are interior points of $\begin{bmatrix}0\\0\end{bmatrix}_n$. Hence, they do not touch $\begin{bmatrix}0\\0\end{bmatrix}_n$.

IF n IS EVEN. We will show a construction with an intersection number $2(n-1)-1$, this construction is a 1-weak covering in the case $n = 4$ and a strong covering for $n \geq 6$. Let be the set:

$$A = \left\{\binom{2i+l(n-1)}{2i+l(n-1)}/i = 0, \ldots, \tfrac{n}{2}-2, l = 0, 1, 2, 3\right\} \cup \left\{\binom{4n-5}{4n-5}, \binom{4n-4}{4n-4}\right\}$$

and the covering,

$$R_{n,2n-3} = \left[A; \binom{4n-2}{4n-2}, \binom{2n}{n-1}\right]_n$$

We give the proof for the case $n \geq 6$ because for the case $n = 4$ it is straightforward from the Figure 2.8.

In first place we observe that the squares of the generator set have their lower left corner on the diagonal $\binom{k}{k}$, $k \in \mathbb{Z}$, also the first vector defining the parallelogram is $\binom{4n-2}{4n-2}$ then we can say the covering is a serie of copies of the squares in the diagonal $\binom{k}{k}$, $k \in \mathbb{Z}$, then every square in the covering has its lower left corner in a point on a diagonal $\binom{k}{k} + c\binom{n+1}{0}$, for some k and c in $\mathbb{Z}$. Of this way, we call first diagonal to all the squares with lower left corner in $\binom{k}{k}$, $k \in \mathbb{Z}$ and second diagonal the set of squares with lower left corner in $\binom{k}{k} + \binom{n+1}{0}$, $k \in \mathbb{Z}$.

To see that every point of the plane is covered by a square of the covering we observe that every diagonal covers a strip of wide $2(n-3)$ and the distance between two

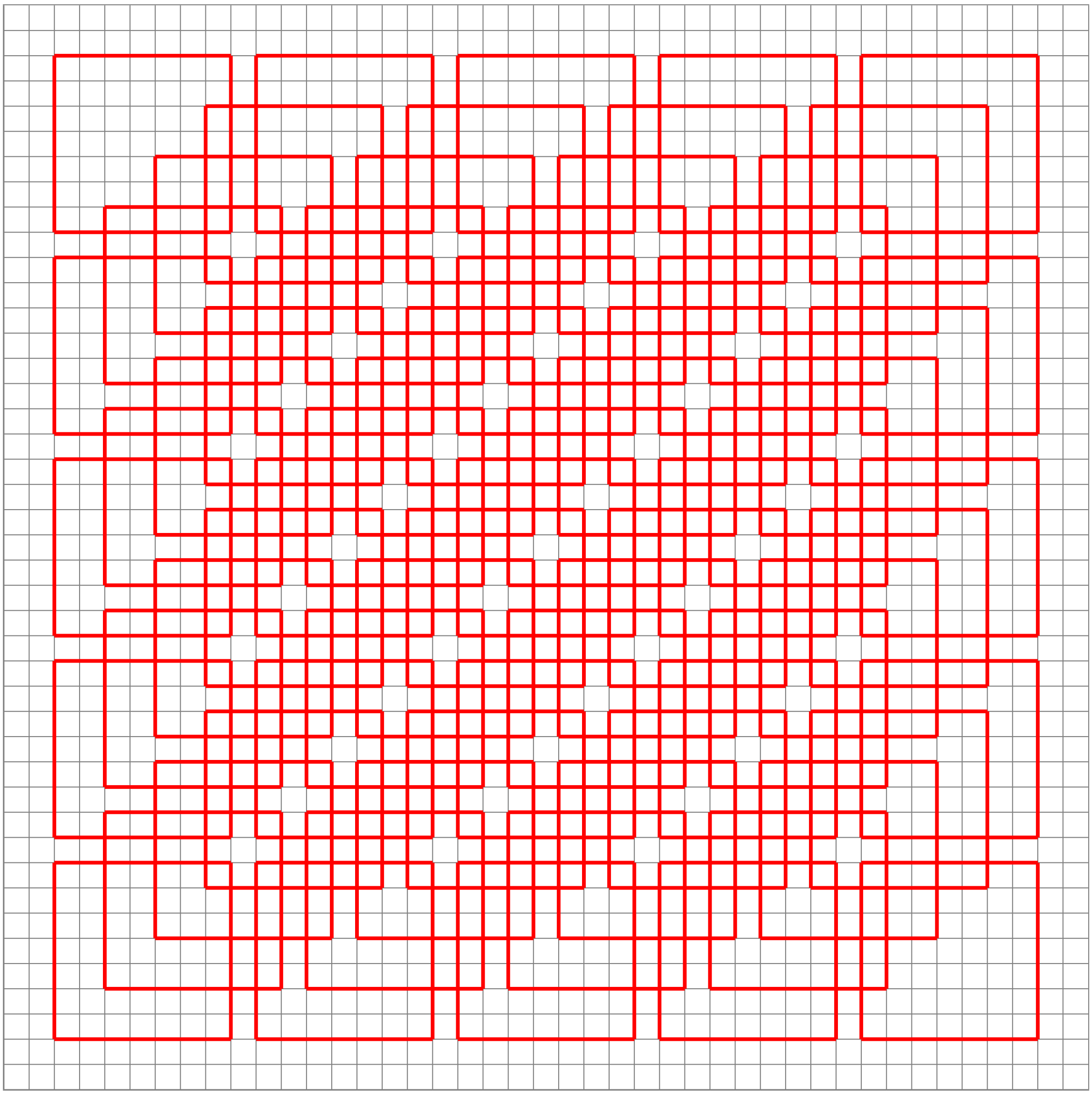


FIGURE 2.7. Covering of Maximum cardinality for n odd.

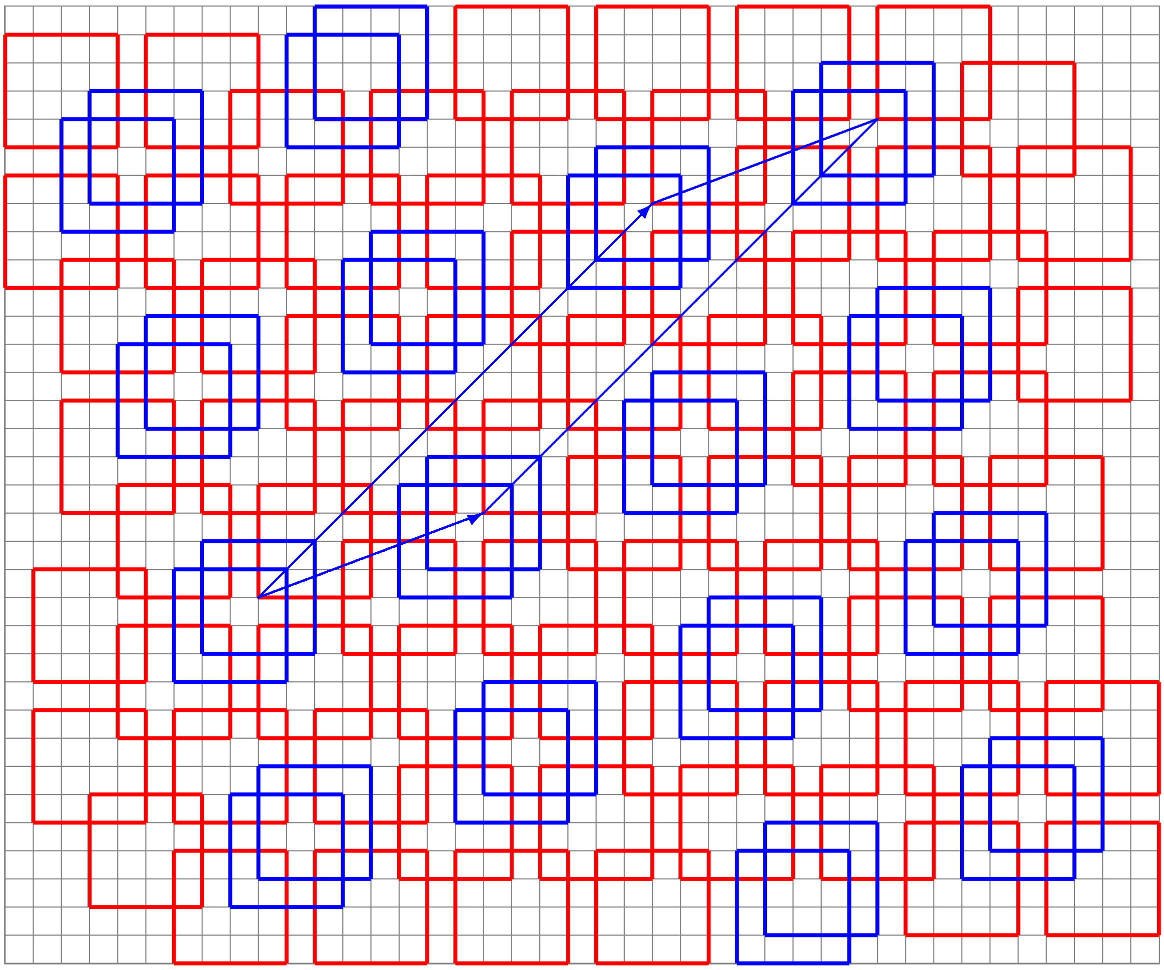


FIGURE 2.8. 1-weak regular covering of width 4 and intersection number 5.

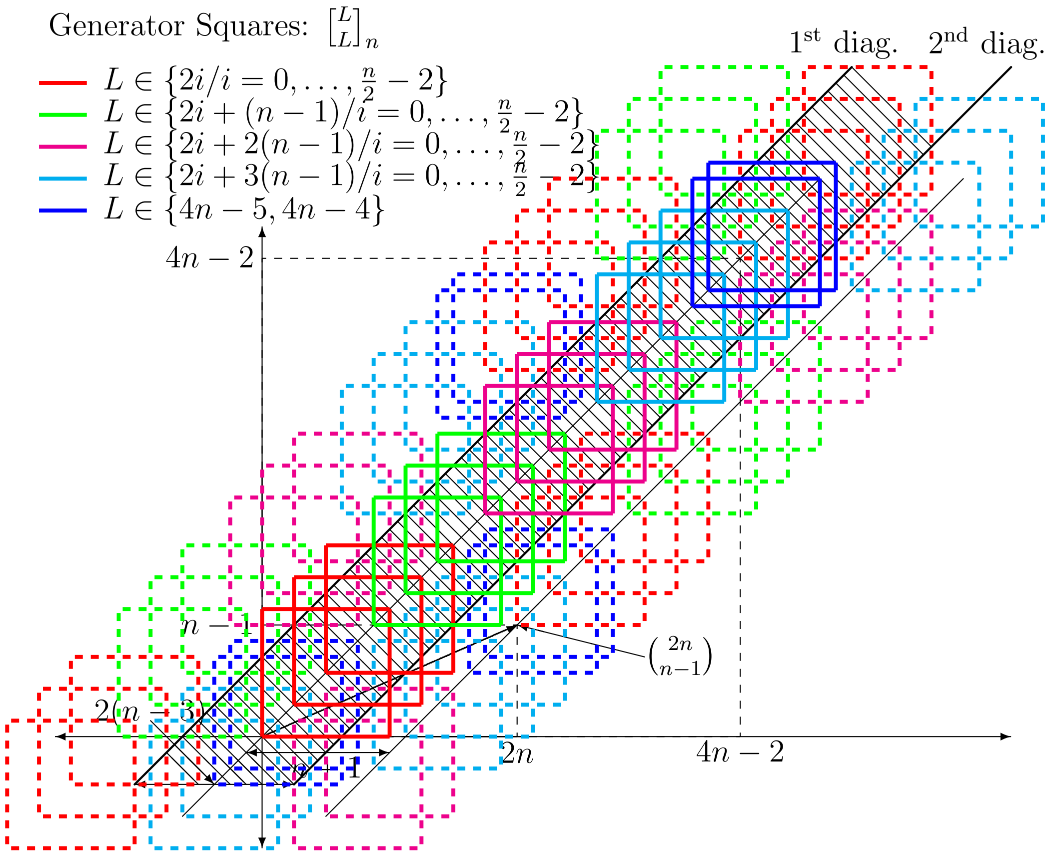


FIGURE 2.9. Covering.

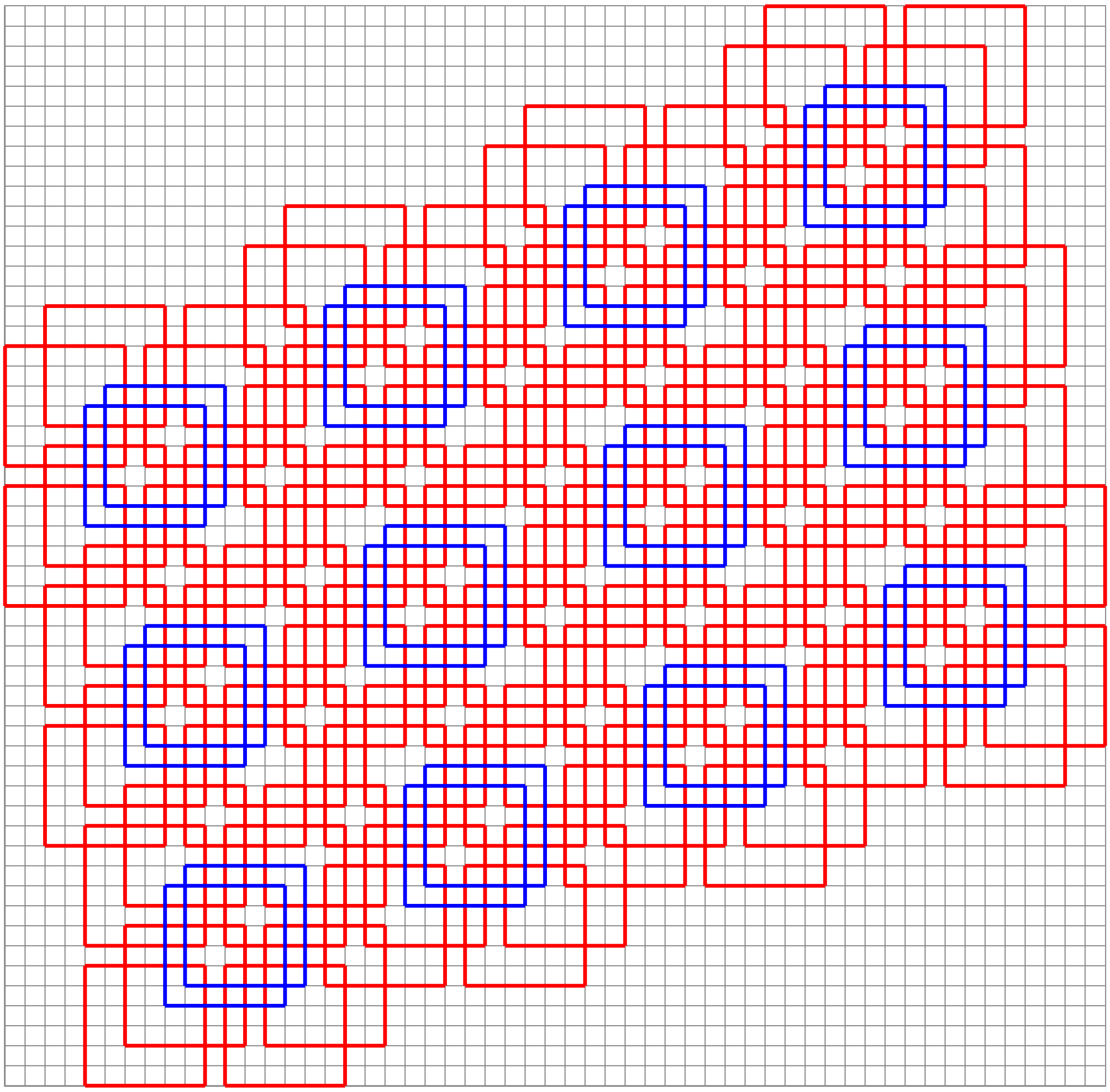


Figure 2.10. strong covering of width 6 and intersection number 9.

adjacent diagonals is $n+1$ (as seen in Figure 2.9) then for $n > 7$ every point of the plane is covered. For the case $n = 6$ the proof is in Figure 2.10.

To verify the intersection number and if the squares in the covering touch another square, we study the squares in the generator set, because every square in the covering is a copy of one of them.

The projection on the parallelogram $P\left(\binom{4n-2}{4n-2}, \binom{2n}{n-1}\right)$ of lower left corners of generator squares are:

$$\begin{array}{l}\binom{0}{0}, \binom{2}{2}, \ldots, \binom{n-4}{n-4} \\ \binom{n-1}{n-1}, \binom{n+1}{n+1}, \ldots, \binom{2n-5}{2n-5} \\ \binom{2n-2}{2n-2}, \binom{2n}{2n}, \ldots, \binom{3n-6}{3n-6} \\ \binom{3n-3}{3n-3}, \binom{3n-1}{3n-1}, \ldots, \binom{4n-7}{4n-7} \\ \binom{4n-5}{4n-5}, \binom{4n-4}{4n-4}\end{array}$$

and upper right corners are:

$$\begin{array}{l}\binom{n}{n}, \binom{n+2}{n+2}, \ldots, \binom{2n-4}{2n-4} \\ \binom{2n-1}{2n-1}, \binom{2n+1}{2n+1}, \ldots, \binom{3n-5}{3n-5} \\ \binom{3n-2}{3n-2}, \binom{3n}{3n}, \ldots, \binom{4n-6}{4n-6} \\ \binom{4n-3}{4n-3}, \binom{1}{1}, \binom{3}{3}, \ldots, \binom{n-5}{n-5} \\ \binom{n-3}{n-3}, \binom{n-2}{n-2}\end{array}$$

We observe all corners have different coordinates, then there is no squares touching in the same diagonal. We have seen squares in the second diagonal have their lower left corner in $\binom{n+1}{0} + \binom{k}{k}$ then, if a square in the second diagonal touch a square in the first diagonal it implies $L - k \in \{1, n\}$, where $\begin{bmatrix} L \\ L \end{bmatrix}_n$ is a generator square. It is enough to prove $L - k \notin \{1, n\}$ for $\begin{bmatrix} L \\ L \end{bmatrix}_n$ a generator square, then the values of $k \in \mathbb{Z} \cap [-n, 4n-2[$ such that $\begin{bmatrix} n+1+k \\ k \end{bmatrix}_n$ belongs to the covering are:

$$\begin{array}{l} n-1, n+1, \ldots, 2n-5 \\ 2n-2, 2n, \ldots, 3n-6 \\ 3n-3, 3n-1, \ldots, 4n-7 \\ -(n-1), -(n-3), \ldots, -5 \\ 4n-4, -2, 0, \ldots, n-4 \\ n-4, n-3 \end{array}$$

From this values we conclude there is no squares touching.

Finally, we prove every square intersect $2n-3$ squares in the covering. Given there are no squares touching we will study the intersection number of every square in the generator set. We classify the squares in the generator set in five goups:

1. $S = \begin{bmatrix} 2i \\ 2i \end{bmatrix}_n$, $i = 0, \ldots, \frac{n}{2} - 2$.

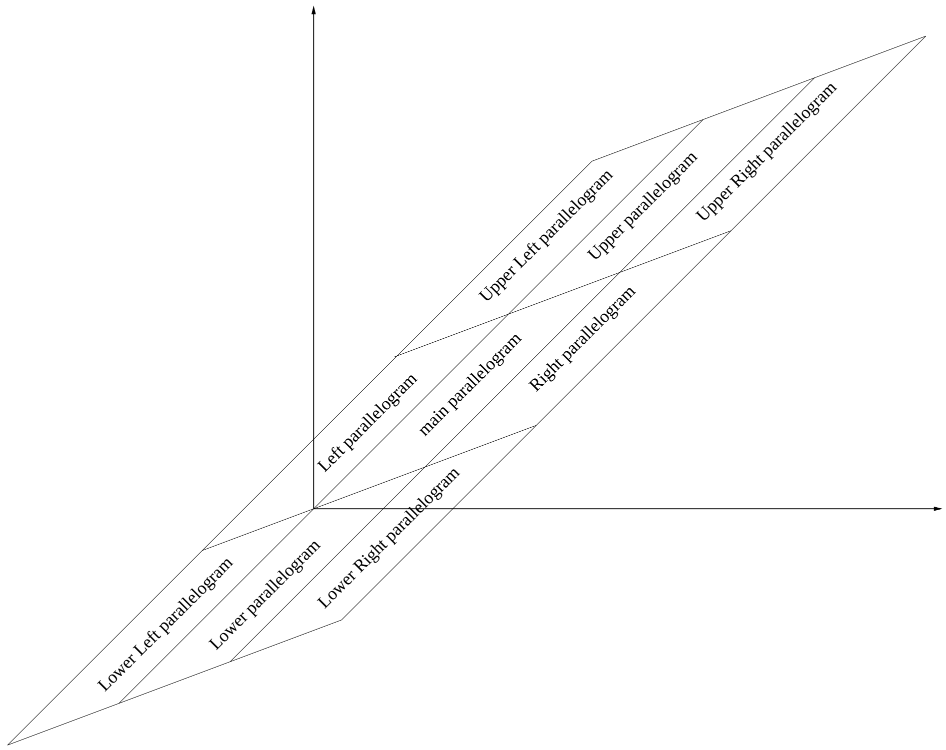


FIGURE 2.11. Scheme of parallelograms of the covering.

2. $S = \begin{bmatrix} 2i+(n-1) \\ 2i+(n-1) \end{bmatrix}_n$, $i = 0, \ldots, \frac{n}{2} - 2$.
3. $S = \begin{bmatrix} 2i+2(n-1) \\ 2i+2(n-1) \end{bmatrix}_n$, $i = 0, \ldots, \frac{n}{2} - 2$.
4. $S = \begin{bmatrix} 2i+3(n-1) \\ 2i+3(n-1) \end{bmatrix}_n$, $i = 0, \ldots, \frac{n}{2} - 2$.
5. $S = \begin{bmatrix} 4n-5 \\ 4n-5 \end{bmatrix}_n$ and $S = \begin{bmatrix} 4n-4 \\ 4n-4 \end{bmatrix}_n$.

For every group we give a table that shows the squares intersecting this type of squares. The squares intersecting are described by the their generator square, the vertex located in the interior of the intersected square (LL: Lower left, LR:Lower right, UL: Upper left and UR:Upper right) and the number of this type of squares intersecting.

- if $S = \begin{bmatrix} 2i \\ 2i \end{bmatrix}_n$, $i = 0, \ldots, \frac{n}{2} - 2$. Then S is intersected by:

Generator square	**vertex**	**number**
$\begin{bmatrix} 2j \\ 2j \end{bmatrix}_n$, $j = i+1, \ldots, \frac{n}{2} - 2$	LL	$\frac{n}{2} - i - 2$
$\begin{bmatrix} 2j+(n-1) \\ 2j+(n-1) \end{bmatrix}_n$, $j = i+1, \ldots, \frac{n}{2} - 2$	LR	$\frac{n}{2} - i - 2$
$\begin{bmatrix} 2j \\ 2j \end{bmatrix}_n$, $j = 0, \ldots, i-1$	UR	i
$\begin{bmatrix} 2j+3(n-1) \\ 2j+3(n-1) \end{bmatrix}_n$, $j = 1, \ldots, i$	LR	i
$\begin{bmatrix} 2j+(n-1) \\ 2j+(n-1) \end{bmatrix}_n$, $j = 0, \ldots, i$	LL	$i+1$
$\begin{bmatrix} 2j+2(n-1) \\ 2j+2(n-1) \end{bmatrix}_n$, $j = 0, \ldots, i$	LR	$i+1$
$\begin{bmatrix} 2j+3(n-1) \\ 2j+3(n-1) \end{bmatrix}_n$, $j = i+1, \ldots, \frac{n}{2} - 2$	UR	$\frac{n}{2} - i - 2$
$\begin{bmatrix} 2j+2(n-1) \\ 2j+2(n-1) \end{bmatrix}_n$, $j = i+1, \ldots, \frac{n}{2} - 2$	UL	$\frac{n}{2} - i - 2$
$\begin{bmatrix} 4n-5 \\ 4n-5 \end{bmatrix}_n$, $\begin{bmatrix} 4n-4 \\ 4n-4 \end{bmatrix}_n$	UR	2
$\begin{bmatrix} 3n-3 \\ 3n-3 \end{bmatrix}_n$	UL	1
Total		$2n - 3$

- if $S = \begin{bmatrix} 2i+(n-1) \\ 2i+(n-1) \end{bmatrix}_n$, $i = 0, \ldots, \frac{n}{2} - 2$. Then S is intersected by:

Generator square	**vertex**	**number**
$\begin{bmatrix} 2j+(n-1) \\ 2j+(n-1) \end{bmatrix}_n$, $j = i+1, \ldots, \frac{n}{2} - 2$	LL	$\frac{n}{2} - i - 2$
$\begin{bmatrix} 2j+2(n-1) \\ 2j+2(n-1) \end{bmatrix}_n$, $j = i+1, \ldots, \frac{n}{2} - 2$	LR	$\frac{n}{2} - i - 2$
$\begin{bmatrix} 2j+(n-1) \\ 2j+(n-1) \end{bmatrix}_n$, $j = 0, \ldots, i-1$	UR	i
$\begin{bmatrix} 2j \\ 2j \end{bmatrix}_n$, $j = 0, \ldots, i-1$	LR	i
$\begin{bmatrix} 2j+2(n-1) \\ 2j+2(n-1) \end{bmatrix}_n$, $j = 0, \ldots, i$	LL	$i+1$
$\begin{bmatrix} 2j+3(n-1) \\ 2j+3(n-1) \end{bmatrix}_n$, $j = 0, \ldots, i$	LR	$i+1$
$\begin{bmatrix} 2j \\ 2j \end{bmatrix}_n$, $j = i, \ldots, \frac{n}{2} - 2$	UR	$\frac{n}{2} - i - 1$
$\begin{bmatrix} 2j \\ 2j \end{bmatrix}_n$, $j = i+1, \ldots, \frac{n}{2} - 2$	UL	$\frac{n}{2} - i - 2$
$\begin{bmatrix} 4n-5 \\ 4n-5 \end{bmatrix}_n$, $\begin{bmatrix} 4n-4 \\ 4n-4 \end{bmatrix}_n$	UL	2
Total		$2n - 3$

- if $S = \begin{bmatrix} 2i+2(n-1) \\ 2i+2(n-1) \end{bmatrix}_n$, $i = 0, \ldots, \frac{n}{2} - 2$. Then S is intersected by:

Generator square	**vertex**	**number**
$\begin{bmatrix} 2j+2(n-1) \\ 2j+2(n-1) \end{bmatrix}_n, j = i+1, \ldots, \frac{n}{2} - 2$	LL	$\frac{n}{2} - i - 2$
$\begin{bmatrix} 2j+3(n-1) \\ 2j+3(n-1) \end{bmatrix}_n, j = i+1, \ldots, \frac{n}{2} - 2$	LR	$\frac{n}{2} - i - 2$
$\begin{bmatrix} 2j+2(n-1) \\ 2j+2(n-1) \end{bmatrix}_n, j = 0, \ldots, i-1$	UR	i
$\begin{bmatrix} 2j+(n-1) \\ 2j+(n-1) \end{bmatrix}_n, j = 0, \ldots, i-1$	LR	i
$\begin{bmatrix} 2j+3(n-1) \\ 2j+3(n-1) \end{bmatrix}_n, j = 0, \ldots, i$	LL	$i+1$
$\begin{bmatrix} 2j \\ 2j \end{bmatrix}_n, j = 0, \ldots, i-1$	LR	i
$\begin{bmatrix} 4n-5 \\ 4n-5 \end{bmatrix}_n, \begin{bmatrix} 4n-4 \\ 4n-4 \end{bmatrix}_n$	LR	2
$\begin{bmatrix} 2j+(n-1) \\ 2j+(n-1) \end{bmatrix}_n, j = i, \ldots, \frac{n}{2} - 2$	UR	$\frac{n}{2} - i - 1$
$\begin{bmatrix} 2j \\ 2j \end{bmatrix}_n, j = i, \ldots, \frac{n}{2} - 2$	UL	$\frac{n}{2} - i - 1$
Total		$2n - 3$

- if $S = \begin{bmatrix} 2i+3(n-1) \\ 2i+3(n-1) \end{bmatrix}_n$, $i = 0, \ldots, \frac{n}{2} - 2$. Then S is intersected by:

Generator square	**vertex**	**number**
$\begin{bmatrix} 2j+3(n-1) \\ 2j+3(n-1) \end{bmatrix}_n, j = i+1, \ldots, \frac{n}{2} - 2$	LL	$\frac{n}{2} - i - 2$
$\begin{bmatrix} 2j \\ 2j \end{bmatrix}_n, j = i, \ldots, \frac{n}{2} - 3$	LR	$\frac{n}{2} - i - 2$
$\begin{bmatrix} 2j+3(n-1) \\ 2j+3(n-1) \end{bmatrix}_n, j = 0, \ldots, i-1$	UR	i
$\begin{bmatrix} 2j+2(n-1) \\ 2j+2(n-1) \end{bmatrix}_n, j = 0, \ldots, i-1$	LR	i
$\begin{bmatrix} 2j \\ 2j \end{bmatrix}_n, j = 0, \ldots, i-1$	LL	i
$\begin{bmatrix} 2j+(n-1) \\ 2j+(n-1) \end{bmatrix}_n, j = 0, \ldots, i-1$	LR	i
$\begin{bmatrix} 2j+2(n-1) \\ 2j+2(n-1) \end{bmatrix}_n, j = i, \ldots, \frac{n}{2} - 2$	UR	$\frac{n}{2} - i - 1$
$\begin{bmatrix} 2j+(n-1) \\ 2j+(n-1) \end{bmatrix}_n, j = i, \ldots, \frac{n}{2} - 2$	UL	$\frac{n}{2} - i - 1$
$\begin{bmatrix} 4n-5 \\ 4n-5 \end{bmatrix}_n, \begin{bmatrix} 4n-4 \\ 4n-4 \end{bmatrix}_n$	UR	2
$\begin{bmatrix} 3n-3 \\ 3n-3 \end{bmatrix}_n$	UR	1
Total		$2n - 3$

- if $S = \begin{bmatrix} 4n-5 \\ 4n-5 \end{bmatrix}_n$ (or $S = \begin{bmatrix} 4n-4 \\ 4n-4 \end{bmatrix}_n$ respect). Then S is intersected by:

Generator square	**vertex**	**number**
$\begin{bmatrix} 2j \\ 2j \end{bmatrix}_n, j = 0, \ldots, \frac{n}{2} - 2$	LL	$\frac{n}{2} - 1$
$\begin{bmatrix} 2j+(n-1) \\ 2j+(n-1) \end{bmatrix}_n, j = 0, \ldots, \frac{n}{2} - 2$	LR	$\frac{n}{2} - 1$
$\begin{bmatrix} 2j+3(n-1) \\ 2j+3(n-1) \end{bmatrix}_n, j = 0, \ldots, \frac{n}{2} - 2$	UR	$\frac{n}{2} - 1$
$\begin{bmatrix} 2j+2(n-1) \\ 2j+2(n-1) \end{bmatrix}_n, j = 0, \ldots, \frac{n}{2} - 2$	UL	$\frac{n}{2} - 1$
$\begin{bmatrix} 4n-5 \\ 4n-5 \end{bmatrix}_n$ (resp. $\begin{bmatrix} 4n-4 \\ 4n-4 \end{bmatrix}_n$)	LL (resp. UR)	1
Total		$2n - 3$

□

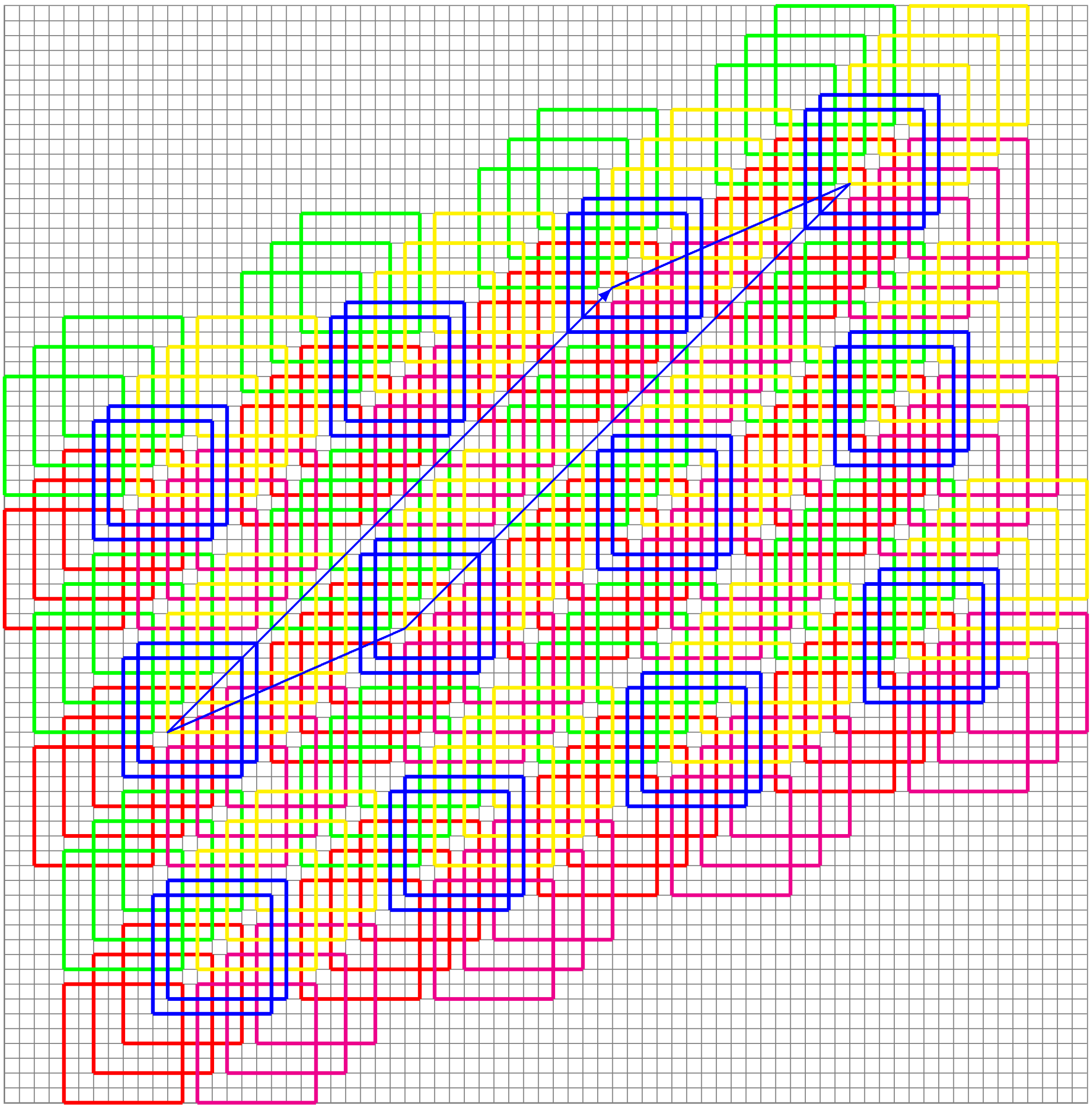


FIGURE 2.12. Maximal intersection number for a regular covering of width n even.

REMARK. If we replace in the generator set the squares:

$$\left\{\binom{4n-5}{4n-5}, \binom{4n-4}{4n-4}\right\}$$

by

$$\left\{\binom{4n-5}{4n-4}, \binom{4n-4}{4n-5}\right\}$$

we obtain a strong covering of squares of width n and intersection number $2n-3$. We observe that the squares in the covering intersecting $\begin{bmatrix} 4n-5 \\ 4n-4 \end{bmatrix}_n, \begin{bmatrix} 4n-4 \\ 4n-5 \end{bmatrix}_n$ are the same than squares intersecting $\begin{bmatrix} 4n-4 \\ 4n-4 \end{bmatrix}_n, \begin{bmatrix} 4n-5 \\ 4n-5 \end{bmatrix}_n$. Then, we can choose one of two pair of squares to use in every copy of parallelogram. Of this way we can have a non-periodic regular covering. And we see the number of feasible covering is not countable.

Theorem 2.2 *Let n be the maximum width of a square in a covering, the intersection number of the covering is lesser or equal than $2(n-1)$ if n is odd and $2(n-1)-1$ if n is even.*

The proof is straigthforward from the above results.

2.3.2 Minimal Conditions for a Covering.

We look for the minimal conditions to have a weak covering and a strong covering. We see that in the case of weak covering these conditions are not very restrictive. On the other hand, in the case of strong covering we find the minimal conditions for the regular case. We prove that the minimum intersection number is equal to 6 and, we obtain that the minimum size of squares is 5. For simplicity, non regular case has not been treated in this article, however we conjecture the minimum intersection number for this case is six as in the regular case.

Fact 2.4 *Given S and S' two squares with the same width and such that S does not touch S'. If $S \cap S' \neq \emptyset$ then $\mathrm{Int}(S) \cap \mathrm{Ver}(S')$ is a singleton.*

Proof. Without loss of generality, we consider $S = \begin{bmatrix} 0 \\ 0 \end{bmatrix}_n, S' = \begin{bmatrix} i \\ j \end{bmatrix}_n$ with $0 < i < n$, $-n < j < n$ and $j \neq 0$.

If $-n < j < 0$ the only vertex in $\mathrm{Int}(S)$ is $\binom{i}{j+n}$ and if $0 < j < n$ the only vertex in $\mathrm{Int}(S)$ is $\binom{i}{j}$. □

Observe that:

1. In Fact 2.4, if we do not have the "do not touch" condition then $|\mathrm{Int}(S) \cap \mathrm{Ver}(S')| \leq 1$ (see Figure 2.13a).
2. In Fact 2.4, if S and S' do not touch and do not have the same width then $|\mathrm{Int}(S) \cap \mathrm{Ver}(S')| \leq 2$ (see Figure 2.13b).

Theorem 2.3 *The squares in a regular weak covering have a width at least 3 and its intersection number is at least 2.*

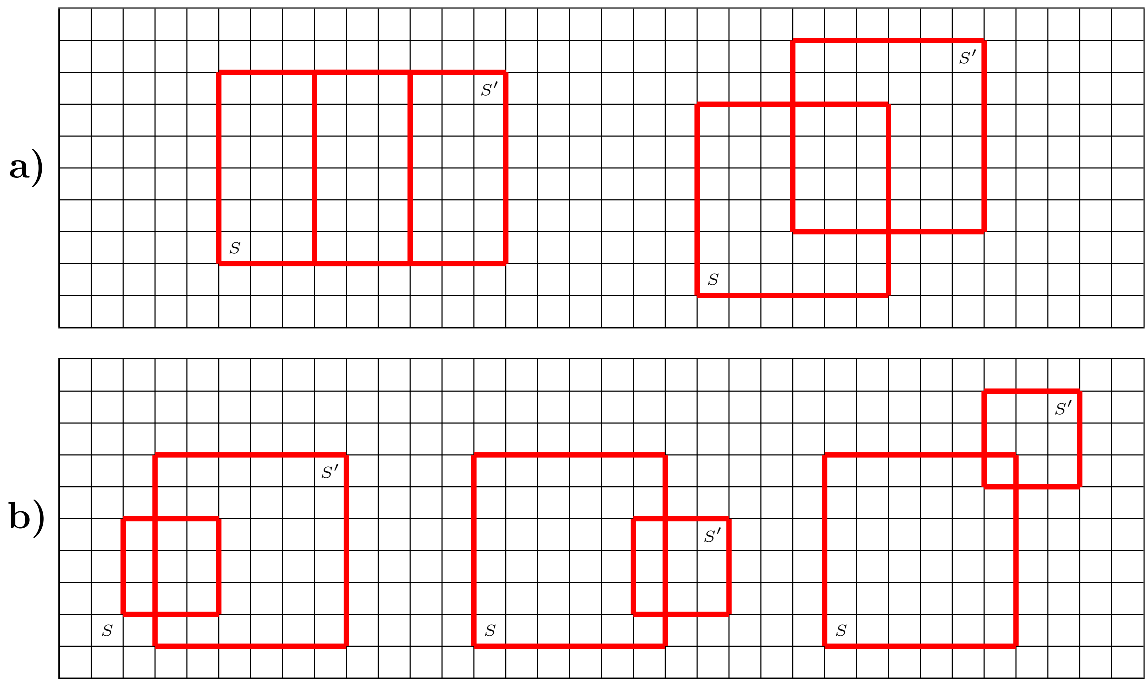


FIGURE 2.13. a) At left, $|\operatorname{Int}(S) \cap \operatorname{Ver}(S')| = 0$ and at right $|\operatorname{Int}(S) \cap \operatorname{Ver}(S')| = 1$. b) At left, $|\operatorname{Int}(S) \cap \operatorname{Ver}(S')| = 0$, at center $|\operatorname{Int}(S) \cap \operatorname{Ver}(S')| = 2$ and at right $|\operatorname{Int}(S) \cap \operatorname{Ver}(S')| = 1$.

PROOF. If the intersection number of the covering is one, the only possible configuration is two squares with a not empty intersection and that does not cover the plane. Then the intersection number of a weak covering has to be at least 2.

Assuming squares of the weak covering have width 2, all square S of the covering has only one interior point. Then, if there exists two squares S' and S'' of width 2 intersecting S, without touching it, by Fact 2.4 $\operatorname{Int}(S) \cap \operatorname{Ver}(S') = \operatorname{Int}(S) \cap \operatorname{Ver}(S'')$, i.e. S' touches S'', which is contradictory with the definition of weak covering.

Figure 2.14 shows a construction of a 2-weak covering with intersection number 2 and squares of width 3. We can see there is only a finite number of points that are not in the frontier or interior of a square in the covering. □

THEOREM 2.4 *The squares in a regular strong covering have a width at least* 5 *and its intersection number is at least* 6.

The proof of this Theorem is by contradiction, for every intersection number lesser than 6, we try to construct the covering and we see that is not possible.

We prove some previous results.

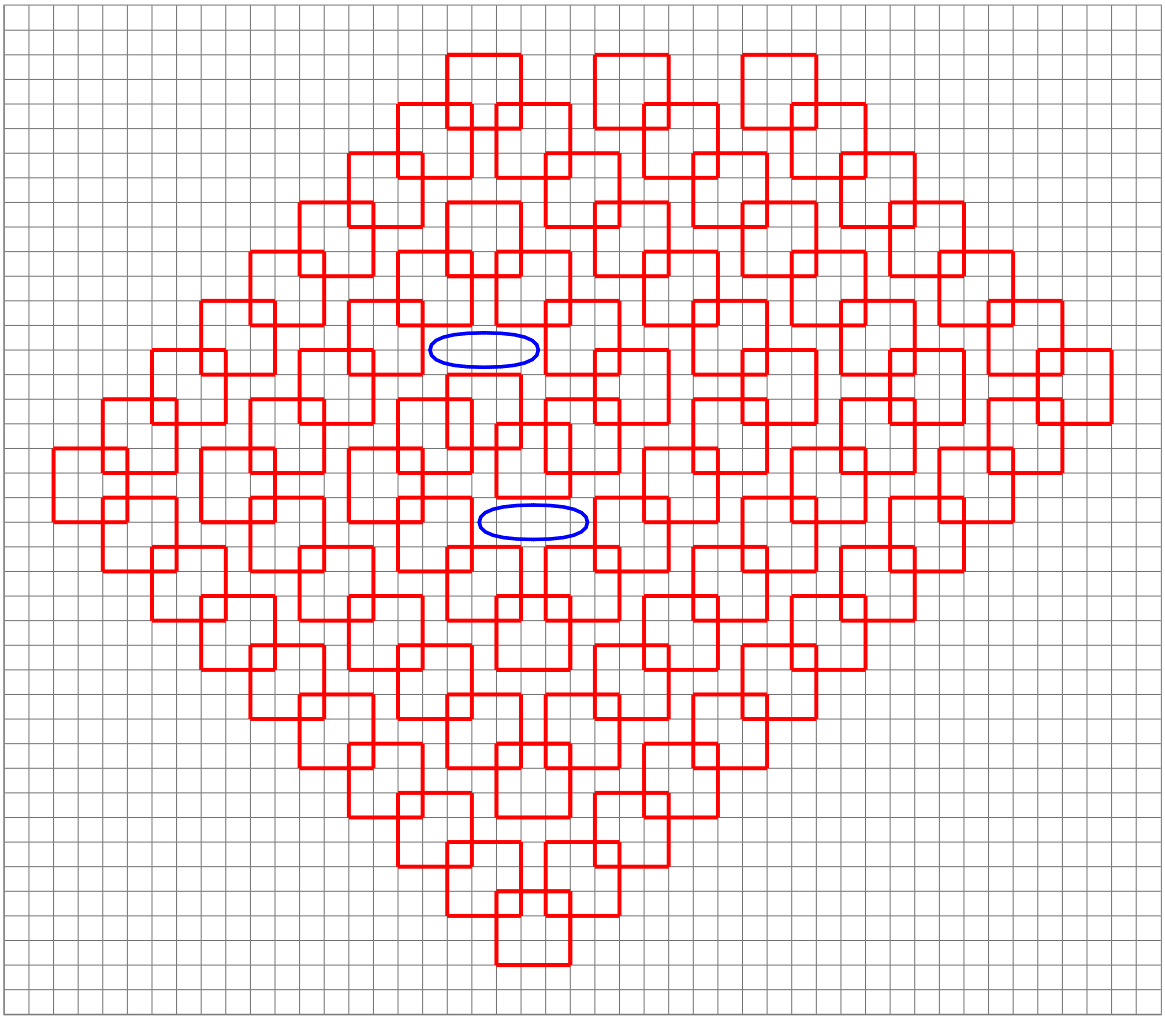


FIGURE 2.14. Minimal 2-weak covering.

Fact 2.5 *Let S' and S'' two squares covering a side of S in a regular strong covering. Then there exists $S''' \neq S$ in the covering such that $S''' \cap S' \neq \emptyset$ and $S''' \cap S'' \neq \emptyset$.*

Proof. We have that $\mathrm{Fr}_*(S') \cap \mathrm{Fr}_*(S'') = \left\{ \binom{i_1}{j_1}, \binom{i_2}{j_2} \right\}$. We can see that any square S_* covering one of these points is such that $S_* \cap S' \neq \emptyset$ and $S_* \cap S'' \neq \emptyset$. Since S' and S'' cover a side of S, S can cover only one of these points, for example $\binom{i_1}{j_1}$, then there necessarily exists a square S''' covering $\binom{i_2}{j_2}$, hence $S''' \cap S' \neq \emptyset$ and $S''' \cap S'' \neq \emptyset$. □

Lemma 2.2 *Let $P = \bigcup_{i=0}^{k} S_i$ where S_i are squares such that $S_1, \ldots, S_k$ cover S_0 in a regular strong covering. If D_j, $j = 1, \ldots, m$ are squares covering the external frontier of P and $D_j \cap S_0 = \emptyset$, $\forall j = 1, \ldots, m$, then $m \geq 8$.*

Proof. Since the squares D_j do not intersect S_0, they have to cover at least a distance $n + 2$ in the four sides of S_0. On the other hand, since the width of squares is n, this distance can be covered by a minimum of two different squares by side, then the minimum of squares covering this surface is 8, as shown in Figure 2.15. □

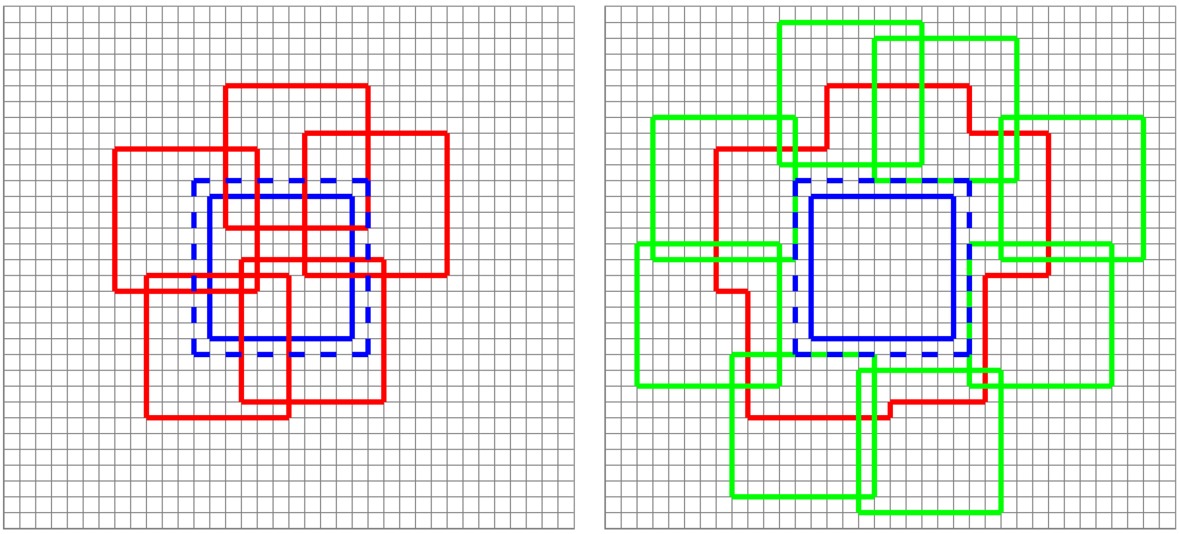


Figure 2.15. Minimum number of squares around S_0.

Lemma 2.3 is the crucial result that allows to find the minimal conditions to have a regular strong covering, the basic idea of the proof is to show that it is impossible have an intersection number lesser than six in a regular strong covering.

Lemma 2.3 *There does not exist a regular strong covering with intersection number $m \leq 5$.*

Proof.
$m \leq 3$. By Fact 2.4 every square in a strong covering has their vertices in the interior of distinct squares, so $m \geq 4$.

$m = 4$. We prove this result by contradiction. For a given square S_0 in a strong covering, let $S_1, \dots, S_4$ be the squares covering its frontier, we prove that one of the squares S_i intersects three others squares among the previous ones and it has two vertices uncovered. Hence, S_i has at least an intersection number five, which is a contradiction.

Without loss of generality, let $S_0 = \left[\begin{smallmatrix}0\\0\end{smallmatrix}\right]_n$ and $S_k = \left[\begin{smallmatrix}i_k\\j_k\end{smallmatrix}\right]_n$, $k = 1, 2, 3, 4$ such that:

- $-(n-1) < i_1 < 0, \quad -(n-1) < j_1 < 0$
- $-(n-1) < i_2 < 0, \quad 0 < j_2 < j_1 + n \quad \Longrightarrow S_1 \cap S_2 \neq \emptyset$
- $0 < i_3 < i_2 + n, \quad 0 < j_3 < n \quad \Longrightarrow S_2 \cap S_3 \neq \emptyset$
- $0 < i_4 < i_1 + n, \quad j_3 - n < j_4 < 0 \quad \Longrightarrow S_3 \cap S_4 \neq \emptyset \wedge S_1 \cap S_4 \neq \emptyset$

From these conditions, we obtain that each S_k, $k = 1, 2, 3, 4$ intersects three squares. Thus to obtain a cover with intersection number $m = 4$. We can add only one square intersecting each S_k. We prove that there exists S_k, $k = 1, 2, 3, 4$, such that S_k has two vertices not covered, then it is impossible have a strong covering with 4 intersections.

From necessary conditions, the vertices $\binom{i_1}{j_1}$ of S_1 and $\binom{i_2}{j_2+n}$ of S_2 are not covered. To cover the vertex $\binom{i_2}{j_2}$ of S_2 the only square which we can use is S_1, and in this case the vertex $\binom{i_1}{j_1+n}$ remains uncovered, and if we cover the vertex $\binom{i_1}{j_1+n}$, the vertex $\binom{i_2}{j_2}$ will be uncovered.

$m = 5$. For a given square $S_0 = \left[\begin{smallmatrix}0\\0\end{smallmatrix}\right]_n$ in a strong covering, let $S_1, \dots, S_5$ be the squares covering its frontiers. Since each square S_k covers a vertex of S_0, there exists a vertex of S_0 which is covered by two squares S_k. Without loss of generality, we consider two squares S_1 and S_2 covering the vertex $\binom{0}{0}$ and S_3, S_4 and S_5 covering the other vertices clockwise (as shown Figure 2.16).

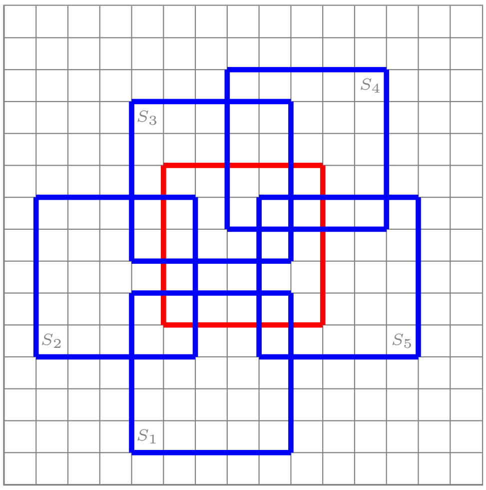


FIGURE 2.16. Covering of square S_0 by 5 squares.

Then, we obtain the conditions:

$$
\begin{array}{lll}
\bullet\ -(n-1) < i_1 < 0, & -(n-1) < j_1 < 0 & \\
\bullet\ -(n-1) < i_2 < 0, & -(n-1) < j_2 < 0 & \Rightarrow S_1 \cap S_2 \neq \emptyset \\
\bullet\ -(n-1) < i_3 < 0, & 0 < j_3 < j_* + n & \Rightarrow (S_1 \cup S_2) \cap S_3 \neq \emptyset \\
\bullet\ 0 < i_4 < i_2 + n, & 0 < j_4 < n & \Rightarrow S_3 \cap S_4 \neq \emptyset \\
\bullet\ 0 < i_5 < i_* + n, & j_3 - n < j_5 < 0 & \Rightarrow S_4 \cap S_5 \neq \emptyset \text{ and} \\
 & & \quad (S_1 \cup S_2) \cap S_5 \neq \emptyset
\end{array}
\tag{2.1}
$$

Where $j_* = \max\{j_1, j_2\}$ and $i_* = \max\{i_1, i_2\}$.

According to the above conditions (2.1) we have S_3, S_4 and S_5 are intersected by three squares. Then their coverings can have only two extra squares. Furthermore, S_1 and S_2 are intersected at least by two squares, and the union of both ones intersects other two squares (S_3 and S_5), then the covering of the union of S_1 and S_2 have at most four other squares. Hence, the covering of the union of all S_i has at most ten squares. Applying the Fact 2.5 to the intersections between S_3 and S_4, S_4 and S_5, S_1 or S_2 with S_3 and S_1 or S_2 with S_5, we reduce the number of squares in the covering of $\bigcup_{i=0}^{5} S_i$ to six, which is a contradiction by Lemma 2.2. Therefore, there does not exist a regular strong covering with intersection number five. $\square$

Now we give the proof of Theorem 2.4.

PROOF. We use the fact that there does not exist a regular strong covering with intersection number 2, 3, 4 or 5. To have a regular covering with intersection number six, by Proposition 2.1 we need a square of width at least five.

Now, we show a construction of a strong covering with intersection number 6 and squares of width $n \geq 5$. Let

$$R_{n,6} = \left[\left\{\binom{0}{0}\right\}; \binom{n-1}{1}, \binom{-2}{n-2}\right]_n$$

The projections of the square sides in the parallelogram are in this case:

$$\begin{array}{llll}
\binom{i}{0} = \binom{i-2}{n-2} & +0\binom{n-1}{1} - 1\binom{-2}{n-2} & & i = 1, \ldots, n-1 \\
\binom{n}{j} = \binom{-1}{j+n-3} & +1\binom{n-1}{1} - 1\binom{-2}{n-2} & & j = 0, 1 \\
\binom{n}{j} = \binom{1}{j-1} & +1\binom{n-1}{1} + 0\binom{-2}{n-2} & & j = 2, \ldots, n-1 \\
\binom{i}{n} = \binom{i-n+3}{1} & +1\binom{n-1}{1} + 1\binom{-2}{n-2} & & i = n-3, n-2, n-1 \\
\binom{i}{n} = \binom{i+2}{2} & +0\binom{n-1}{1} + 1\binom{-2}{n-2} & & i = 0, \ldots, n-4 \\
\binom{0}{j} = \binom{2}{j-n+2} & +0\binom{n-1}{1} + 1\binom{-2}{n-2} & & j = n-1, n \\
\binom{0}{j} = \binom{0}{j} & +0\binom{n-1}{1} + 0\binom{-2}{n-2} & & j = 0, \ldots, n-2
\end{array}$$

On account of the above conditions we observe that the projections of the horizontal sides of the square do not intersect between them, and the same property holds for the projections of the vertical sides.

Now, we prove that every point of the discrete plane belongs to the interior of a square of the covering, that is:

$$(\forall \tbinom{i}{j} \in \mathbb{Z}^2), (\exists l, k \in \mathbb{Z}) : \tbinom{i}{j} \in \text{Int} \begin{bmatrix} k(n-1)-2l \\ k+l(n-2) \end{bmatrix}_n$$

By periodicity this is equivalent to:

$$(\forall \tbinom{i'}{j'} \in P\left(\tbinom{x_1}{y_1}, \tbinom{x_2}{y_2}\right)), (\exists l, k \in \mathbb{Z}) : \tbinom{i'}{j'} \in \text{Int} \begin{bmatrix} k(n-1)-2l \\ k+l(n-2) \end{bmatrix}_n$$

- If $i' < 1$ then $\binom{i'}{j'} \in \text{Int} \begin{bmatrix} -(n-1) \\ -1 \end{bmatrix}_n$
- If $i' \geq 1$ then $\binom{i'}{j'} \in \text{Int} \begin{bmatrix} 0 \\ 0 \end{bmatrix}_n$

Finally, we study the intersection number of every square in the covering. It is enough to count the number of intersections of the square $\begin{bmatrix} 0 \\ 0 \end{bmatrix}_n$. We can observe that the only squares intersecting $\begin{bmatrix} 0 \\ 0 \end{bmatrix}_n$ are:

$$\left\{ \begin{bmatrix} n-1 \\ 1 \end{bmatrix}_n, \begin{bmatrix} -(n-1) \\ -1 \end{bmatrix}_n, \begin{bmatrix} -2 \\ n-2 \end{bmatrix}_n, \begin{bmatrix} 2 \\ -(n-2) \end{bmatrix}_n, \begin{bmatrix} n-3 \\ n-1 \end{bmatrix}_n, \begin{bmatrix} -(n-3) \\ -(n-1) \end{bmatrix}_n \right\}$$

□

This construction is not unique, it is not difficult to find out a lot of others regular strong coverings with intersection number 6.

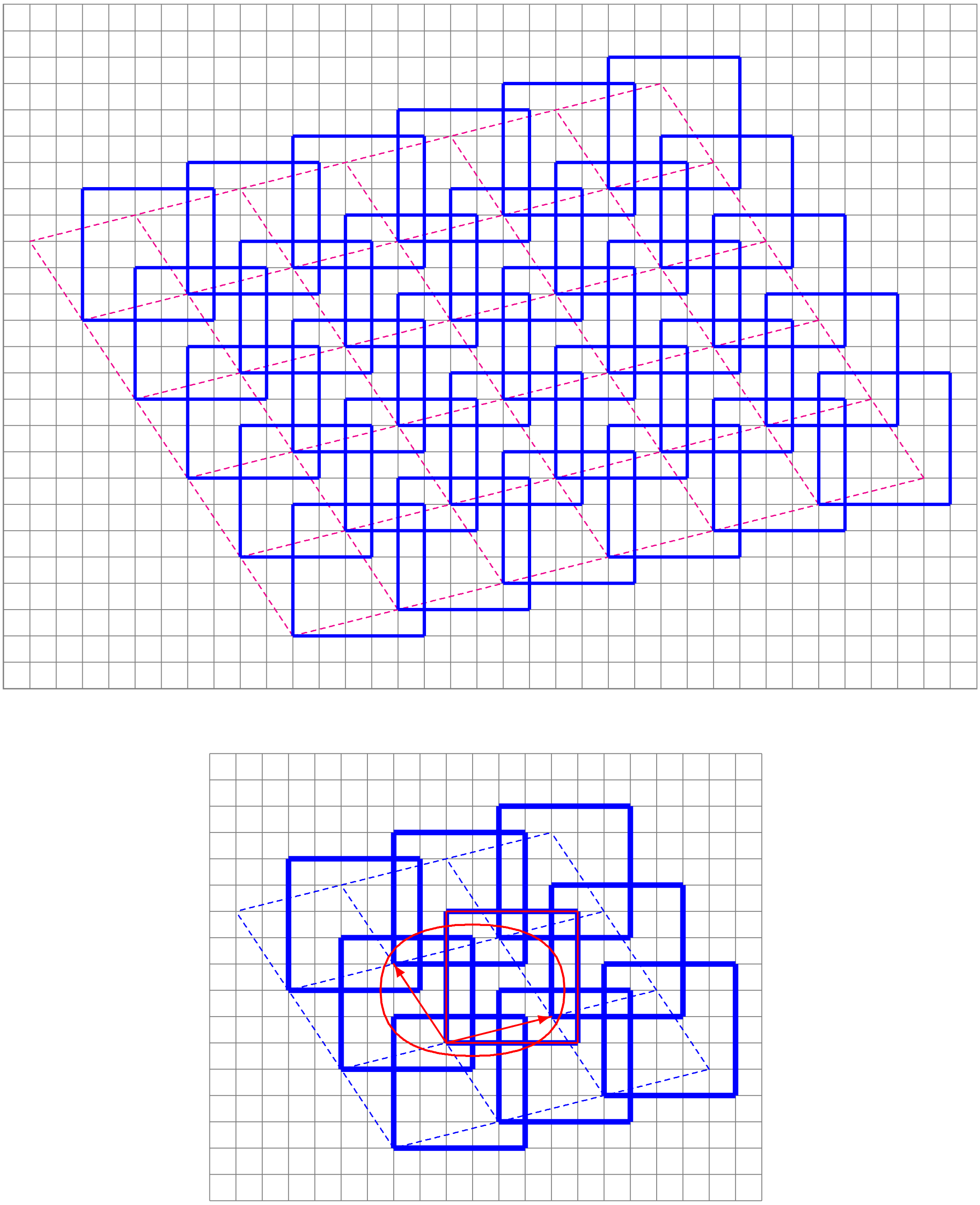


FIGURE 2.17. Periodic regular strong covering.

2.4 Other related problems

One question still unanswered is wether non-regular coverings have a behavior similar to regular coverings. For example if we study the minimal intersection number it is easy to see that for a weak covering we need an intersection number two in the regular case and non-regular. But for strong covering is an open question, we conjecture that minimal intersection number is six as in regular case.

Also we could study the coverings from the point of view of how much times is covered every point of the discrete plane and study the regularity of the covering from this point of view. This problem could be seen as a generalization of tiling problem because in tiling problem we have to covering each point by only one tile and in this problem we can have an arbitrary number of tiles covering every point.

CHAPTER 3

Boolean Networks with graph by layers

Boolean networks have applications in many areas including circuit theory, computer science [15, 35] and molecular biology [22, 23, 24]. These networks are defined by a set of states, a transition function and an update schedule. We are interested to study its limit behavior, i.e. its attractors. In biology attractors can represent a memory trace, a pattern of motor nerve activity, a state of an immune network or a cell type. For example, in the modeling of gene regulatory networks, the attractors are associated to distinct cell states defined by patterns of gene activity. In particular, the fixed points are often associated with phenomena such as cell proliferation and apoptosis [21]. Consequently, the knowledge of the number of attractors is essential to understand the function of the studied system.

The transition function of the network defines a directed graph, which we call the graph associated to the network. Some properties of this graph can help us to know some features about the attractors of the network [10, 11, 18, 34], for example, the existence of dynamical cycles and the length of them.

In this chapter, we study the particular case of a network where the associated graph does not have circuits of length $k \geq 2$, we call this kind of graphs a *graph by layers*. In these Boolean networks every strongly connected component in the associated graph is a singleton, this quality allows found some characteristics on the attractors of this network. In fact, we obtain some results about the length of the attractors of the

[2]work published in: Goles E., Salinas L., "Comparison between parallel and serial dynamics of Boolean Networks", Theoretical Computer Science, Volume 396, Number 1–3, 10 May 2008.

Boolean networks and the length of the attractor basins.

3.1 Notation

A Boolean network $N = (F, s)$ is defined by:

1) A finite set of *variable states* $\{x_1, \ldots, x_n\}$, where $x_i \in \{0, 1\}$,
2) A *global activation function* $F : \{0, 1\}^n \to \{0, 1\}^n$, where:

$$F(x) = (f_1(x), \ldots, f_n(x)) \text{ and } x = (x_1, \ldots, x_n),\ x_i \in \{0, 1\}$$

3) An *update schedule* defined by an update function that we denote $s : \{1, \ldots, n\} \to \{1, \ldots, n\}$.

The iteration of the Boolean network with an update function s is:

$$x_i^{r+1} = f_i(x_1^{l_1}, \ldots, x_n^{l_n}), \tag{3.1}$$

where $l_j = r$ if $s(i) \le s(j)$ and $l_j = r + 1$ if $s(i) > s(j)$.

This is equivalent to apply a function $F^s : \{0, 1\}^n \to \{0, 1\}^n$ in a parallel way, with $F^s(x) = (f_1^s(x), \ldots, f_n^s(x))$ defined by:

$$f_i^s(x) = f_i(g_{i,1}^s(x), \ldots, g_{i,n}^s(x)),$$

where the function $g_{i,j}^s$ is defined by $g_{i,j}^s(x) = x_j$ if $s(i) \le s(j)$ and $g_{i,j}^s(x) = f_j^s(x)$ if $s(i) > s(j)$. Thus, the function F^s corresponds to the dynamical behavior of the network $N = (F, s)$.

Since $\{0, 1\}^n$ is a finite set we have two limit behaviors for the iteration of a network:

- *Fixed Point.* We define a fixed point as $x \in \{0, 1\}^n$ such that $F^s(x) = x$.
- *Cycle.* We define a cycle of length p as the sequence $[x^0, \ldots, x^{p-1}, x^0]$ such that $x^j \in \{0, 1\}^n, p > 1$, x^j are pairwise distinct and $F^s(x^j) = x^{j+1}$, for all $j = 0, \ldots, p - 2$ and $F^s(x^{p-1}) = x^0$.

Fixed points and cycles are called *attractors* of the network.

The *graph associated* to $N = (F, s)$ is the directed digraph $G^F = (V, A)$, where:

G_s^F :

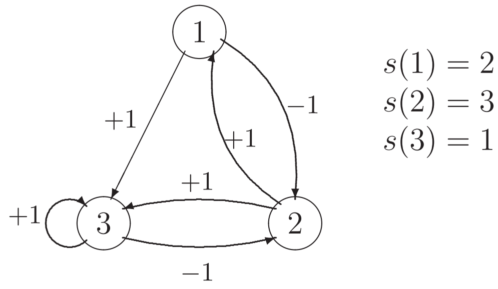


FIGURE 3.1. Example of signed graph

- $V = \{1 \dots, n\}$
- $(i, j) \in A$ if and only if f_j depends on x_i, i.e., if there exists $x \in \{0, 1\}^n$ such that

$$f_j(x_1, \dots, x_{i-1}, 0, x_{i+1}, \dots, x_n) \neq f_j(x_1, \dots, x_{i-1}, 1, x_{i+1}, \dots, x_n).$$

The node set of G^F is referred to as $V(G^F)$, its arc set as $A(G^F)$.

A *circuit* of G^F is a sequence of distinct nodes (except eventually the extreme ones) $i_1, i_2, \dots, i_k, i_1$ of V where $(i_l, i_{l+1}) \in A$ for $l = 1, \dots, k-1$ and $(i_k, i_1) \in A$. k is the length of the circuit. A *loop* is a circuit of length one.

We define the *signed graph associated* to a Boolean network $N = (F, s)$ as: $G_s^F = (G^F, \text{sign}_s)$, where every arc has associated a sign given for the function $\text{sign}_s : A(G^F) \to \{-1, +1\}$ in the digraph and defined by:

$$\text{sign}_s(i, j) = \begin{cases} +1 & \text{if } s(i) \geq s(j) \\ -1 & \text{if } s(i) < s(j) \end{cases}$$

We define the followings elemental sequential schedules which are elemental permutations very useful in the sequel.

$$\pi_{i,j}(k) = \begin{cases} j & \text{if } k = i \\ i & \text{if } k = j \\ k & \text{otherwise.} \end{cases}$$

Also we denote by π_0 the schedule function such as: $\pi_0(i) = i$ and the parallel schedule $s_p(i) = 1$

We denote $I(j) = \{i \in \{1, \dots, n\} / (i, j) \in A\}$. Thus, we can say $f_j(x) = f_j(x_i : i \in I(j))$.

A function $f : \{0,1\}^n \to \{0,1\}$ is monotonic on input i if for every $x \in \{0,1\}^n$

$$f(x_1, \ldots, x_{i-1}, 0, x_{i+1}, \ldots, x_n) \leq f(x_1, \ldots, x_{i-1}, 1, x_{i+1}, \ldots, x_n).$$

A loop in i is monotonic if f_i is monotonic on input i.

A *graph by layers* is a digraph where there is not circuits of length $k \geq 2$. i.e. the only circuits are the loops. As seen in Figure 3.2, in this kind of graph we can define different layers of vertices.

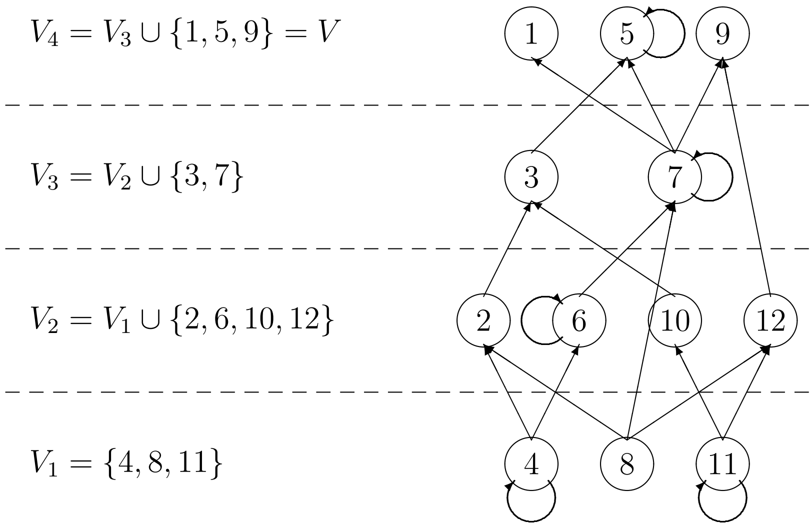


FIGURE 3.2. Example of a graph by layers.

3.2 Attractors in Boolean Networks with graph by layers

In this section we show some results about the length of the attractors in a Boolean Networks with a graph by layers, we observe that this characteristic in the Boolean Network allows to found of a simple way the attractors of networks, and bound its length.

PROPOSITION 3.1 *Let $N = (F, s)$ be a Boolean network such that there are no circuits of length $k \geq 2$ in its associated graph. Then if N has any cycles, these cycles have a length 2^p, $p \in \mathbb{N}$ for any s schedule function. Moreover, in the absence of non-monotonic loop the only attractors are fixed points.*

PROOF. As shown in Figure 3.2, we can define a sequence of set of nodes $\{V_i\}_{i=1}^{M}$ such that:

- $i \in V_1 \iff I(i) \subseteq \{i\}$.
- $i \in V_r \iff I(i) \subseteq \{i\} \cup V_{r-1}$.
- $V_M = V$

Let $N_A = (F^A, s)$ be, a Boolean network such as the $F^A : \{0,1\}^n \to \{0,1\}^n$:

$$f_i^A(x) = \begin{cases} f_i(x) & \text{if } i \in A \\ 0 & \text{otherwise} \end{cases}$$

where $A \subseteq V$

Then, it is easy to see that:

- $N_{V_M} \equiv N$
- $\forall x \in \{0,1\}^n$ and $\forall i \in V_r$, $f_i(x) = f_i^{V_r}(x)$

Hence, given $[x^0, \ldots, x^{p-1}, x^0]$, a cycle for the boolean network $N = (F, s)$ then $[x^{r,0}, \ldots, x^{r,m(r)-1}, x^{r,0}]$ is a cycle for $N_{V_r} = (F^{V_r}, s)$, where:

$$x_i^{r,l} = \begin{cases} x_i^l & \text{if } i \in V_r \\ 0 & \text{otherwise} \end{cases}$$

and,

$$m(r) = \min\left\{m \in \{0, \ldots, p-1\} / \forall i \in V_r, x_i^{r,m} = x_i^{r,0}\right\}$$

And then, we have:

- if $r < r'$ then for all $i \in V_r$ and $l < m(r)$, $x_i^{r,l} = x_i^{r',l}$.
- $m(r+1)$ is a multiple of $m(r)$. Indeed, if there exist k, d such that $m(r+1) = km(r) + d$, where $0 < d < m(r)$, then:
  $$d = \min\left\{m \in \{0, \ldots, p-1\} / \forall i \in V_r, x_i^{r,m} = x_i^{r,0}\right\}$$
  which contradicts the definition of $m(r)$.

We say the cycle $[x^{r,0}, \ldots, x^{r,m(r)-1}, x^{r,0}]$ is a restriction of the cycle $[x^0, \ldots, x^{p-1}, x^0]$ to the set of nodes V_r.

Now, we will use induction on r to prove that $m(r)$ is a power of two for all $r = 1, \ldots, M$, and then l is a power of two, and in the absence of non-monotonic loops, $l = 1$.

BASE $r = 1$. By definition of V_1 for all $i \in V_1$, we have three possibilities:

1. $f_i^1(x_i) = c_i$ then for all $q = 0, \ldots, l-1$, $x_i^q = c_i$ and $x_i^{1,l} = c_i$,
2. $f_i^1(x_i) = x_i$ then for all $q = 0, \ldots, l-1$, $x_i^q = x_i^1$ and $x_i^{1,l} = x_i^0$,
3. $f_i^1(x_i) = \neg x_i$ then for all $q = 0, \ldots, l-1$, $x_i^q = \neg x_i^{q+1}$, and hence $x_i^{1,0} = x_i^1$ and $x_i^{1,1} = \neg x_i^1$.

Thus in monotonic case $m(1) = 1$ and if there exist a non-monotonic loop, we have a function in the third class and $m(1) = 2 = 2^1$.

HYPOTHESIS OF INDUCTION. For all $k \leq r$, $m(k)$ is a power of 2 and in the absence of non-monotonic loops $m(k) = 1$.

CASE $r+1$. Since the cycle $[x^0, \ldots, x^{p-1}, x^0]$ restricted to V_r has length $m(r)$, for every $i \in V_{r+1} \setminus V_r$, the cycle $[x^0, \ldots, x^{p-1}, x^0]$ restricted to $\{i\} \cup V_r$ has length at most $2m(r)$ and this length has to be a multiple of $m(r)$, then this length is either $m(i,r) = m(r)$ or $m(i,r) = 2m(r)$. Now, $m(r+1)$ is the minimum common multiple of $m(i,r), i \in V_{r+1} \setminus V_r$ then either $m(r+1) = m(r)$ or $m(r+1) = 2m(r)$.

In the case of non-monotonic loops, by hypothesis of induction $m(r)$ is a power of two, then $m(r+1)$ is a power of two.

On the other hand, in the absence of non-monotonic loops $m(r) = 1$. Let $x^* = x^{r,0}$. Now we have only two possibilities $m(r+1) = 1$ or $m(r+1) = 2$. If $m(r+1) = 2$ then there exists $i \in V_{r+1} \setminus V_r$ such that:

$$f_i(x_1^*, \ldots, x_{i-1}^*, 0, x_{i+1}^*, \ldots, x_n^*) = 1 \text{ and } f_i(x_1^*, \ldots, x_{i-1}^*, 1, x_{i+1}^*, \ldots, x_n^*) = 0$$

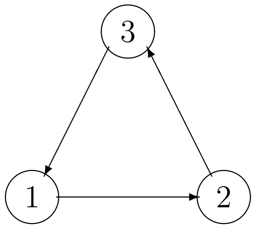
which is a contradiction with the monotonicity of the loops, then $m(r+1) = 1$. □

At this point it is worth remarking that not all Boolean networks have cycles of length a power of 2. Indeed, in Figure 3.3 we can see an example of a Boolean network having a cycle of length 3.

Now we are interested in the comparison between the dynamics of a boolean network with different update schedule, this topics is treated in more depth in Chapter 4, but now, it is given a first approach studying the particular case of Boolean Networks with graph by layers.

The next Proposition was proved by Tchuente [34] and it is a corollary of a theorem that we prove in this thesis, this result will be showed after.

PROPOSITION 3.2 *Let N be a Boolean network such that for all $i = 1, \ldots, n$, $I(i) \subseteq \{i, \ldots, n\}$ then sequential and parallel dynamics are identical.*



$F : \{0,1\}^3 \to \{0,1\}^3$
$f_1(x_1, x_2, x_3) = x_3$
$f_2(x_1, x_2, x_3) = x_1$
$f_3(x_1, x_2, x_3) = x_2$

Fixed Points: $(0,0,0), (1,1,1)$
Cycles: $[(1,0,0),(0,1,0),(0,0,1),(1,0,0)]$
$[(1,1,0),(0,1,1),(1,0,1),(1,1,0)]$

FIGURE 3.3. Network with an attractor of length 3.

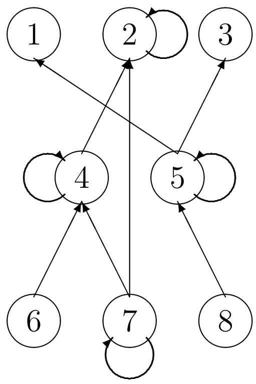


FIGURE 3.4. Graph of a network such that $I(i) \subseteq \{i, i+1, \ldots, n\}$.

Now, we are interested in the converse of this Proposition. The graphs of these networks do not have circuits of length $k \geq 2$, the only circuits possible are the loops, i.e., they are a particular case of graphs by layers. An example of graph of these networks is depicted in Figure 3.4.

Notice that in the next proposition, we consider networks where the associated graph does not have loops, then these networks satisfy the hypothesis of Proposition 3.1 without non-monotonic loops, and then all their attractors are fixed points.

THEOREM 3.1 *Let $F : \{0,1\}^n \to \{0,1\}^n$ be a Boolean transition function such that its associated graph does not have any loop. If the dynamics of $N_P = (F, s_p)$ and $N_S = (F, \pi_0)$ are identical then, for all $i = 1, \ldots, n$, $I(i) \subseteq \{i+1, \ldots, n\}$.*

PROOF. By contradiction, let us suppose that there exists i such that f_i depends on the value x_j where $j < i$. Let

$$j_* = \min\{j \in \{1, \dots, n\} / \exists i > j, f_i \text{ depends on } x_j\}, \text{ and} \tag{3.2}$$
$$i_* = \min\{i \in \{j_* + 1, \dots, n\} / f_i \text{ depends on } x_{j_*}\} \tag{3.3}$$

Since f_{i_*} depends on x_{j_*} then there exists $x' = (x'_1, \dots, x'_{j_*-1}, 0, x'_{j_*+1}, \dots, x'_n)$ and $x'' = (x'_1, \dots, x'_{j_*-1}, 1, x'_{j_*+1}, \dots, x'_n)$ such that, $f_{i_*}(x') \neq f_{i_*}(x'')$. Next, we apply the function F^{s_p} (defined in (3.1)) to x', that is equivalent to use a sequential update schedule.

$$f^{s_p}_{i_*}(x') = f_{i_*}(f^{s_p}_1(x'), \dots, f^{s_p}_{i_*-1}(x'), x'_i, \dots, x'_n)$$

But, f_{i_*} depends on states of variables whose indices are greater or equal than j_*, and then:

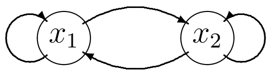
$$f^{s_p}_{i_*}(x') = f_{i_*}(f^{s_p}_{j_*}(x'), \dots, f^{s_p}_{i_*-1}(x'), x'_i, \dots, x'_n) \tag{3.4}$$

Thanks to (3.3), for $j_* \leq k < i_*$, f_k does not depend on x_{j_*}, thus $f^{s_p}_k$ does not depend on x_{j_*}, either. And then (3.4) becomes,

$$f^{s_p}_{i_*}(x') = f_{i_*}(f^{s_p}_{j_*}(x''), \dots, f^{s_p}_{i_*-1}(x''), x'_i, \dots, x'_n)$$
$$f^{s_p}_{i_*}(x') = f^{s_p}_{i_*}(x'')$$

Therefore, there exist vectors $x' \neq x''$ such that the values on the input i_* after a parallel update are different ($f_{i_*}(x') \neq f_{i_*}(x'')$), and equal after a sequential update ($f^{s_p}_{i_*}(x') = f^{s_p}_{i_*}(x'')$), which is a contradiction. □

Last theorem does not hold for networks with loops as in Figure 3.5. In fact we see the associated graph is not by layers and one of the attractors is a cycle, which it is not possible for networks that satisfy the hypothesis of Theorem 3.1.



$F : \{0,1\}^2 \to \{0,1\}^2$
$f_1(x) = x_1 \vee x_2$
$f_2(x) = x_1 \wedge \bar{x}_2$

x_1	x_2	s_p		π_0	
0	0	0	0	0	0
0	1	1	0	1	0
1	0	1	1	1	1
1	1	1	0	1	0

ATTRACTORS: *Fixed point:* $(0,0)$ *Cycle:* $[(1,0),(1,1),(1,0)]$

FIGURE 3.5. Example of a Network with the same sequential and parallel update where $I(i) \nsubseteq \{i+1,\ldots,n\}$.

CHAPTER 4

Robustness of a Boolean Network

A dynamical property of a Boolean network is said to be robust if it is not affected by small changes in the network. There are different kinds of perturbations in a Boolean network: perturbations of the states of the nodes in a given global state of the network, of the local activation functions, or of the type of update schedule. The last two ones correspond to changes in the definition of the network and therefore they can yield variations on the set of attractors.

In the modeling of genetic regulatory networks, the attractors are usually identified with distinct types of cells defined by patterns of gene activity. In particular, the fixed points are often associated with phenomena such as cell proliferation and apoptosis [21] and the dynamical cycles with cellular cycle, division, etc.

On the other hand, there does not exist enough evidence about the activation schedule of genes in a regulatory network. Thus, an important aspect in the modeling of the genetic regulatory networks by Boolean networks is the study of robustness of the set of attractors with regard to the kind of update schedule used.

The robustness of Boolean networks has been widely studied, mainly from a statistical point of view, in random Boolean networks. However, there exist only a few analytical studies. Aldana et al. [6] show that random Boolean networks with scale-free architecture, where a small set of nodes are highly connected and the rest poorly connected, are robust. Schmulevich et al. [32] study the robustness of random Boolean networks whose local functions belong to certain Post classes.

The effect of function perturbation has been studied by Gerhernson et al. [16], but without emphasis on the attractors. Xiao and Dougherty [37] study the impact of function perturbations on attractors in homogenous synchronous Boolean networks. Regarding to perturbations of the update schedule, Chaves et al. [14] study the effect of different asynchronous updates of the nodes on the dynamics of Boolean networks for the Drosophila Melanogaster segment polarity genes. Willadsen and Wiles [36] propose a method for quantifying robustness and dynamics in terms of state-space structures, for Boolean models of known genetic regulatory systems.

Some analytical works about this kind of perturbations have been made in a particular class of discrete dynamical system where the connection digraph is symmetric or equivalently an undirected graph. For this class of networks the team of Morveit and Reidys [28] studied the set of update schedules preserving the whole dynamical behavior of the network and the set of attractors in a certain class of Cellular Automata (Hansson et al. [19]).

We define the graph with signs associated to a Boolean network $N = (F, s)$ as: $G^F_s = (G^F, \text{sign}_s)$, where every arc has associated a sign given for the function $\text{sign}_s : A(G^F) \to \{-1, +1\}$ defined as:

$$\text{sign}_s(i,j) = \begin{cases} +1 & \text{if } s(i) \geq s(j) \\ -1 & \text{if } s(i) < s(j) \end{cases}$$

See example of graph with signs in Figure 4.1.

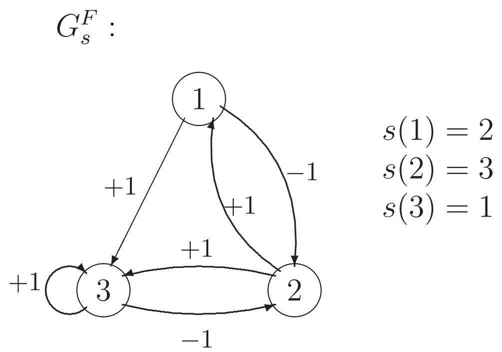


FIGURE 4.1. Example of graph with signs.

We define the following elemental sequential schedules which are elemental permutations very useful in the sequel.

$$\pi_{i,j}(k) = \begin{cases} j & \text{if } k = i \\ i & \text{if } k = j \\ k & \text{otherwise.} \end{cases}$$

Also we denote by π_0 the schedule function such as: $\pi_0(i) = i$. Observe that $\forall i,\ \pi_{i,i} = \pi_0$.

We denote $I(j) = \{i \in \{1,\ldots,n\}/(i,j) \in A\}$. Thus, we can say $f_j(x) = f_j(x_i : i \in I(j))$.

4.1 Equivalent update schedules

THEOREM 4.1 *Let $N_1 = (F, s_1)$ and $N_2 = (F, s_2)$ be two Boolean networks which are different only in the update schedule. If $G^F_{s_1} = G^F_{s_2}$, then both dynamical behaviors are identical.*

PROOF. Without loss of generality, we suppose s_1 is such that, for all $i \in \{1,\ldots,n\}$, $s_1(i+1) \geq s_1(i)$ and $s_1(1) = 1$. Now, we prove by induction that $\forall j = 1,\ldots,n$, $f^{s_1}_j(x) = f^{s_2}_j(x)$.

BASE. After the assumptions, if f_1 depends on x_i, then $s_1(i) \geq s_1(1)$, and by the condition $G^F_{s_1} = G^F_{s_2}$, $s_2(i) \geq s_2(1)$. Thus:

$$f^{s_1}_1(x) = f_1(g^{s_1}_{1,j}(x) :\ j\ \in I(1)) = f_1(x_j :\ j \in I(1)) = f_1(g^{s_2}_{1,j}(x) :\ j\ \in I(1)) = f^{s_2}_1(x).$$

HYPOTHESIS OF INDUCTION. For all $j \leq k$

$$f^{s_1}_j(x) = f^{s_2}_j(x).$$

CASE $k+1$. By definition of $f^{s_1}_{k+1}$

$$f^{s_1}_{k+1}(x) = f_{k+1}(g^{s_1}_{k+1,j}(x) :\ j \in I(k+1)).$$

On the other hand, since $G^F_{s_1} = G^F_{s_2}$,

$$\forall j \in I(k+1) :\ s_1(j) \geq s_1(k+1) \Longleftrightarrow s_2(j) \geq s_2(k+1).$$

Thus, $\forall j \in I(k+1)$ such that $\text{sign}_{s_1}(j,k+1) = \text{sign}_{s_2}(j,k+1) = 1$:

$$g^{s_1}_{k+1,j}(x) = x_j = g^{s_2}_{k+1,j}(x).$$

And $\forall j \in I(k+1)$ such that $\text{sign}_{s_1}(j,k+1) = \text{sign}_{s_2}(j,k+1) = -1$:

$$g^{s_1}_{k+1,j}(x) = f^{s_1}_j(x) \ \text{ and } \ g^{s_2}_{k+1,j}(x) = f^{s_2}_j(x).$$

Because of s_1, $\forall j \in I(k+1)$, $\text{sign}_{s_1}(j,k+1) = -1$ if and only if $j < k+1$. Hence, according to hypothesis of induction: $f_j^{s_1}(x) = f_j^{s_1}(x)$ for all $j \in I(k+1)$ such that $\text{sign}_{s_1}(j,k+1) = -1$.

Therefore, for all $j \in I(k+1)$, $g_{k+1,j}^{s_1}(x) = g_{k+1,j}^{s_2}(x)$, and thus, $f_{k+1}^{s_1}(x) = f_{k+1}^{s_2}(x)$. □

As a corollary of this theorem is this result proved by Tchuente in [34]:

THEOREM 4.2 *Let N be a Boolean network such that $\forall i = 1,\ldots,n$, $\forall j \in I(i)$, $s(i) \leq s(j)$. Then the dynamics of N with the update schedule s and with the parallel update schedule are identical.*

PROOF. It is easy to see that a parallel update is equivalent to have a schedule function $s_p : V \to \{1,\ldots,n\}$ such that $s_p(i) = 1$, $\forall i = 1,\ldots,n$, and in this case $\text{sign}_{s_p}(i,j) = +1$, $\forall (i,j) \in A$ and if for all $i = 1,\ldots,n$, $s(i) \leq s(j)$, $\forall j \in I(i)$, $\text{sign}_s(i,j) = +1$, $\forall (i,j) \in A$, then $G_{s_p}^F = G_s^F$. □

For a given global activation function F, we would like to classify the schedules that yield the same dynamical behavior. If we consider the relation between updates schedules s_1 and s_2 defined by having $G_{s_1}^F = G_{s_2}^F$, Theorem 4.1 shows that is yields a partition which is *finer* than the partition of identical dynamical behavior.

In fact, the partition is strictly finer, since the converse of Theorem 4.1 is not true. Figure 4.2 shows two different graphs with signs, without loops and strongly connected, associated to Boolean networks $N_1 = (F,\pi_0)$ and $N_2 = (F,\pi_{2,3})$ respectively, where $f_1(x) = x_2 \vee x_4$, $f_2(x) = x_4$, $f_3(x) = x_1 \vee x_2$ and $f_4(x) = x_3$. Both Boolean networks have the same dynamical behavior, shown in Figure 4.3. However, in the following

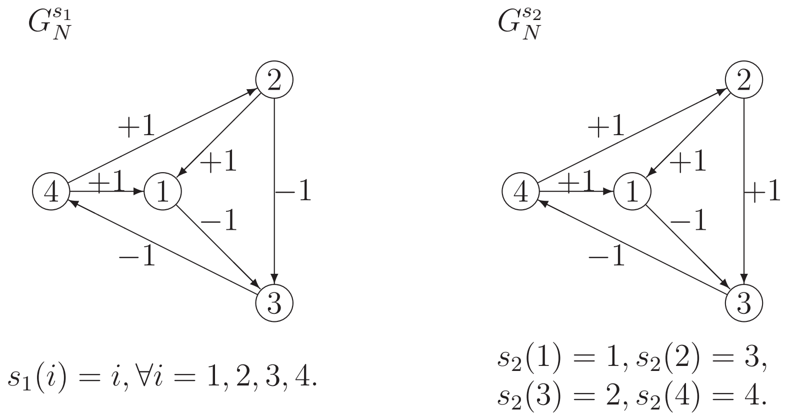


FIGURE 4.2. Boolean networks with two non-equivalent schedules that have the same dynamical behavior.

Proposition we show that, when two update schedules are dynamically equivalent but

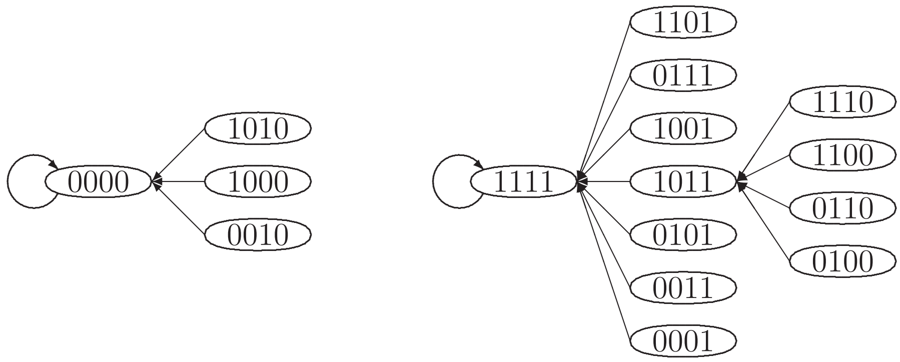


FIGURE 4.3. Dynamical behavior of N_1 and N_2.

with different graphs with signs, then a minimal perturbation of the activation function can be found which preserves the graphs with signs, while causing a different dynamical behavior.

PROPOSITION 4.1 *Let $N_1 = (F, s_1)$ and $N_2 = (F, s_2)$ be two Boolean networks such that $G^F_{s_1} \neq G^F_{s_2}$ and their dynamical behavior are identical. Then, there exists $\tilde{F}$, different from F in at most two local activation functions, such that $G^{\tilde{F}} = G^F$ and the dynamical behavior of $\tilde{N}_1 = (\tilde{F}, s_1)$ and $\tilde{N}_2 = (\tilde{F}, s_2)$ are different.*

PROOF. Without loss of generality, we suppose s_1 is such that, for all $i \in \{1, \ldots, n\}$, $s_1(i+1) \geq s_1(i)$ and $s_1(1) = 1$. Let be:

$$i_* = \min \left\{ i \in \{1, \ldots, n\} : \exists j \in I(i), \operatorname{sign}_{s_1}(j,i) \neq \operatorname{sign}_{s_2}(j,i) \right\},$$

which is well-defined, because by hypothesis $G^F_{s_1} \neq G^F_{s_2}$. Let us suppose that there exists $j_* \in I(i_*)$ and $x^* \in \{0,1\}^n$ such that $\operatorname{sign}_{s_1}(j_*, i_*) \neq \operatorname{sign}_{s_2}(j_*, i_*)$ and $f^{s_1}_{j_*}(x^*) \neq x^*_{j_*}$. Then, we define the function $\tilde{F}$ as:

$$\tilde{f}_i(x) = f_i(x) \qquad \forall i \neq i_*$$

$$\tilde{f}_{i_*}(x) = \begin{cases} f_{i_*}(y^1) & \text{if } x = y^1 \\ \neg f_{i_*}(y^2) & \text{if } x = y^2 \\ f_{i_*}(x) & \text{otherwise.} \end{cases}$$

where $y^1, y^2 \in \{0,1\}^n$ are such that $f^{s_1}_{i_*}(x^*) = f_{i_*}(y^1)$ and $f^{s_2}_{i_*}(x^*) = f_{i_*}(y^2)$.

Observe that $f^{s_1}_{j_*}(x^*) \neq x^*_{j_*}$ implies $y^1 \neq y^2$, and hence $\tilde{f}_{i_*}$ is well defined.

Thus, $\tilde{F}_{i_*}^{s_1}(x^*) = \tilde{f}_{i_*}^{s_1}(x^*) = f_{i_*}(y^1)$ and $\tilde{F}_{i_*}^{s_2}(x^*) = \tilde{f}_{i_*}^{s_2}(x^*) = f_{i_*}(y^2)$. Since by hypothesis $f_{i_*}(y^1) = f_{i_*}(y^2)$, $\tilde{F}_{i_*}^{s_1}(x^*) \neq \tilde{F}_{i_*}^{s_2}(x^*)$.

On the other hand, $\forall j \in I(i^*)$, $\exists x = (x_1, \ldots, x_j, \ldots, x_n) \neq y^2$ and $x' = (x_1, \ldots, \neg x_j, \ldots, x_n) \neq y^2$ such that $f_{i^*}(x) \neq f_{i^*}(x')$.

Hence, $\tilde{f}_{i^*}(x) \neq \tilde{f}_{i^*}(x')$ and therefore, $G^F = G^{\tilde{F}}$.

If $\forall x \in \{0,1\}^n$, $\forall j \in I(i_*)$ such that $\text{sign}_{s_1}(j, i_*) \neq \text{sign}_{s_2}(j, i_*)$, $f_j^{s_1}(x) = x_j$, then we can define $\hat{f}_{j_*} = \neg f_{j_*}$ and $\hat{f}_i = f_i$, $\forall i \neq j^*$, where $j_* \in I(i_*)$ and $\text{sign}_{s_1}(j_*, i_*) \neq \text{sign}_{s_2}(j_*, i_*)$. Since

$$f_{j_*}(x_1, \ldots, x_{k-1}, 0, x_{k+1}, \ldots, x_n) \neq f_{j_*}(x_1, \ldots, x_{k-1}, 1, x_{k+1}, \ldots, x_n)$$

if and only if

$$\hat{f}_{j_*}(x_1, \ldots, x_{k-1}, 0, x_{k+1}, \ldots, x_n) \neq \hat{f}_{j_*}(x_1, \ldots, x_{j-1}, 1, x_{j+1}, \ldots, x_n),$$

hence $G^{\hat{F}} = G^F$. If $\hat{F}^{s_1} \neq \hat{F}^{s_2}$ we obtain the result of this proposition. Otherwise, we can apply the above reduction from $\hat{N} = (\hat{F}, s_1)$. □

If we apply the above Proposition to the example given in Figure 4.2, we obtain that $i_* = 3$ and $j_* = 2$. Thus, for $x^* = (0,0,0,1)$: $\tilde{f}_3(y^1) = f_3(y^1) = y_1^1 \vee y_2^1 = 1 \vee 1 = 1$; $\tilde{f}_3(y^2) = f_3(y^2) = \neg(y_1^2 \vee y_2^2) = \neg(1 \vee 0) = 0$, and $\tilde{f}_3(x) = f_3(x)$, $\forall x \neq y^1, y^2$, where $y^1 = (1,1,0,1)$ and $y^2 = (1,0,0,1)$.

4.2 Robustness of attractors

In this section, we study different changes in the update schedule of a Boolean network which keep or change its attractors. It is known that the set of fixed points of a discrete network does not change with respect to different update schedules. Therefore, in the following we focus on the dynamical cycles.

Given $N = (F, s)$ a Boolean network and $[x^0, \ldots, x^{p-1}, x^0]$ a dynamical cycle of length $p \geq 1$, we will say that the arc $(i,j) \in A(G^F)$ is critical for the cycle if either there exists $r \in \{0, \ldots, p-2\}$ such that $F^{s_{i,j}}(x^r) \neq x^{r+1}$ or $F^{s_{i,j}}(x^{p-1}) \neq x^0$, where $s_{i,j}$ denote the update schedule defined by $s_{i,j} = s \circ \pi_{i,j}$ (in particular $s_{i,i} = s$). In other words, the arc (i,j) is critical for a dynamical cycle if the Boolean network with update schedule $s_{i,j}$ does not preserve the cycle. Hence, a loop $(i,i) \in A(G^F)$ is never a critical arc.

Figure 4.4 shows an example of a Boolean network $N = (F, s = \pi_0)$, where

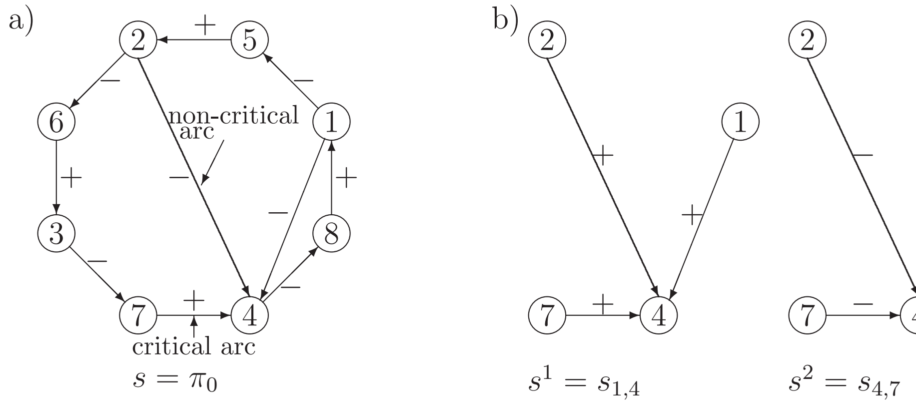


FIGURE 4.4. a) Critical and non-critical arcs for the cycle C_0. b) Application of conditions of Theorem 4.3 on the node 4: $i = 4$, $q = 1$,$r = 7$.

$F : \{0,1\}^8 \to \{0,1\}^8$ is defined by:

$$\begin{array}{llll} f_1(x) = x_8 & f_2(x) = x_5 & f_3(x) = x_6 & f_4(x) = (x_1 \wedge x_2) \vee x_7 \\ f_5(x) = x_1 & f_6(x) = x_2 & f_7(x) = x_3 & f_8(x) = x_4 \end{array}$$

N has a cycle

$$C_0 = [(10001000), (01000100), (00100010), (00010001), (10001000)].$$

For this cycle the arc $(2,4)$ is non-critical, since C_0 is also a cycle of the Boolean network $N_1 = (F, s_{2,4})$. On the other hand, the arc $(7,4)$ is a critical C_0, because the Boolean network $N_2 = (F, s_{7,4})$ does not have the cycle C_0 as attractor.

THEOREM 4.3 *Let $N = (F,s)$ be a Boolean network and $C = [x^0, \ldots, x^{p-1}, x^0]$ a dynamical cycle of length $p > 1$. Then, for every node i such that $\exists l \in \{0, \ldots, p-1\}$, $x_i^l \neq x_i^{l+1}$ and $\exists q, r \in I(i) \cup \{i\}$, $\forall j \in I(i)$, $s_{i,q}(j) \geq s_{i,q}(i)$ and $s_{i,r}(j) < s_{i,r}(i)$, either (q,i) or (r,i) must be a critical arc for C.*

PROOF. Let $C = [x^0, \ldots, x^{p-1}, x^0]$ a dynamical cycle of length $p > 1$ of $N = (F,s)$.

Let us now prove the result by contradiction. Let us suppose that $\exists q, r \in I(i) \cup \{i\}$, $\forall j \in I(i)$, $s_{i,q}(j) \geq s_{i,q}(i)$ and $s_{i,r}(j) < s_{i,r}(i)$, and C is cycle of $N = (F, s_{i,q})$ and $N = (F, s_{i,r})$. Hence, $\forall l = 0, \ldots, p-1$:

$$f_i^s(x_j^l : j \in I(i)) = f_i^{s_{i,q}}(x_j^l : j \in I(i)) = f_i^{s_{i,r}}(x_j^l : j \in I(i)).$$

But

$$f_i^{s_{i,q}}(x_j^l : j \in I(i)) = f_i(x_j^l : j \in I(i))$$

and

$$f_i^{s_{i,r}}(x_j^l : j \in I(i)) = f_i(x_j^{l+1} : j \in I(i)).$$

From here,

$$f_i(x_j^{l+1} : j \in I(i)) = f_i(x_j^l : j \in I(i)), \forall\, l = 0, \ldots, p-1,$$

where $x^p \equiv x^0$. Thus, $f_i^s(x^l) = x_i^l = a,\ a \in \{0,1\}\,\forall l = 1, \ldots, p-1$, which is a contradiction with the hypothesis of x_i non-constant. $\square$

An example of application of Theorem 4.3 is shown in Figure 4.4.

Observe from the above proof that if $\forall j \in I(i)$, $s(j) \geq s(i)$ and $\exists r \in I(i)$, $s_{i,r}(j) < s_{i,r}(i)$ or $\forall j \in I(i)$, $s(j) < s(i)$ and $\exists r \in I(i)$, $s_{i,r}(j) \geq s_{i,r}(i)$, then (r,i) is a critical arc. Besides, the condition: $\exists r \in I(i) \cup \{i\}$, $\forall j \in I(i)$, $s_{i,r}(j) < s_{i,r}(i)$ is not satified by a node j with a loop associated. However, it is easy to show that the result is also valid if a monotonic loop in the node is allowed. Thus, the following is a direct corollary of Theorem 4.3.

Corollary 4.1 *Let $N = (F,s)$ and $N' = (F,s')$ be two Boolean network with different update schedules, and $j \in V(G^F)$ a node without a loop or with a monotonic loop. If* $\text{sign}_s(i,j) = +1$, $\forall i \in I(j)$ *and* $\text{sign}_{s'}(i,j) = -1$, $\forall i \in I(j) \setminus \{j\}$, *then N and N' do not share dynamical cycles with non-constant value in the node j.*

The following result allows us to define a new update shedule for a given Boolean network such that the dynamical cycles are not kept.

Theorem 4.4 *Let $N = (F,s)$ be a Boolean network where the loops are monotonic. There exists an update schedule s' such that the dynamical cycles of $N' = (F,s')$ and $N = (F,s)$ are different.*

Proof. Let $\{i_1, i_2, \ldots, i_n\}$ be a labelling of the nodes of G^F so that $i_j \leq i_k \Longleftrightarrow s(i_j) \leq s(i_k)$. We define s' by: $s'(i_j) = n + 1 - j$, $\forall j = 1, \ldots, n$. Thus, $s'(i_1) > s'(i_2) > \cdots > s'(i_n)$.

Given $[x^0, \ldots, x^{p-1}, x^0]$ a dynamical cycle of length $p > 1$ of N, let i_* be the node of G^F such that $s'(i_*) = \max\{s'(i) :\ \exists l \in \{0, \ldots, p-1\},\ x_i^l \neq x_i^{l+1}\}$.

Suppose that $[x^0, \ldots, x^{p-1}, x^0]$ is also a dynamical cycle of N'. Then, $\forall r = 0, \ldots, p-1$:

$$f_{i_*}^s(x_j^r : j \in I(i)) = f_{i_*}^{s'}(x_j^r : j \in I(i)),$$

with

$$f_{i_*}^{s'}(x_j^r : j \in I(i)) = f_{i_*}(x_j^{r+1} : j \in I(i) \setminus I^*(i_*);\ a_j : j \in I^*(i_*)),$$

where $I^*(i_*) = \{j \in I(i) : x_j^r = a_j,\ a_j \in \{0,1\},\ \forall r = 0, \ldots, p-1\}$.

Let us suppose that f_{i_*} does not depend on i_*, i.e. there does not exist the loop (i_*, i_*) in G^F. Then,

$$x_{i^*}^{r+1} = f_{i_*}^s(x_j^r : j \in I(i)) = f_{i_*}(x_j^r : j \in I(i) \setminus I^*(i_*);\ a_j : j \in I^*(i_*)),$$

Hence,

$$f_{i_*}(x_j^r : j \in I(i) \setminus I^*(i_*);\ a_j : j \in I^*(i_*)) = f_{i_*}(x_j^{r+1} : j \in I(i) \setminus I^*(i_*);\ a_j : j \in I^*(i_*)).$$

Therefore, x_{i_*} has constant value in the dynamical cycle, which is a contradiction with the definition of i_*.

Suppose now that f_{i_*} depends on i_*.

Observe that if there exists $l = 0, \ldots, p-1$ such that $x_{i_*}^{l-1} = x_{i_*}^l$ then

$$\begin{aligned} x_{i_*}^l &= f_{i_*}^{s'}(x_j^{l-1} : j \in I(i)) = f_{i_*}(x_j^l : j \in I(i) \setminus I^*(i_*);\ a_j : j \in I^*(i_*)) \\ x_{i_*}^{l+1} &= f_{i_*}^s(x_j^l : j \in I(i)) = f_{i_*}(x_j^l : j \in I(i) \setminus I^*(i_*);\ a_j : j \in I^*(i_*)) \end{aligned}$$

Thus $x_{i_*}^l = x_{i_*}^{l+1}$ and by induction we obtain that the i_*-th component of the vectors in the cycle is constant, which contradicts again the definition of i_*.

Now, we suppose that f_{i_*} depends on x_{i_*} and $x_{i_*}^l \neq x_{i_*}^{l+1}, \forall l = 0, \ldots, p-1$. Then, there exists $l = 0, \ldots, p-1$, such that $x_{i_*}^{l-1} = 1, x_{i_*}^l = 0$ and $x_{i_*}^{l+1} = 1$:

$$\begin{aligned} x_{i_*}^l &= 0 = f_{i_*}(x_j^l : j \in I(i) \setminus \{i_*\}; x_{i_*}^l = 1) \\ x_{i_*}^{l+1} &= 1 = f_{i_*}(x_j^l : j \in I(i) \setminus \{i_*\}; x_{i_*}^l = 1) \end{aligned}$$

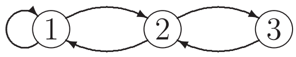
This is a contradiction with the monotonicity of f_{i_*} with respect to x_{i_*}. Therefore, $[x^0, \ldots, x^{p-1}, x^0]$ is not a dynamical cycle of $N' = (F, s')$. □

As a Corollary of this Theorem we have:

COROLLARY 4.2 *Let N be a Boolean network such that the loops are monotonic, if $[x^0, \ldots, x^{p-1}, x^0]$ is a cycle, of N for parallel update, then $[x^0, \ldots, x^{p-1}, x^0]$ is not a cycle of N for sequential update.*

PROOF. Observe that if s is a synchronous update schedule, then each sequential update schedule s' verifies that $s'(i_1) > s'(i_2) > \cdots > s'(i_n)$ with $i_1, \ldots, i_n$ nodes of G^F. Thus, no sequential update schedule can share a dynamical cycle with the synchronous one (for a given Boolean network without non-monotonic loops)

The hypotesis of monotonicity in the loops is essential for the previous theorem, as shown by the example of Figure 4.5.



$f_1 = \bar{x}_1 \wedge x_2$
$f_2 = x_2 \vee x_3$
$f_3 = x_2$

FIGURE 4.5. This Boolean network $N = (F, s)$ has a dynamical cycle $C = [(0,1,1),(1,1,1),(0,1,1)]$, which is invariant against any change in the update schedule s. Here, $(1,1)$ is a non-monotonic loop of G^F.

4.3 Update schedules in symmetric networks

One of main studies of equivalent update schedules in discrete networks has been made in sequential dynamical systems [19, 28]. These networks correspond to Boolean networks with sequential schedules and where the connection digraph is symmetric, that is $(i,j) \in A(G^F) \iff (j,i) \in A(G^F)$. Besides, each node has also a loop.

In the following, we work with Boolean networks where the update schedule is sequential and G^F is a symmetric digraph.

Mortveit et al. in [19, 28] characterized the set of equivalent sequential schedules, yielding a same dynamical behavior of a given sequential dynamical systems $N = (F, s_1)$, through the following relation:

$$s_1 \sim s_2 \iff \exists \{i_1, \ldots, i_l\} \subseteq V(G^F),\ (s_1 = s_2 \circ \pi_{i_1,i_2} \circ \pi_{i_2,i_3} \circ \cdots \circ \pi_{i_{l-1},i_l}) \wedge$$
$$(\forall j = 1, \ldots, l-1,\ |s_1(i_j) - s_1(i_{j+1})| = 1 \ \wedge\ (i_j, i_l) \notin A(G^F) \ \wedge\ (i_l, i_j) \notin A(G^F)).$$

They also estimated the number of schedules in each class.

In this section, we prove that the equivalence classes, determined by the relation $\sim$ defined above, coincide, in this particular family of Boolean networks, with those defined in Section 4.2.

THEOREM 4.5 *Let $N_1 = (F, s_1)$ and $N_2 = (F, s_2)$ be two Boolean networks with symmetric connection digraph and s_1, s_2 sequential update functions. Then, $s_1 \sim s_2$ if and only if $G^F_{s_1} = G^F_{s_2}$.*

PROOF.

SUFFICIENT CONDITION. It is easy to see that if $s_1 = s_2 \circ \pi_{i_1,i_2}$ with $|s_1(i_1) - s_1(i_2)| = 1$ and such that $(i_1, i_2) \notin A(G^F)$ and $(i_2, i_1) \notin A(G^F)$, then $G^F_{s_1} = G^F_{s_2}$. Thus, by using induction on the number of permutations needed to transform s_2 into s_1, $G^F_{s_1} = G^F_{s_2}$.

NECESSARY CONDITION. We prove now that if $G^F_{s_1} = G^F_{s_2}$, then there exists a sequence of permutations $\pi_{i,j}$ such that the update schedule s_1 is the composition of these permutations with s_2, that is $s_1 = s_2 \circ \pi_{i_1,i_2} \circ \pi_{i_2,i_3} \circ \cdots \circ \pi_{i_{l-1},i_l}$.

Without loss of generality, we suppose $s_1 = \pi_0$, and therefore for all $(i,j) \in A$ if $i \geq j$ then $s_1(i) \geq s_1(j)$, and if $i < j$ then $s_1(i) < s_1(j)$.

Now we proceed by induction on k to prove that $\forall k \in \{1, \ldots, n\}$, $\exists i_1, \ldots i_l$, $\forall j \leq k$, $s_1(j) = j = s_2 \circ \pi_{i_1,i_2} \circ \cdots \circ \pi_{i_{l-1},i_l}(j)$ and $G^F_{s_2 \circ \pi_{i_1,i_2} \circ \cdots \circ \pi_{i_{l-1},i_l}} = G^F_{s_1}$.

BASE. Let us suppose that $s_2(1) = l \neq 1$, since $\forall j \in I(1), s_1(j) = j > 1$ and by hypothesis $G^F_{s_1} = G^F_{s_2}$, so that $s_2(j) > s_2(1) = l$, $\forall j \in I(1)$.

Therefore, $\forall j \in \{1, \ldots, n\}$ such that $s_2(j) < l, (j,l) \notin A$ and $(l,j) \notin A$. Thus,

$$s_1(1) = 1 = s_2 \circ \pi_{i_1,i_2} \circ \cdots \circ \pi_{i_{l-1},i_l}(1)$$

where i_j is such that $s_2(i_j) = j$, $\forall j = 1, \ldots, l$. In particular, $i_1 = 1$ and $i_l = l$. Besides, by Sufficient Condition result, $G^F_{s_2 \circ \pi_{i_1,i_2} \circ \cdots \circ \pi_{i_{l-1},i_l}} = G^F_s$.

HYPOTHESIS OF INDUCTION. There exists a sequence of permutations such that, for all $j \leq k$:

$$s_1(j) = j = s'(j),$$

with $s' = s_2 \circ \pi_{i_1,i_2} \circ \cdots \circ \pi_{i_{p-1},i_p}$ and $G^F_{s'} = G^F_s$.

CASE $k+1$. If $s'(k+1) = k+1 = s_1(k+1)$, then the result is direct.

Suppose that $s'(k+1) = l \neq k+1$. Thus, $l > k+1$. Let $i_{k+1}, i_{k+2}, \ldots, i_{l-1}$ be such that $s'(i_j) = j$, $\forall j = k+1, \ldots, l$. Hence, $i_j > k+1$, $\forall j = k+1, \ldots, l-1$ and $i_l = k+1$.

Let us suppose that $(i_j, i_l) \in A$. Then, $\text{sign}_{s'}(i_j, i_l) = -1$. Since by hypothesis $G^F_{s'} = G^F_s$, $\text{sign}_s(i_j, i_l) = -1$. This implies that $i_j < i_l = k+1$ and hence $s'(i_j) = i_j < k+1$, which contradicts $s'(i_j) = j \geq k+1$.

Therefore, $(i_j, i_l) \notin A(G^F)$ and $(i_l, i_j) \notin A(G^F)$ for all $j = k+1, \ldots, l-1$.

And by Sufficient Condition result, $G^F_s = G^F_{s'} = G^F_{s' \circ \pi_{i_{k+1},i_{k+2}} \circ \cdots \circ \pi_{i_{l-1},i_l}}$ and

$$s_1(j) = s' \circ \pi_{i_{k+1},i_{k+2}} \circ \cdots \circ \pi_{i_{l-1},i_l}(j), \ \forall j = 1, \ldots, k+1.$$

□

Note that the relation $\sim$ defined above, as well as the proof of Theorem 4.5, is valid in any Boolean network, not only for those with symmetric connection digraphs. Therefore, the results of Morveit et al. in [28], respect to the equivalence relation $\sim$, are also valid in another family of Boolean networks differerent from sequential dynamical systems. However, the problem of determining whether two update functions are equivalent is much more simple when the characterization given by its signed digraphs is used.

CHAPTER 5

Sequential Boolean Networks

A great amount of collected data by Harris et al. [20] about the updating rules of different real genes, and some models of real genetic networks (for example, Aracena [12]; Aracena et al. [9]; Mendoza and Alvarez-Buylla [27]; Sánchez and Thieffry [31]) show that interactions between gene and gene products are mainly of the activation or inhibition type. We define a class of Boolean networks, called regulatory Boolean networks, where each interaction between the elements of the network corresponds either to a positive or to a negative interaction. This family of networks includes the Boolean networks with hierarchically canalizing functions, also known as nested canalyzing functions (Kauffman et al. [25]), introduced by Szallasi and Liang [33] and recently studied by Nikolajewa et al. [29](in press).

In this chapter we propose an algorithm, polynomial with respect to number of vertices in the graph associated to the Boolean network, that allow "filter" the cycles of a Boolean network with a graph without negative circuits, i.e. the algorithm transforms the Boolean network in a new Boolean network with the same set of fixed points and without dynamical cycles in its dynamical behavior. Also in this new Boolean network the fixed points are reached in at most n updates, where n is the number of vertices in the graph associated to the Boolean network.

5.1 Notation

A Boolean function $f : \{0,1\}^n \to \{0,1\}$ is increasing monotonic on input i if

$$\forall x \in \{0,1\}^n \ , \ f(x_1, \ldots, x_{i-1}, 0, x_{i+1}, \ldots, x_n) \leq f(x_1, \ldots, x_{i-1}, 1, x_{i+1}, \ldots, x_n),$$

and decreasing monotonic on input i if

$$\forall x \in \{0,1\}^n, \ , \ (x_1, \ldots, x_{i-1}, 0, x_{i+1}, \ldots, x_n) \geq f(x_1, \ldots, x_{i-1}, 1, x_{i+1}, \ldots, x_n).$$

A Boolean function $f : \{0,1\}^n \to \{0,1\}$ is said to be a sign-definite function, also known as unate function (see [7]), if for each $i = 1, \ldots, n$, is either increasing monotonic or decreasing monotonic on input i. Equivalently, a Boolean function is sign-definite if it can be represented by a formula in disjunctive normal form in which all occurrences of any given literal are either negated or nonnegated [7]. Examples of sign-definite Boolean functions are the hierarchically canalyzing functions [25, 29], where the literals appear once in the disjunctive normal form. Another example of sign-definite functions are the threshold Boolean functions, where the sign of the weight of each interaction is associated to the type of monotony. On the other hand, there are sign-definite functions which are neither hierarchically canalyzing functions nor threshold functions, for example: $f(x_1, x_2, x_3, x_4) = (x_1 \wedge x_2) \vee (x_3 \wedge x_4)$. A well-known example of non-sign-definite Boolean function is "$\veebar$" (XOR), that is, $x_1 \veebar x_2 = (\neg x_1 \wedge x_2) \vee (x_1 \wedge \neg x_2)$. An analysis of Harris' collected data revealed that 134 of the 139 rules are sign-definite functions.

Given a sign-definite function $F : \{0,1\}^n \to \{0,1\}^n$, such that $F(x) = (f_1(x), \ldots, f_n(x))$, we denote by $I^+(j)$ and $I^-(j)$ the set of indices where f_j is increasing monotonic and decreasing monotonic respectively.

Hence, for every regulatory Boolean network $N = (F, s)$ we can define a sign function $w_F : A(G^F) \to \{-1, 1\}$ with

$$w_F(i,j) = \begin{cases} -1 & \text{if } i \in I^-(j) \\ +1 & \text{if } i \in I^+(j) \end{cases}$$

An arc $(i,j) \in A(G^F)$ will be called positive if $w_F(i,j) = 1$ and negative otherwise. We will say that a path is positive if the number of its negative arcs is even, and negative otherwise. (G^F, w_F) will be called graph with sign of N.

We denote by $\mathcal{N}_n = \{N = (F, s_p)/F : \{0,1\}^n \to \{0,1\}^n\}$ Boolean networks with n vertices in its associated graph and parallel update schedule. And, we define the operator $\mathcal{S}^\pi : \mathcal{N}_n \to \mathcal{N}_n$ as $\mathcal{S}^\pi(F, s_p) = (F^\pi, s_p)$, where π is a permutation of $\{1, \ldots, n\}$.

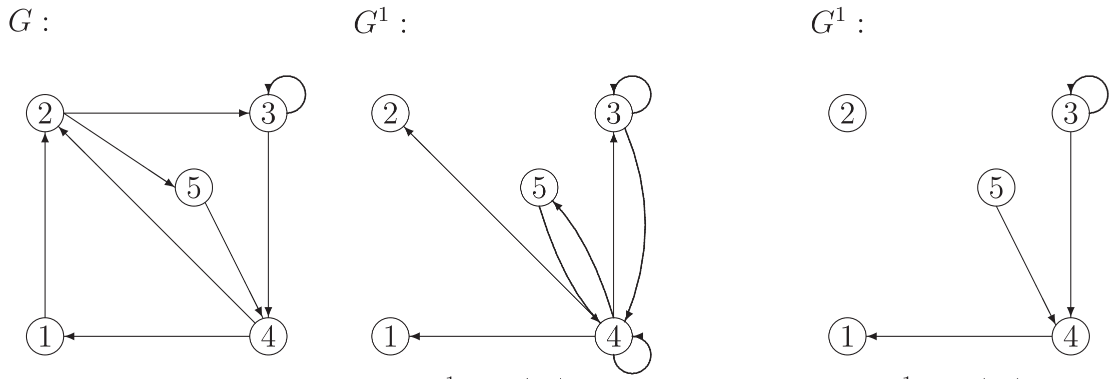
We observe that, $\mathcal{S}^{\pi}(F, s_p) = (F, \pi)$. Also, without loss of generality we will study only the permutation π_0, then we denote $\mathcal{S} = \mathcal{S}^{\pi_0}$ and $F^{\pi_0}(x) = (f_1^{(1)}(x), \ldots, f_n^{(1)}(x))$, where:

$$
\begin{aligned}
f_1^{(1)}(x) &= f_1(x) \\
f_i^{(1)}(x) &= f_i(f_1^{(1)}(x), \ldots, f_{i-1}^{(1)}(x), x_i \ldots, x_n) \qquad \forall i = 2, \ldots, n
\end{aligned}
$$

We see that we can define the graph associated to the sequential Boolean network, i.e, if $G = (V, A)$ is the graph associated to N we will call $G^1 = (V, A^1)$ the graph associated to $N^1 = \mathcal{S}(N)$. We observe that the set of vertex is the same in both cases, but the set of arcs is different. In fact we can see that:

$$(i, j) \in A^1 \Longrightarrow (i \geq j \wedge (i, j) \in A) \vee ((\exists k < j), (i, k) \in A^1 \wedge (k, j) \in A) \tag{5.1}$$

Figure 5.1 shows on the left a Boolean network N and its associated graph, on the center the graph associated that we obtain if we have "$\Longleftrightarrow$" instead "$\Longrightarrow$" in (5.1), and on the right we have the effective graph associated to $\mathcal{S}(N)$.



N :
$f_1(\vec{x}) = x_4$
$f_2(\vec{x}) = x_1 \vee \neg x_4$
$f_3(\vec{x}) = x_2 \wedge x_3$
$f_4(\vec{x}) = x_3 \wedge x_5$
$f_5(\vec{x}) = \neg x_2$

$N^1 = \mathcal{S}(N)$
$f_1^{(1)}(\vec{x}) = x_4$
$f_2^{(1)}(\vec{x}) = x_4 \vee \neg x_4$
$f_3^{(1)}(\vec{x}) = (x_4 \vee \neg x_4) \wedge x_3$
$f_4^{(1)}(\vec{x}) = x_3 \wedge (x_4 \vee \neg x_4) \wedge x_5$
$f_5^{(1)}(\vec{x}) = \neg(x_4 \vee \neg x_4)$

$N^1 = \mathcal{S}(N)$
$f_1^{(1)}(\vec{x}) = x_4$
$f_2^{(1)}(\vec{x}) = 1$
$f_3^{(1)}(\vec{x}) = x_3$
$f_4^{(1)}(\vec{x}) = x_3 \wedge x_5$
$f_5^{(1)}(\vec{x}) = 0$

FIGURE 5.1. Graph associated to $\mathcal{S}(N)$

In this way we define recursively the k-sequential network of N denoted by $N^k = \mathcal{S}(N^{k-1})$.

5.2 Boolean networks with associated graph without negative circuits

In this section we will restrict our attention to the Boolean networks with associated graph without negative circuits, and we give a Theorem that induces an algorithm polynomial in the number of vertices in the graph associated to the Boolean network; this algorithm allows to “filter” the dynamical cycles of a Boolean network. Also, this algorithm allows to find a fixed point in polynomial time. In networks associated graph without negative circuits, we can say that the dependence of a variable on itself is always positive, and it is a kind of Boolean network where it is known that there exist fixed points [8].

LEMMA 5.1 *Let N be a Boolean network such that all the circuits are positive, and let $N^1 = \mathcal{S}(N)$ be the sequential Boolean network of N. Then all the circuits of N^1 are positive.*

PROOF. Let $G = (V, A)$ be the graph associated to N and $G^1 = (V, A^1)$ the graph associated to N^1.

To prove this lemma we need to prove that if $(i, j) \in A^1$ then there exists a path $i_0 i_1 \ldots i_k$ in G where $i_0 = i$ and $i_k = j$, and if all the paths from i to j have the same sign then $w_{F^{(1)}}(i, j) = \prod_{l=1}^{k} w_F(i_{l-1}, i_l)$. In this way, we prove that any path in G^1, in particular the circuits, comes from a path in G, and the sign of the path in G is related to the sign of the path in G.

We know that:

$$f_j^{(1)}(x) = f_j(f_1^{(1)}, \ldots, f_{j-1}^{(1)}, x_j, \ldots, x_n)$$

Then:

$$(i, j) \in A^1 \Longrightarrow (i \geq j \wedge (i, j) \in A) \vee ((\exists k < j), (i, k) \in A^1 \wedge (k, j) \in A)$$

By induction on j, we prove that for all $(i, j) \in A^1$ there exists a path from i to j.

BASE. For $j = 1$, if $(i, 1) \in A^1$, then $(i, 1) \in A$, thus there exists a path of length one between i and j in G. The sign of this path is the sign of the arc $(i, 1) \in A$.

HYPOTHESIS OF INDUCTION. We suppose that for all $k \leq j$, if $(i, k) \in A^1$, then there exists a path from i to k in G. And, if all the paths from i to k have the same sign in G then the sign of (i, k) in G^1 is the sign of the paths.

Case $j+1$. Given $(i,j+1)\in A^1$, we prove that there exists a path from i to $j+1$ in G. We study two cases:

1. If $i \geq j+1$ and $(i,j+1)\in A$ we have a path of length one in G.
2. if $(i,j+1)$ is such that there exists $k<j+1, (i,k)\in A^1, (k,j+1)\in A$, then by hypothesis of induction there exists a path from i to k in G. Since $(k,j+1)\in A$, thus there exists a path from i to $j+1$.

Now, we prove that if all the paths from i to j have the same sign in G the sign of (i,j) in G^1 is the sign of the paths. We give the proof for the case where the sign of the paths is positive, the negative case is analogous. We prove that if the sign of path is positive then the function $f^{(1)}_{j+1}$ is increasing on input i.

$$f^{(1)}_{j+1}(x) = f_{j+1}(f^{(1)}_1(x),\ldots,f^{(1)}_j(x),x_{j+1},\ldots,x_n)$$

1. If $i\geq j+1$ and $(i,j+1)\in A$ we have a path of length one in G and $w_F(i,j+1) = +1$ then $f_{j+1}(x)$ is increasing on input i, and thus $f^{(1)}_{j+1}(x)$ is increasing on input i.
2. if $(i,j+1)$ is such that there exists $k<j+1, (i,k)\in A^1, (k,j+1)\in A$ then by hypothesis of induction there exists a path from i to k in G and $w_{F^{(1)}}(i,k) = \prod_{l=1}^{p} w_F(i_{l-1},i_l)$. Since the path is positive if $w_{F^{(1)}}(i,k)=+1$ then $w_F(k,j+1) = +1$. Therefore $f^{(1)}_k(x)$ is increasing on input i and $f_{j+1}(x)$ is increasing on input k, and hence $f_{j+1}(x)^{(1)}$ is increasing on input i. Now, if $w_{F^{(1)}}(i,k) = -1$ then $w_F(k,j+1) = -1$. Therefore $f^{(1)}_k(x)$ is decreasing on input i and $f_{j+1}(x)$ is decreasing on input k, and then $f_{j+1}(x)^{(1)}$ is increasing on input i.

□

As a Corollary of the last Lemma, we can conclude that in a Boolean nework with associated graph without negative circuits all the loops in the k-sequential network are positive. This point is very important, because the fact the loops are positive is one of the hypothesis of the next Lemma, which is the base of the proof of the main result of this chapter.

Lemma 5.2 *Let N be a Boolean network such that its parallel and sequential dynamics are identical and all the loops are positive. Then, all the attractors of the network are fixed points, and they are reached in at most n updates. Also, if we denote $\underbrace{F\circ\cdots\circ F}_{k\ times}(x^0) = x^k$, then:*

$$x^{l+1}_{n-l} = x^k_{n-l}, \forall k > l, l = 0,\ldots,n-1.$$

PROOF. We proceed by induction on l.

BASE. In first place we prove that $x_n^k = x_n^{k+1}$ implies $x_n^p = x_n^k, \forall p \geq k$. Since sequential dynamic is equal to parallel dynamic:

$$\begin{aligned} x_n^{k+1} &= f_n(x_1^{k+1}, \ldots, x_{n-1}^{k+1}, x_n^k) && \text{Sequential update} \\ x_n^{k+2} &= f_n(x_1^{k+1}, \ldots, x_{n-1}^{k+1}, x_n^{k+1}) && \text{Parallel update} \end{aligned}$$

Hence if $x_n^k = x_n^{k+1}$ then $x_n^{k+1} = x_n^{k+2}$ and in this way it is clear that, $x_n^p = x_n^k, \forall p \geq k$.

Now we show, $x_n^1 = x_n^2$. If $x_n^0 = x_n^1$, the previous sentence applies. Let us suppose $x_n^0 = x$, $x_n^1 = \neg x$, then

$$\begin{aligned} x_n^1 &= f_n(x_1^1, \ldots, x_{n-1}^1, x) = \neg x && \text{Sequential update} \\ x_n^2 &= f_n(x_1^1, \ldots, x_{n-1}^1, \neg x) && \text{Parallel update} \end{aligned}$$

If f_n does not depend on x_n then $x_n^2 = x_n^1$. If f_n depends on x_n, f_n is monotonic respect to x_n, then $x_n^2 = \neg x = x_n^1$.

HYPOTHESIS OF INDUCTION.

$$x_{n-j}^{j+1} = x_{n-j}^k, \quad \forall k > j, \quad j = 0, \ldots, l-1.$$

CASE l. In first place we prove that $x_{n-l}^{l+1} = x_{n-l}^{l+2}$ implies $x_{n-l}^p = x_{n-l}^{l+1}, \forall p > l$. Since sequential update is equal to paralel update:

$$\begin{aligned} x_{n-l}^{l+2} &= f_{n-l}(x_1^{l+2}, \ldots, x_{n-l-1}^{l+2}, x_{n-l}^{l+1}, \ldots, x_n^{l+1}) && \text{Sequential update} \\ x_{n-l}^{l+3} &= f_{n-l}(x_1^{l+2}, \ldots, x_{n-l-1}^{l+2}, x_{n-l}^{l+2}, \ldots, x_n^{l+2}) && \text{Parallel update} \end{aligned}$$

By hypothesis of induction $x_{n-j}^{l+1} = x_{n-j}^{l+2} \forall j < l$, then:

$$\begin{aligned} x_{n-l}^{l+2} &= f_{n-l}(x_1^{l+2}, \ldots, x_{n-l-1}^{l+2}, x_{n-l}^{l+1}, x_{n-l+1}^{l+1}, \ldots, x_n^{l+1}) \\ x_{n-l}^{l+3} &= f_{n-l}(x_1^{l+2}, \ldots, x_{n-l-1}^{l+2}, x_{n-l}^{l+2}, x_{n-l+1}^{l+1}, \ldots, x_n^{l+1}) \end{aligned}$$

Then if $x_{n-l}^{l+1} = x_{n-l}^{l+2}$, this implies $x_{n-l}^p = x_{n-l}^{l+1}, \forall p > l$.

Now, we prove that $x_{n-l}^{l+1} = x_{n-l}^{l+2}$:

$$\begin{aligned} x_{n-l}^{l+1} &= f_{n-l}(x_1^{l+1}, \ldots, x_{n-l-1}^{l+1}, x_{n-l}^l, x_{n-l+1}^l, \ldots, x_n^l) && \text{Sequential update} \\ x_{n-l}^{l+2} &= f_{n-l}(x_1^{l+1}, \ldots, x_{n-l-1}^{l+1}, x_{n-l}^{l+1}, x_{n-l+1}^{l+1}, \ldots, x_n^{l+1}) && \text{Parallel update} \end{aligned}$$

By hypothesis of induction:

$$x_{n-l}^{l+1} = f_{n-l}(x_1^{l+1}, \ldots, x_{n-l-1}^{l+1}, x_{n-l}^{l}, x_{n-l+1}^{l}, \ldots, x_n^{l})$$
$$x_{n-l}^{l+2} = f_{n-l}(x_1^{l+1}, \ldots, x_{n-l-1}^{l+1}, x_{n-l}^{l+1}, x_{n-l+1}^{l}, \ldots, x_n^{l})$$

We have three possibilities:

1. if f_{n-l} does not depend on x_{n-l} then $x_{n-l}^{l+1} = x_{n-l}^{l+2}$.
2. if f_{n-l} depends on x_{n-l} and $x_{n-l}^{l} = x_{n-l}^{l+1}$ then $x_{n-l}^{l+1} = x_{n-l}^{l+2}$, by sentence showed above.
3. if f_{n-l} depends on x_{n-l} and $x_{n-l}^{l} = x$, $x_{n-l}^{l+1} = \neg x$

$$\neg x = f_{n-l}(x_1^{l+1}, \ldots, x_{n-l-1}^{l+1}, x, x_{n-l+1}^{l}, \ldots, x_n^{l})$$
$$x_{n-l}^{l+2} = f_{n-l}(x_1^{l+1}, \ldots, x_{n-l-1}^{l+1}, \neg x, x_{n-l+1}^{l}, \ldots, x_n^{l})$$

Since f_{n-l} is monotonic on input x_{n-l}, $x_{n-l}^{l+2} = x_{n-l}^{l+1} = \neg x$.

□

Notice that, in a Boolean network with graph by layers, with negative loops and such that $\forall (i,j) \in A$, $s(i) \geq s(j)$ we can have identical parallel and sequential dynamics, and also we can have cycles as attractors.

LEMMA 5.3 *Let $N = (F, s_p)$ be a Boolean network such that $F : \{0,1\}^n \to \{0,1\}^n$ and $\mathcal{S}(N) = (F^{(1)}, s_p)$. If we consider a Boolean network $N_{k,\vec{y}} = (F_k, s_p)$, $k < n$ such athat $F_k : \{0,1\}^k \to \{0,1\}^k$, and, $F_k(x_1, \ldots, x_k) = F(x_1, \ldots, x_k, y_1, \ldots, y_{n-k})$, then $\mathcal{S}(N_{k,\vec{y}}) = (F_k^{(1)}, s_p)$ where $F_k^{(1)}(x_1, \ldots, x_k) = F^{(1)}(x_1, \ldots, x_k, y_1, \ldots, y_{n-k})$.*

PROOF. Let denote by $f_i^{1,k}$ the i-th component of the function $F_k^{(1)}$ and by f_i^k the i-th component of the function F_k . We prove by induction on i that $f_i^{1,k}(\vec{x}) = f_i^{(1)}(\vec{x}, \vec{y})$ for all $x \in \{0,1\}^k$ and for all $i = 1, \ldots, n$.

BASE.
$$f_1^{1,k}(\vec{x}) = f_1^k(\vec{x}) = f_1(\vec{x}, \vec{y}) = f_1^{(1)}(\vec{x}, \vec{y})$$

HYPOTHESIS OF INDUCTION. $f_l^{1,k}(\vec{x}) = f_l^{(1)}(\vec{x}, \vec{y})$ for all $l = 1, \ldots, i$.

CASE $i+1$.

$$\begin{aligned} f_{i+1}^{1,k}(\vec{x}) &= f_{i+1}^{k}(f_1^{1,k}(\vec{x}),\ldots,f_i^{1,k}(\vec{x}),x_{i+1},\ldots,x_k) \\ &= f_{i+1}(f_1^{1,k}(\vec{x}),\ldots,f_i^{1,k}(\vec{x}),x_{i+1},\ldots,x_k,y_1,\ldots,y_{n-k}) \end{aligned}$$

By hypothesis of induction,

$$\begin{aligned} f_{i+1}^{1,k}(\vec{x}) &= f_{i+1}(f_1^{(1)}(\vec{x},\vec{y}),\ldots,f_i^{(1)}(\vec{x},\vec{y}),x_{i+1},\ldots,x_k,y_1,\ldots,y_{n-k}) \\ &= f_{i+1}^{(1)}(\vec{x},\vec{y}) \end{aligned}$$

Then, $F_k^{(1)}(x_1,\ldots,x_k) = F^{(1)}(x_1,\ldots,x_k,y_1,\ldots,y_{n-k})$. □

LEMMA 5.4 *Let N be a Boolean network where the loops, if they exist, are positive. If $N^i = (F^{(i)}, s_p)$ is the i–sequential network of N and for all $k \le i$, $f_k^{(k)}(x) = f_k^{(k-1)}(x)$ then the sequences:*

1. $X(i,x)^0 = (x_1,\ldots,x_i,x_{i+1},\ldots,x_n)$
   $X(i,x)^{k+1} = (f_1^{(i+1)}(X(i,x)^k),\ldots,f_i^{(i+1)}(X(i,x)^k),x_{i+1},\ldots,x_n)$
2. $Y(i,x)^0 = (x_1,\ldots,x_i,x_{i+1},\ldots,x_n)$
   $Y(i,x)^{k+1} = (f_1^{(i+1-k)}(Y(i,x)^k),\ldots,f_i^{(i+1-k)}(Y(i,x)^k),x_{i+1},\ldots,x_n)$
3. $Z(i,x)^0 = (x_1,\ldots,x_i,x_{i+1},\ldots,x_n)$
   $Z(i,x)^{k+1} = (f_1^{(i-k)}(Z(i,x)^k),\ldots,f_i^{(i-k)}(Z(i,x)^k),x_{i+1},\ldots,x_n)$

are identical.

PROOF. Notice that by Lemma 5.3 the sequence $X(i,x)$ is the update of a Boolean network with i variable states, and hence the hypothesis of Lemma 5.2 apply. Then the sequence converges to a fixed point in i updates, i.e., $X(i,x)^i = X(i,x)^{i+1}$.

In this proof we denote: $X(i,x)^k = x^k, Y(i,x)^k = y^k, Z(i,x)^k = z^k$. And, we notice that by hypothesis of the Lemma:

1. $x^0 = (x_1,\ldots,x_i,x_{i+1},\ldots,x_n)$
   $x^{k+1} = (f_1^{(0)}(x^k), f_1^{(1)}(x^k),\ldots,f_i^{(i-1)}(x^k),x_{i+1},\ldots,x_n)$
2. $y^0 = (x_1,\ldots,x_i,x_{i+1},\ldots,x_n)$
   $y^{k+1} = (f_1^{(0)}(y^k),\ldots,f_{i+2-k}^{(i+1-k)}(y^k),\ldots,f_i^{(i+1-k)}(y^k),x_{i+1},\ldots,x_n)$
3. $z^0 = (x_1,\ldots,x_i,x_{i+1},\ldots,x_n)$
   $z^{k+1} = (f_1^{(0)}(z^k),\ldots,f_{i+1-k}^{(i-k)}(z^k),\ldots,f_i^{(i-k)}(z^k),x_{i+1},\ldots,x_n)$

Now, we proceed by induction on k.

Base. Clearly $x^0 = y^0 = z^0$

Hypothesis of induction. For all $j \leq k$

$$x^j = y^j = z^j$$

Case $k+1$. We will only give the proof for sequence z, the proof for sequence y is analogous.

It is easy to see that:

$$x_l^{k+1} = z_l^{k+1}, \qquad \forall l \leq i+1-k$$

Now, if $l > i+1-k \iff k-1 > i-l$:

$z_l^{k+1} = f_l^{(i-k)}(z^k)$

Since $z^k = (f_1^{(i+1-k)}(z^{k-1}), \ldots, f_i^{(i+1-k)}(z^{k-1}), x_{i+1}, \ldots, x_n)$

$$\begin{aligned} z_l^{k+1} &= f_l^{(i-k)}(f_1^{(i+1-k)}(z^{k-1}), \ldots, f_i^{(i+1-k)}(z^{k-1}), x_{i+1}, \ldots, x_n) \\ &= f_l^{(i-k)}(f_1^{(i+1-k)}(z^{k-1}), \ldots, f_{l-1}^{(i+1-k)}(z^{k-1}), f_l^{(i+1-k)}(z^{k-1}), \ldots, f_i^{(i+1-k)}(z^{k-1}), x_{i+1}, \ldots, x_n) \\ &= f_l^{(i-k)}(f_1^{(i+1-k)}(z^{k-1}), \ldots, f_{l-1}^{(i+1-k)}(z^{k-1}), z_l^k, \ldots, z_i^k, x_{i+1}, \ldots, x_n) \end{aligned}$$

by hypothesis of induction:

$$z_l^{k+1} = f_l^{(i-k)}(f_1^{(i+1-k)}(z^{k-1}), \ldots, f_{l-1}^{(i+1-k)}(z^{k-1}), x_l^k, \ldots, x_i^k, x_{i+1}, \ldots, x_n)$$

Since $k-1 > i-l$, by Lemma 5.2:

$$z_l^{k+1} = f_l^{(i-k)}(f_1^{(i+1-k)}(z^{k-1}), \ldots, f_{l-1}^{(i+1-k)}(z^{k-1}), x_l^{k-1}, \ldots, x_i^{k-1}, x_{i+1}, \ldots, x_n)$$

by hypothesis of induction:

$$\begin{aligned} z_l^{k+1} &= f_l^{(i-k)}(f_1^{(i+1-k)}(z^{k-1}), \ldots, f_{l-1}^{(i+1-k)}(z^{k-1}), z_l^{k-1}, \ldots, z_i^{k-1}, x_{i+1}, \ldots, x_n) \\ z_l^{k+1} &= f_l^{(i+1-k)}(z^{k-1}) = z_l^k \end{aligned}$$

Then by hypothesis of induction and Lemma 5.2:

$z_l^{k+1} = x_l^k = x_l^{k+1}$

□

5.3 Algorithm

Now we present an algorithm such that its input is a Boolean network N with associated graph without negative circuits and n variable states. Its output is a Boolean network with n variable states with the same fixed points than the input, but without cycles, and where the fixed points are reached in at most n updates.

```
Filter(N)
{
    while (N ≠ S(N))
        N ⟵ S(N)
    return(N)
}
```

The next Theorem proves that this algorithm stop in at most n iterations and it gives a Boolean network without cycles where the fixed point are reached in at most n updates.

Theorem 5.1 *Let $N = (F, s)$ be a Boolean network where $F : \{0,1\}^n \rightarrow \{0,1\}^n$ such that all the circuits are positive. Let $N^{n-1} = \underbrace{\mathcal{S} \circ \cdots \circ \mathcal{S}}_{n-1 \text{ times}}(N)$ then $N^{n-1} = \mathcal{S}(N^{n-1})$, and also the only attractors of this network are fixed points, that are reached in at most n updates.*

Proof. We only need to prove that:

$$\forall F : \{0,1\}^n \rightarrow \{0,1\}^n, \forall i = 1, \ldots, n, f_i^{(i)}(x) = f_i^{(i-1)}(x)$$

because the fact that the only attractors of this network are fixed points, that are reached in at most n updates, is given by Lemma 5.2.

We proceed by induction on i, we will prove that:

$$f_i^{(i)}(x) = f_i^{(i-1)}(x)$$

Base. For $i = 1$

$$f_1^{(1)}(x) = f_1^{(0)}(x) = f_1(x)$$

Hypothesis of induction. For all $j \leq i$, and for all $x \in \{0,1\}^n$

$$f_j^{(j)}(x) = f_j^{(j-1)}(x)$$

Case $i+1$. If we consider the sequences defined in Lemma 5.4, we obtain:

$$\begin{aligned}
f_{i+1}^{(i+1)}(x) &= f_{i+1}^{(i)}(f_1^{(i+1)}(x),\ldots,f_1^{(i+1)}(x),x_{i+1},\ldots,x_n) = f_{i+1}^{(i)}(Y(i,x)^1)\\
f_{i+1}^{(i+1)}(x) &= f_{i+1}^{(i-1)}(f_1^{(i)}(Y(i,x)^1),\ldots,f_1^{(i)}(Y(i,x)^1),x_{i+1},\ldots,x_n) = f_{i+1}^{(i-1)}(Y(i,x)^2)\\
&\vdots\\
f_{i+1}^{(i+1)}(x) &= f_{i+1}(Y(i,x)^{i+1})
\end{aligned}$$

also,

$$\begin{aligned}
f_{i+1}^{(i)}(x) &= f_{i+1}^{(i-1)}(f_1^{(i)}(x),\ldots,f_1^{(i)}(x),x_{i+1},\ldots,x_n) = f_{i+1}^{(i-1)}(Z(i,x)^1)\\
f_{i+1}^{(i)}(x) &= f_{i+1}^{(i-2)}(f_1^{(i-1)}(Z(i,x)^1),\ldots,f_1^{(i-1)}(Z(i,x)^1),x_{i+1},\ldots,x_n) = f_{i+1}^{(i-2)}(Z(i,x)^2)\\
&\vdots\\
f_{i+1}^{(i)}(x) &= f_{i+1}(Z(i,x)^i)
\end{aligned}$$

By hypothesis of induction $f_j^{(j)}(x) = f_j^{(j-1)}(x), \forall j \le i$ then, by Lemma 5.4:

$$Y(i,x)^{i+1} = X(i,x)^{i+1}, \quad Z(i,x)^i = X(i,x)^i$$

and, by Lemma 5.2 and Lemma 5.3 $X(i,x)^{i+1} = X(i,x)^i$. Thus,

$$f_{i+1}^{(i+1)}(x) = f_{i+1}^{(i)}(x)$$

□

Figure 5.2 shows the algorithm applied on a particular Boolean network, we observe that the algorithm converges in $n-1$ time steps, however we can find some sequential update schedule that allows the algorithm to converge faster (see Figure 5.3).

5.4 Discussion of the result

In first place, it is well-kown that the problem of finding a fixed point, in the general case, is NP-complete, but in this case we can found one fixed point in polynomial time. In fact, we note that in the i-th step of the algorithm `Filter` we modify only $n-i$ functions and thus the algorithm is $O(n^2)$. Since in the $(n-1)-$sequential network the fixed points are reached in at most n updates, then we can find a fixed point of the Boolean network in $O(n^2)$.

Also, if we have a Boolean network N without cycles, the algorithm allows to find the fixed point with shorter transient (see Figure 5.4).

The worst case for the algorithm is to converge in n time steps, but if we use an appropiate update sequential schedule the algorithm converges faster. For example, Figure 5.5 shows a Boolean network that converges in one iteration of the algorithm. A good strategy to accelerate the convergence is to choose an update schedule that minimizes the number of edges $(i, j) \in A$ such that $s(i) \geq s(j)$. In fact, we observe that if a circuit has only one arc (i, j) such that $s(i) \geq s(j)$, this circuit becomes a loop in the vertex i and an arc from i to every vertex in the circuit as shown in Figure 5.6. Also we see that using this update schedule the algorithm gives us a Boolean network where the fixed points are reached in 1 time step. Then an open problem is to found a polynomial algorithm, if there exists, that allows to get the convergence of the algorithm in one time step and such that the Boolean network obtained reaches the fixed point in one time step. Also, we need to note that, since the algorithm `Filter` converges in $O(n^2)$ this new algorithm would need a lower order of convergence to be useful.

Now, if we have a graph by layers with positive loops only, and we use an update schedule such that $\forall i \in V_{k_i}, \forall j \in V_{k_j}$ such that $k_i < k_j$ then $s(i) < s(j)$, this Boolean network converges in one iteration of the algorithm and the fixed points are reached in one update. Now, it is interesting to discuss about the length of the transient. In chapter 3 we have seen that the length of the transient in a graph by layers depends on the number of layers in the graph. In the general case we can do a decomposition of the graph in its strongly connected components as shown in Figure 5.7.

The length of the transient depends of the length of transient of each strongly connected component. In Figure 5.7 we see that a strongly connected component can be represented as a vertex of a graph by layers in a discrete network (not Boolean necessarily). In this way, following the same technic used in proof of Proposition 3.1, the length of transient is at most the addition of the lengths of the transients in every layer. Since every strongly connected component verifies the hypothesis of Lemma 5.2, then every strongly connected component has a transient of length n_i, where n_i is the number of vertices in the i-th strongly connected component. Thus, the transient in every layer is the maximun number of vertices in a strongly connected component in this layer. It is important to remark that in some cases, the output of the algorithm is a Boolean network where the associated graph is a graph with only one strongly connected component, and in this case, we cannot reduce the length of transient (see Figure 5.8).

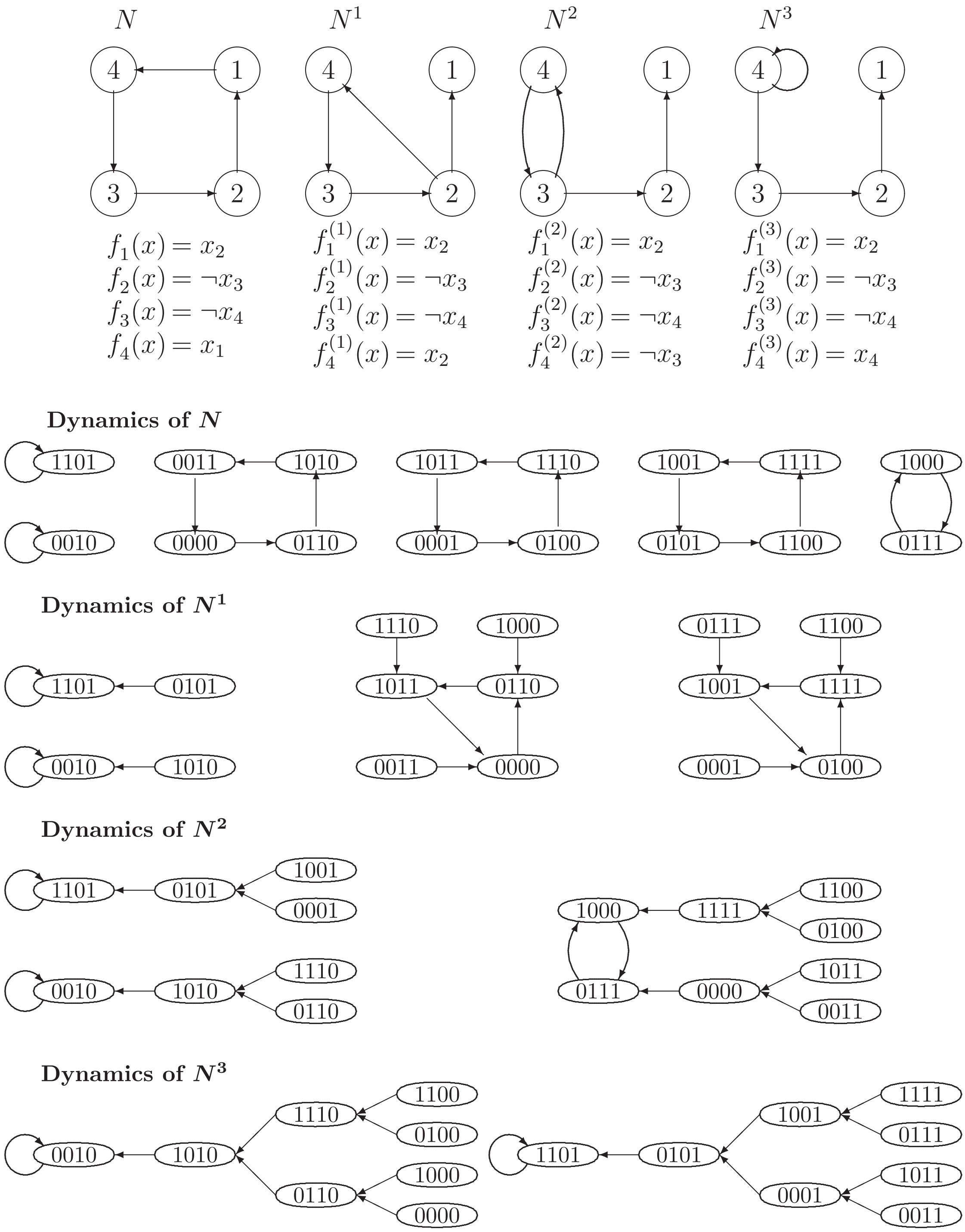
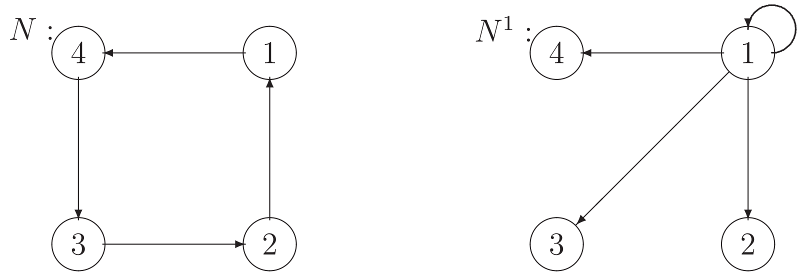


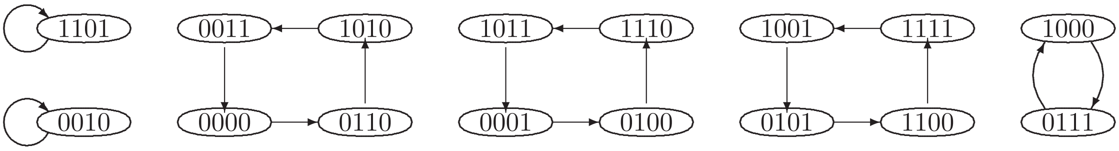
FIGURE 5.2. Algorithm applied on a particular Boolean network with sequential update schedule $s(i) = i$



$$f_1(x) = x_2$$
$$f_2(x) = \neg x_3$$
$$f_3(x) = \neg x_4$$
$$f_4(x) = x_1$$

$$f_1^{(1)}(x) = x_1$$
$$f_2^{(1)}(x) = x_1$$
$$f_3^{(1)}(x) = \neg x_1$$
$$f_4^{(1)}(x) = x_1$$

Dynamics of N



Dynamics of N^1

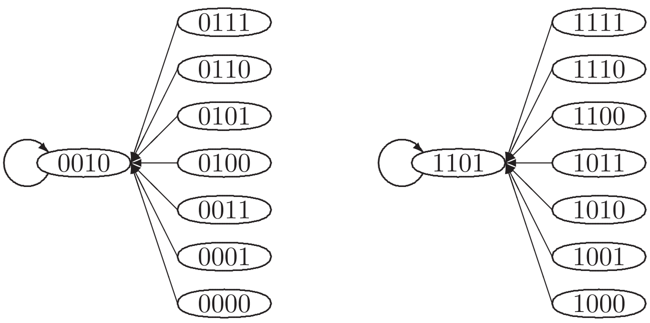
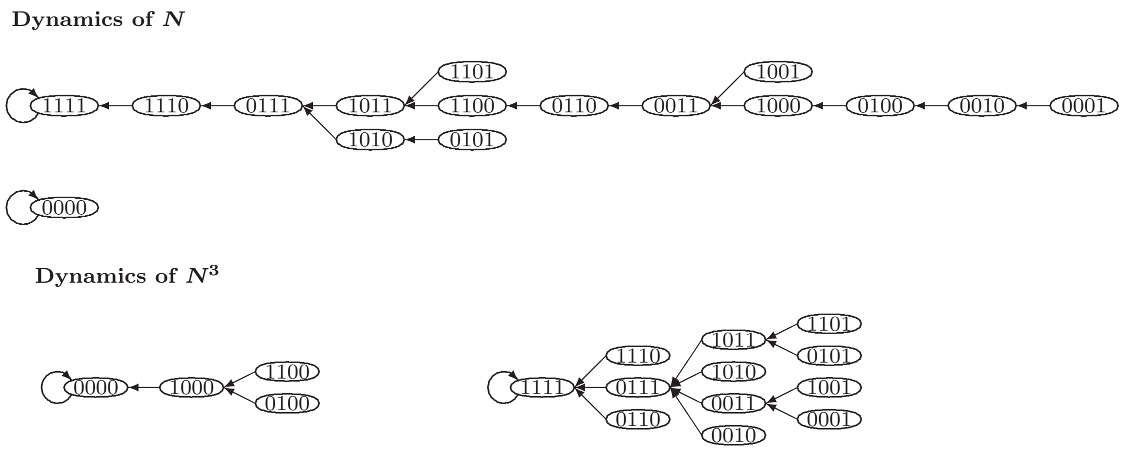


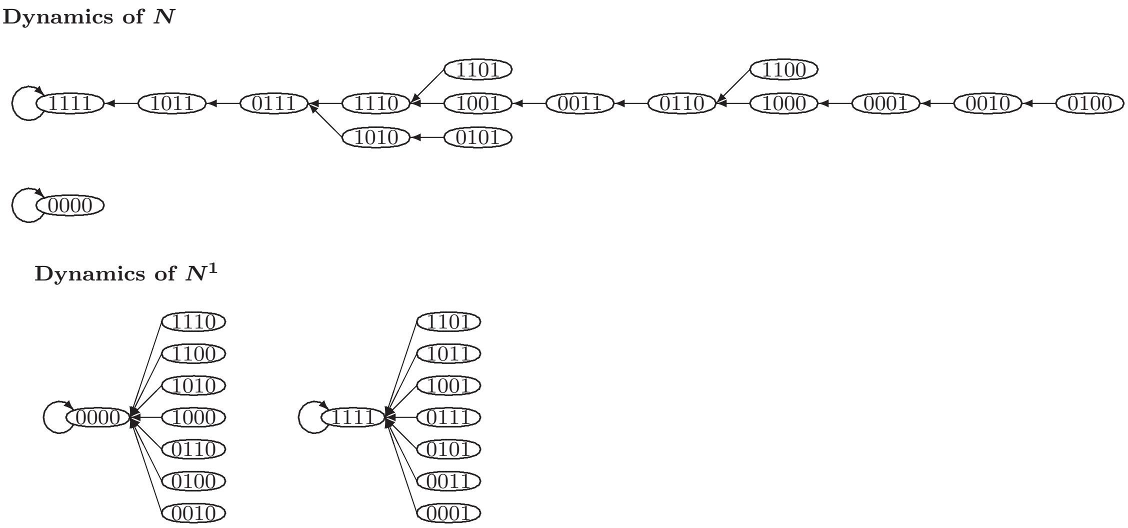
FIGURE 5.3. Algorithm applied on a particular Boolean network with sequential update schedule $s(i) = 5 - i$.



Functions

N :	N^3 :
$f_1 = x_2$	$f_1^{(3)} = x_2$
$f_2 = x_3$	$f_2^{(3)} = x_3$
$f_3 = x_1 \vee x_4$	$f_3^{(3)} = x_3 \vee x_4$
$f_4 = x_1$	$f_4^{(3)} = x_3 \vee x_4$

FIGURE 5.4. Boolean network without cycles but with a long transient



Functions

N :	N^1 :
$f_1 = x_4$	$f_1^{(1)} = x_4$
$f_2 = x_1$	$f_2^{(1)} = x_4$
$f_3 = x_1 \vee x_2$	$f_3^{(1)} = x_4$
$f_4 = x_3$	$f_4^{(1)} = x_4$

FIGURE 5.5. Boolean network that converges in one iteration of the algorithm

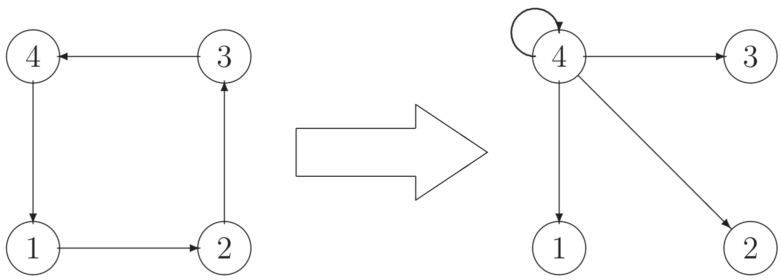


FIGURE 5.6. Circuit that converges in one iteration of the algorithm

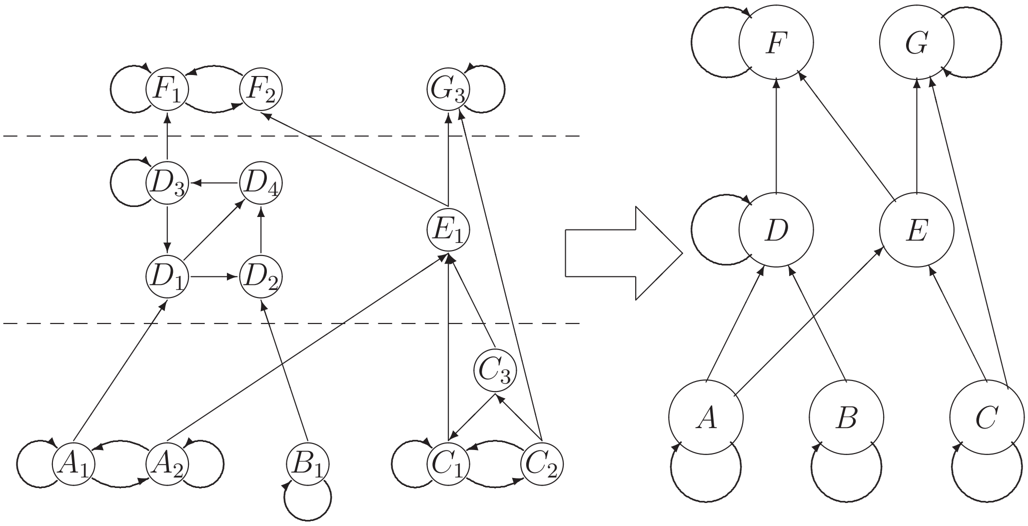
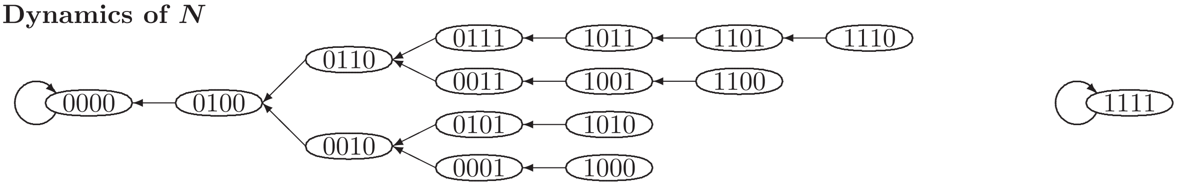
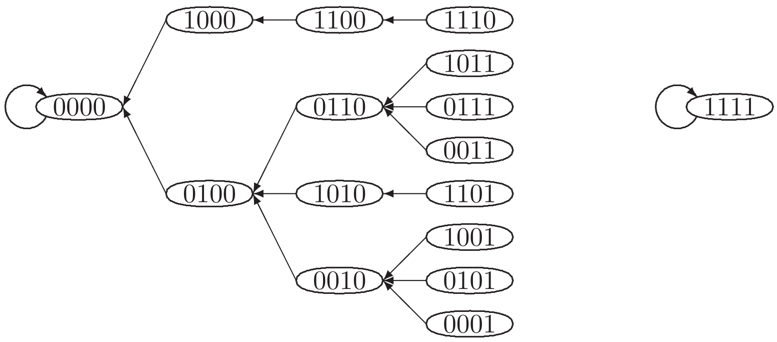


FIGURE 5.7. Decomposition of a graph in strongly connected components.

Dynamics of N



Dynamics of N^3



Functions.

$f_1 = x_1 \wedge x_2$	$f_1^{(3)} = x_1 \wedge x_2$
$f_2 = x_3$	$f_2^{(3)} = x_3$
$f_3 = x_4$	$f_3^{(3)} = x_4$
$f_4 = x_1$	$f_4^{(3)} = x_1 \wedge x_2 \wedge x_3 \wedge x_4$

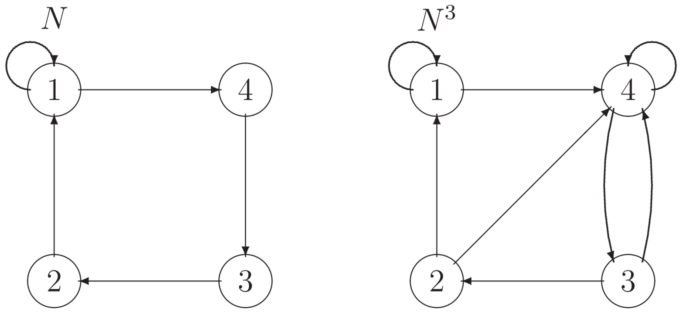


FIGURE 5.8.

CHAPTER 6

Conclusions

6.1 Covering by squares

In the covering by squares problem we have concentrated our attention on the existence of regular covering with respect to two parameters: the size of squares and the intersection number. In first place we have observed that these parameters are related. In fact, we have proved that the maximum intersection number for a square of size n in a regular covering is $2(n-1)$ if n is odd and $2(n-1)-1$ if n is even. In second place, we have found minimal conditions to have a strong and a weak covering, and we have proved that the minimum intersection number for a strong covering is six, which induces a size square of at least five. Also, we gave the minimal conditions for a regular weak covering, where the minimum size of squares is three and minimum intersection number is two.

In the case of non-regular covering the most interesting case is where the size of squares is not bounded, because in the the other case we can found results very similar to the regular case studying the largest square in the covering. For example, we have seen that the maximum intersection number is the maximum intersection number for the largest square, then if the size of the largest square is n the maximum intersection number will be bounded by $2(n-1)$. If n is odd the construction given in the regular case proves this bound is reached, but if n is even we need to found a non-regular covering where the bound is reached. In fact, for weak coverings we can use as a base Figure 2.5. For strong covering, we do not know if the bound is reached. If we analize the problem of minimal conditions, we observe that to have a strong covering we need a minimum intersetion number of six, for the same reasons of the regular case, applied now to the largest square.

Non-regular coverings problems where the size of squares is not bounded are an open problem.

6.2 Boolean Networks

In this thesis we have studied different aspects of the dynamical behavior of Boolean networks with deterministic update schedule. We have studied three problems:

1. Dynamics of Boolean networks with graphs by layers.
2. Robustness of the dynamics of Boolean networks with respect to the update schedule.
3. A Filter of cycles in Boolean networks which associated graphs have only positive circuits.

We observe that the dynamics of Boolean networks with graphs by layers is very simple, and the attractor it reaches is completely determined by the initial states of the first layer. In fact, the number of attractors is bounded by $2^{|V_1|}$, where V_1 is the set of vertices in the first layer. We have studied the length of the attractors, and we see that the length of cycles is a power of two. It is important to note that the existence of cycles in this kind of Boolean networks comes from the existence of decreasing loops, in fact, we have proved that if all the loops are increasing, then the attractors will be only fixed points. Also, the length of the transient to reach the fixed points is bounded by the number of layers of the associated graph. These results are true for any deterministic update schedule, because the associated graph to the Boolean network is by layers in every case.

In the study of robustness of Boolean network with respect to the update schedule we have studied the robustness of the dynamical behavior with respect to different update schedules, and the robustness of cycles with respect to the update schedule. In both cases we have concentrated our attention on deterministic update schedules (parallel, block-sequential, sequential). In first place, for a given Boolean network we have defined some equivalence classes of updates schedule such that their dynamical behaviors are identical. These equivalence classes are defined using a graph with signs, and they generalize the equivalence proposed by Morveit and Reidys [28]. However, the problem of determining whether two update functions are equivalent is much more simple when the characterization given by the graph with signs is used.

It is well-known that fixed points are the same for any update schedule; hence, we have studied when a change in the update schedule preserves the dynamical cycles. In chapter 3 we have shown a class of Boolean networks with graph by layers, where the parallel and sequential dynamics are identical, if these Boolean networks have only decreasing loops we can be sure that their attractors are only cycles, and therefore the cycles are preserved in any two update schedules. The question now becomes, how a dynamical cycle can be disrupted by a change in the update schedule. For this, given a dynamical cycle C for a Boolean network (F, s), we say the arc $(i, j) \in A$ is a critical arc for C, if C is not an attractor of $(F, s_{i,j})$ where $s_{i,j}(i) = s(j)$, $s_{i,j}(j) = s(i)$ and $s_{i,j}(k) = s(k)$ if $k \neq i$ and $k \neq j$. We prove that, for almost any cycle we can find a critical arc. In fact, since the sign of a loop is always positive, for any update schedule, the cycles generated for a decreasing loop are always preserved for any update shedule.

As a consequence of the above results we show that, given a Boolean network (F, s), we can find another update schedule s' such that (F, s) and (F, s') do not share any cycle. As a corollary of this theorem we have that if all the loops are increasing, then the parallel and sequential dynamics do not share any dynamical cycle.

The last chapter presents an algorithm that allows to filter out the dynamical cycles for the Boolean networks which associated graph has only positive circuits. This algorithm is polynomial and it can be used to find a fixed point of the Boolean network in polynomial time. Also it returns a new Boolean network with the same fixed points than the input Boolean network but without any cycle. We note that in this procedure, positive circuits are turned into positive loops. In the resultant network, the fact that we have only positive loops prevent the existence of cycles in the dynamical behavior. This behavior is similar to the behavior of Boolean networks with graph by layers.

6.3 Open problems

In the problem of covering by squares an open problem is the non-regular case without bound for the size of the squares.

In Boolean networks we have several open problems. In robustness, given a Boolean network, we would like to count the number of equivalence classes of update schedules and to estimate the size of these equivalence classes. Also, we want to study the robustness of the attractors with respect to other variables, for example the conectivity, i.e. what happens with attractors if we remove or add an arc. In this case the fixed points can be affected too.

In sequential Boolean networks we are interested to know what happens if the associated graph has any negative circuit. From experimental information, we have observed that the algorithm finds a sequence of dynamical behavior. This sequence is reached in a linear number of iterations of the algorithm.

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Covering by squares

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