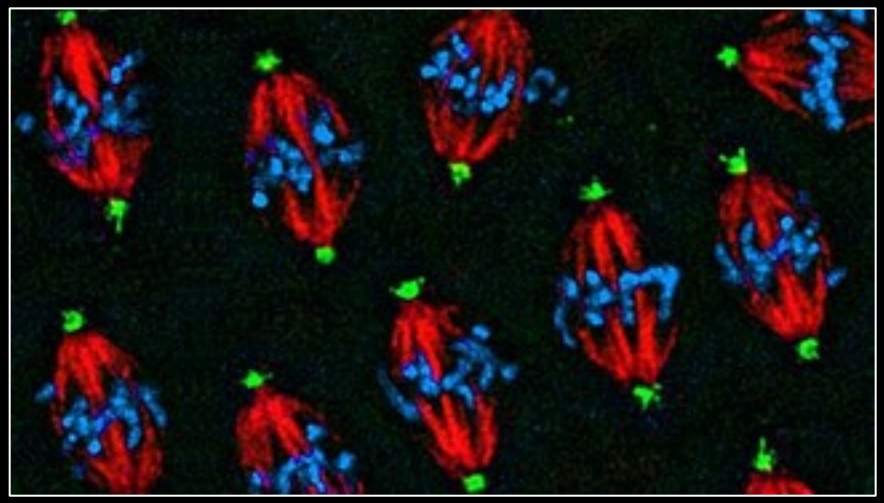
AÜTF Dönem-1; 2017-2018.

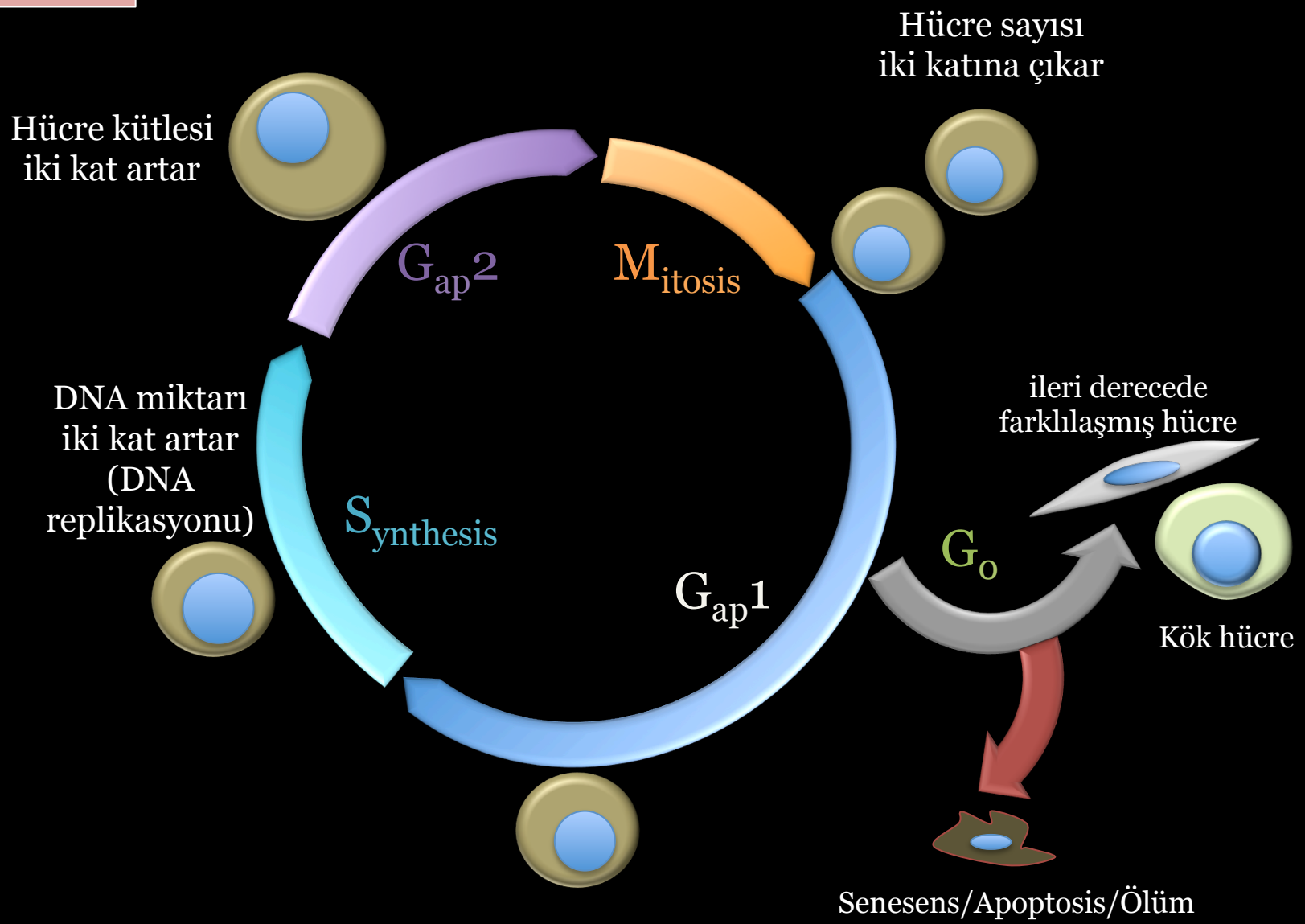


Hücre Bölünmesi Mekaniği ve Sitokinez

Prof.Dr. Alp Can
Histoloji-Embriyoloji
Anabilim Dalı

www.alpcan.com

Hücrenin Yaşam Döngüsü

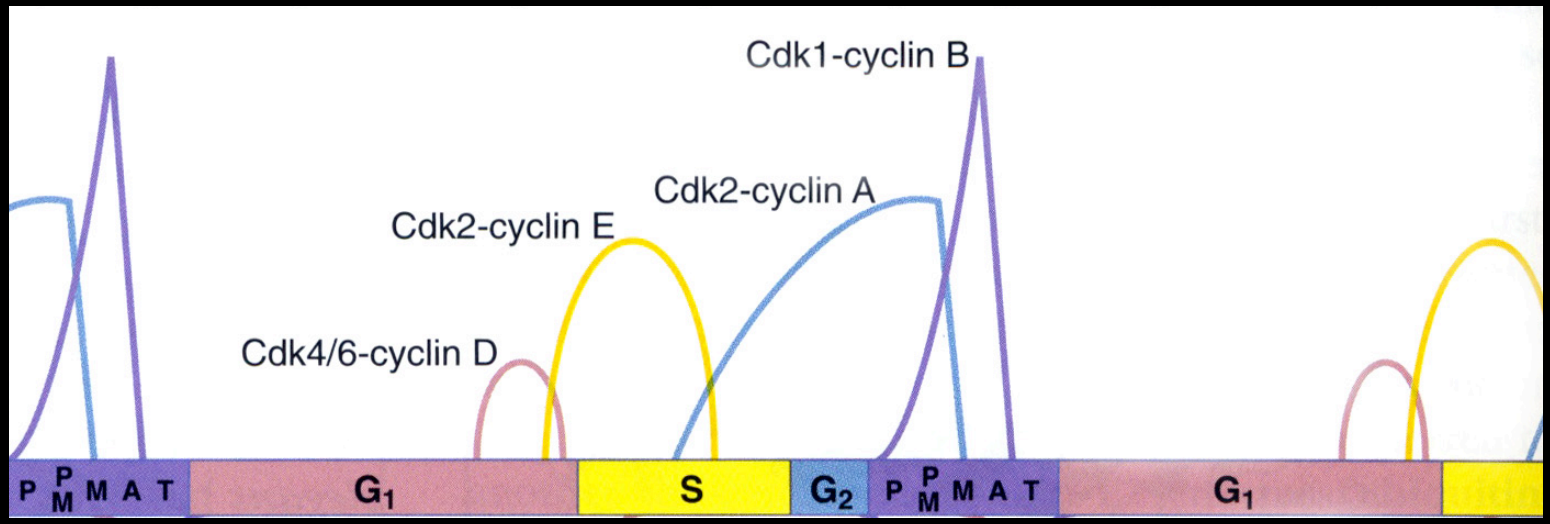


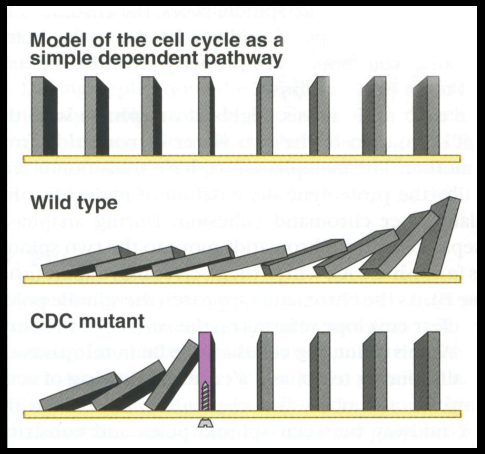
Siklin (Cyclin) ve Siklin Bağımlı Kinazlar (CDK)

- Hücre döngüsünün ilerlemesinde yer alan bir grup protein.
- Siklinler, siklin bağımlı kinazlarla birleşerek bunların protein kinaz işlevini aktive ederler.
- Adlarına uygun olarak hücre döngüsü süresince yapım ve yıkım döngüleri geçirirler.
- Sitoplazma düzeyleri düşünce CDK'lardan ayrılırlar ve böylece onların enzim aktivitelerinin düşmesine neden olurlar.

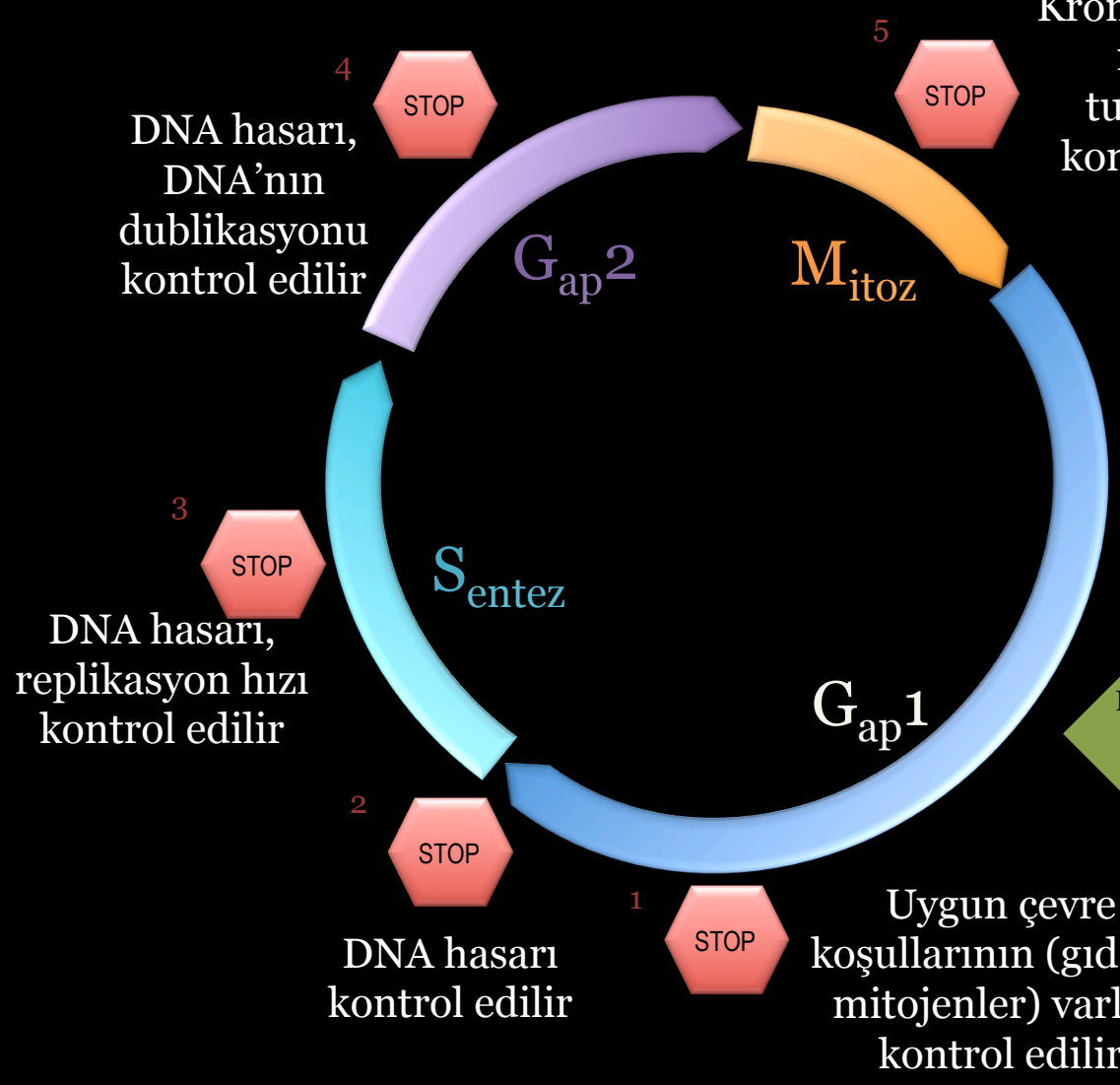
CDK'lar (sabit)	Siklin'ler (dalgalı)	
CDK-1 ($p34^{cdc2}$)	Cyclin-A	CDK-1/Cyclin-B
CDK-2	Cyclin-B	CDK-2/Cyclin-E
CDK-4	Cyclin-D	CDK-2/Cyclin-A
CDK-6	Cyclin-E	CDK-4/Cyclin-D
CDK-7 (RNA replikasyonu)		CDK-6/Cyclin-D

CDK aktivitesi





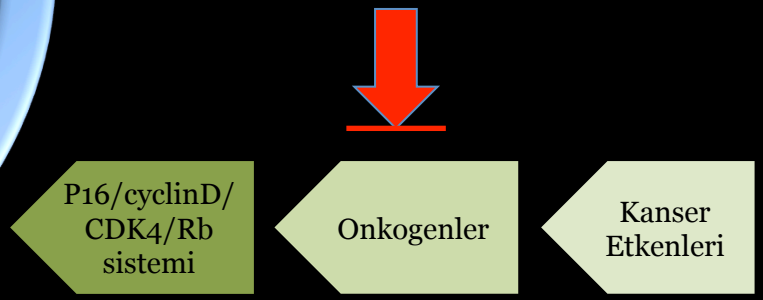
Hücrenin Döngüsündeki Kontrol Noktaları

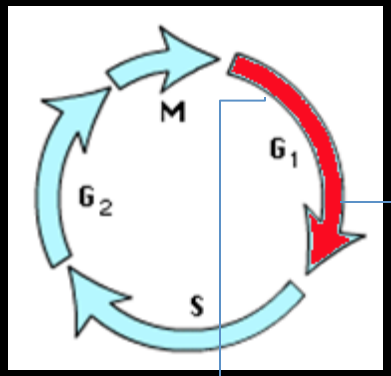


kültür hücresinde fazların uzunlukları

Faz	Süre (saat)
G1	10
S	7,5
G2	3,5
M	1,0
Yeni bir hücrenin oluşma zamanı	22

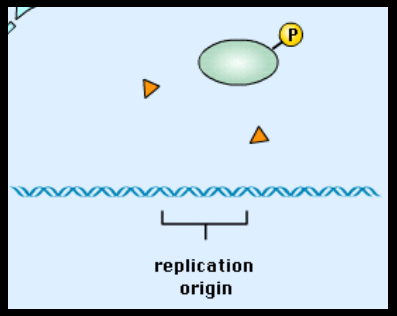
Tümör baskılayıcı genler



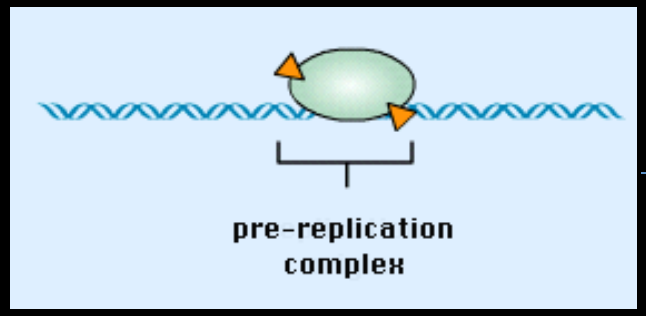


Geç G1

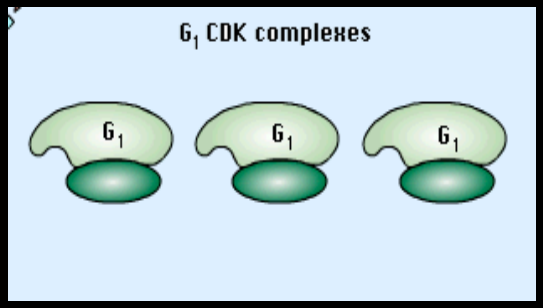
Erken G1



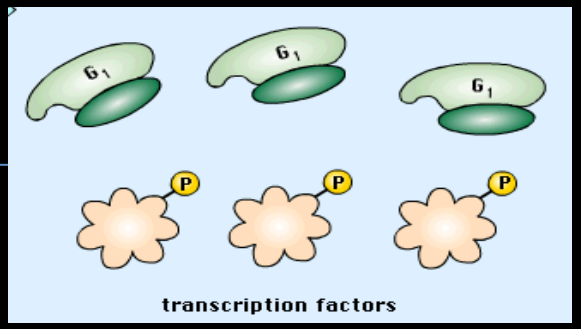
DNA prereplikasyon kompleksi defosforile olur.



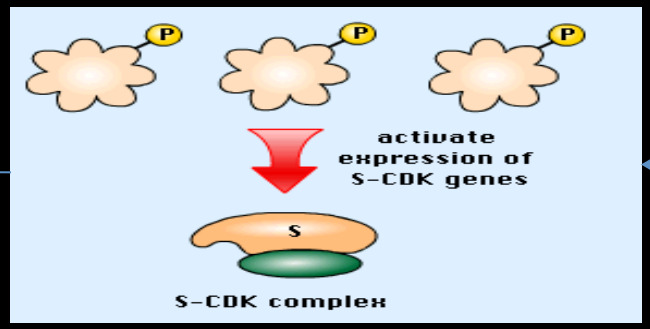
ve kromozomlarında replikasyonun başlayacağı bölgeye tutunur.



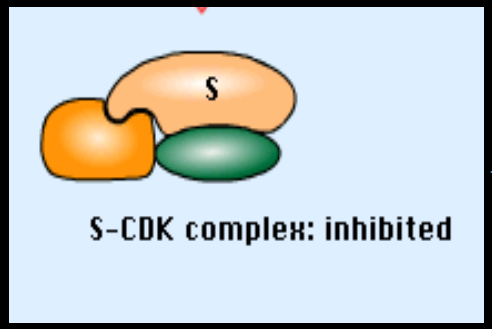
G_1 CDK kompleksleri sentezlenir



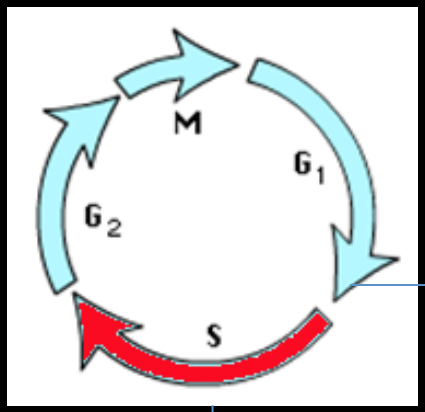
CDK kompleksleri transkripsiyon faktörlerini fosforile ederek aktifleştirir



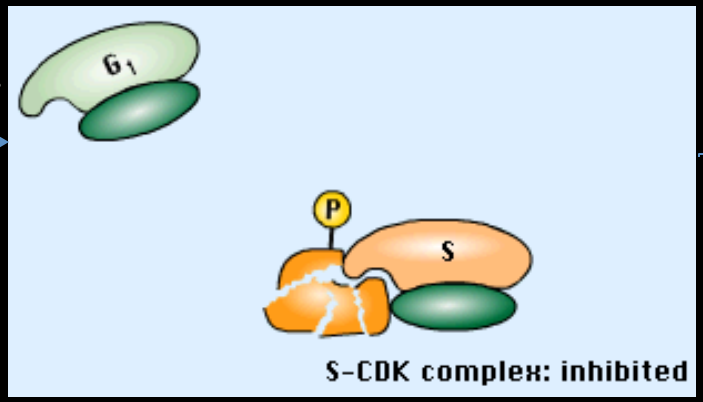
Transkripsiyon faktörleri S fazı CDK genlerini aktive eder



Bu aşamada S fazı CDK spesifik inhibitörü ile blokedir



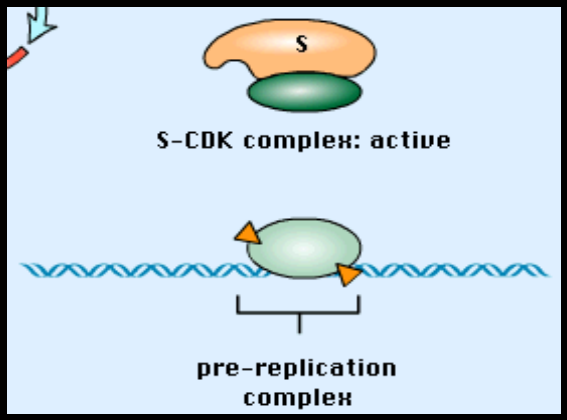
G_1-S geçişi



S fazının başlangıcı

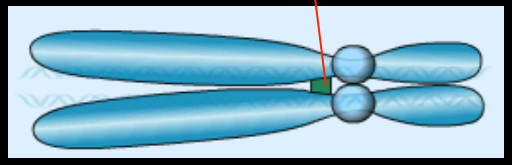
Bir G_1-CDK kompleksi S-CDK kompleksini fosforile ederek onu parçalar ve inhibisyonu kaldırır

S fazı boyunca

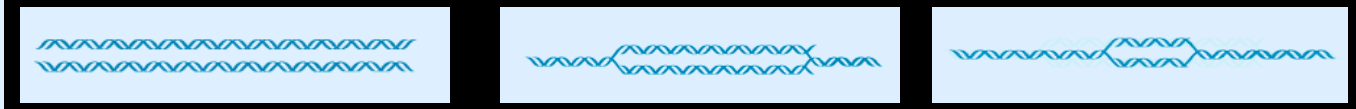


S-CDK kompleksi prereplikasyon kompleksini fosforile ederek onun bir kez replikasyonunu sağlar

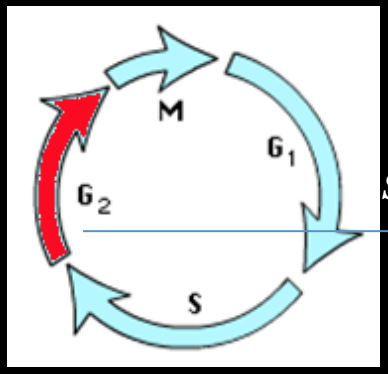
Kohezin



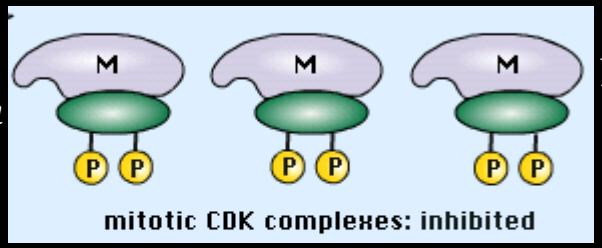
İki kardeş kromatid oluşur



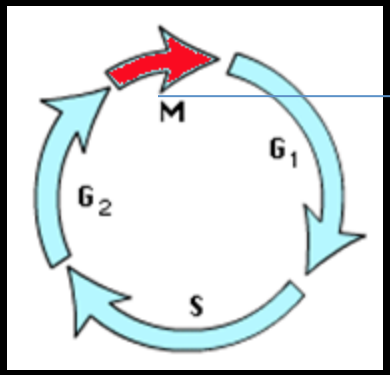
Her kromozom kendilerini eşler



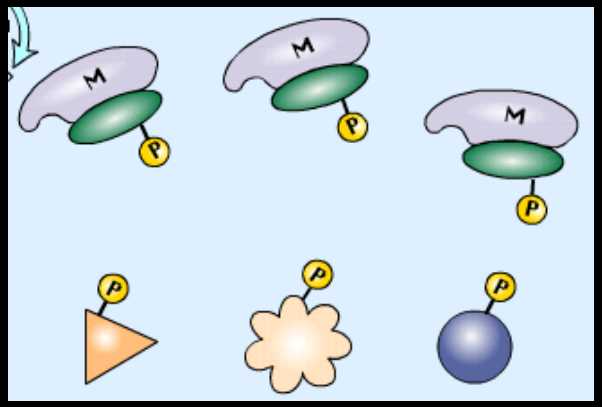
S fazının sonu ve G_2 fazı



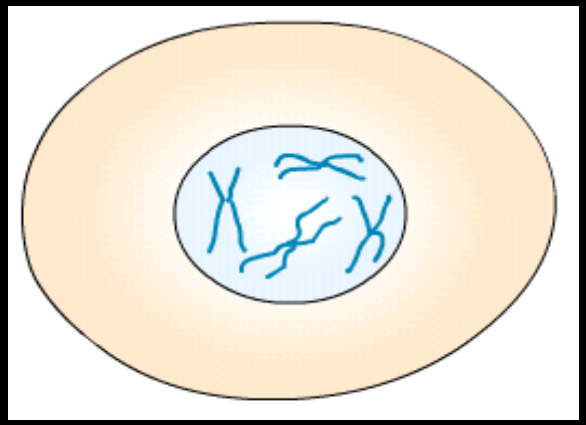
Mitotik CDK kompleksleri sentezlenir ancak aktiviteleri DNA sentezi bitene kadar durdurulmuştur



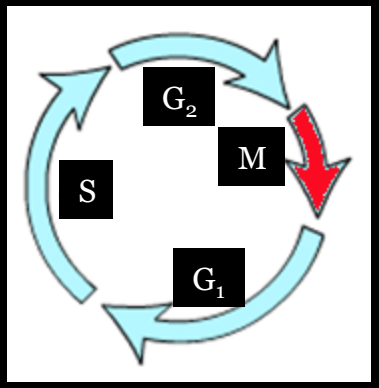
M fazı

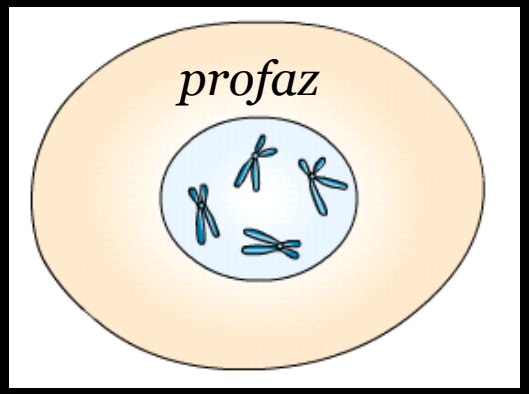


Mitotik CDK kompleksleri M fazında aktifleşir ve bir takım sübstratları fosforile eder

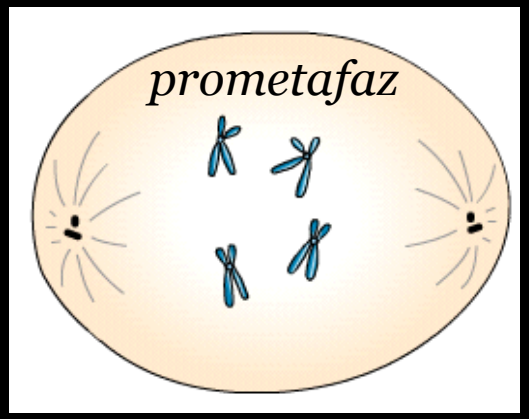


Böylece mitozun ilk aşaması başlar



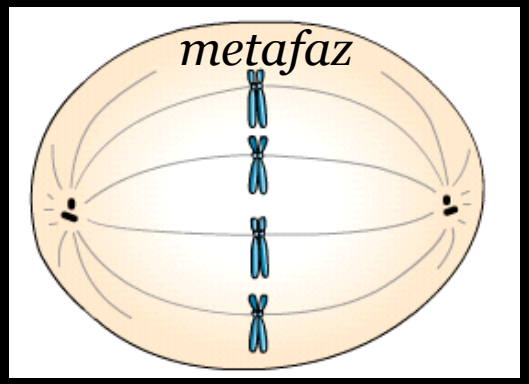


Kromozomlar paketlenir

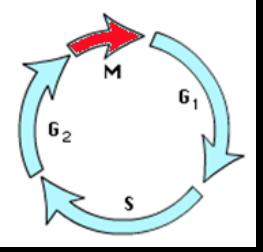


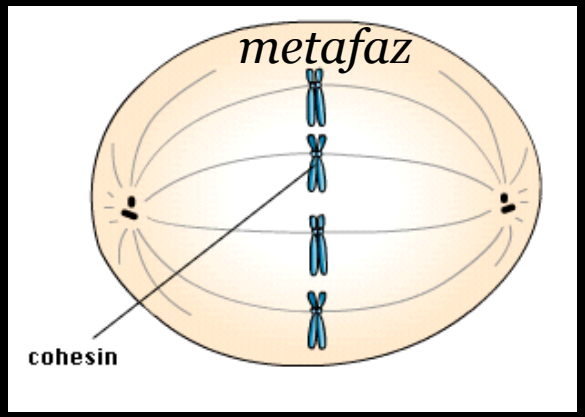
Sentrozomlar karşı kutuplara göç eder

Mekik oluşur

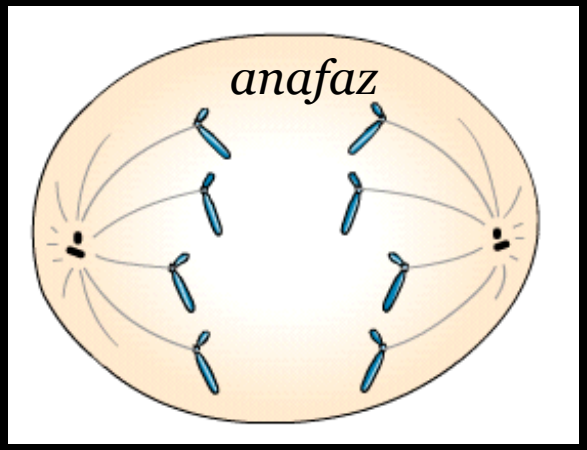


Anafaz Uyarıcı Kompleks (APC) aktive olur

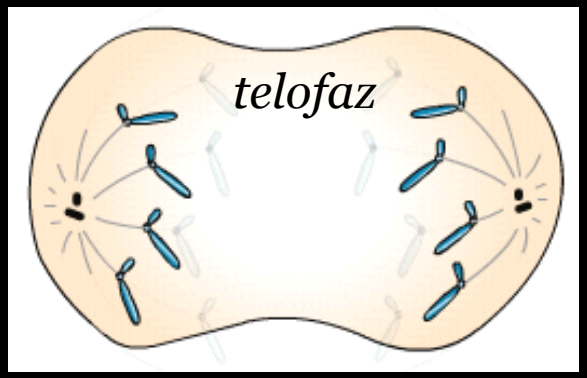




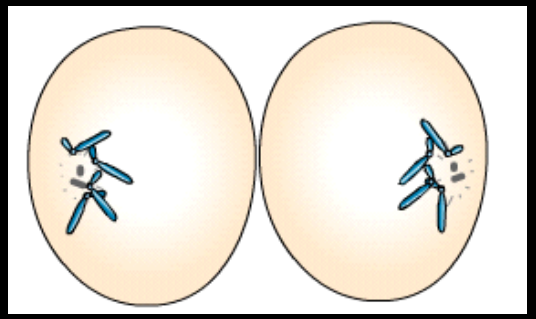
Aktif APC, kohezin düzenleyicilerini parçalar



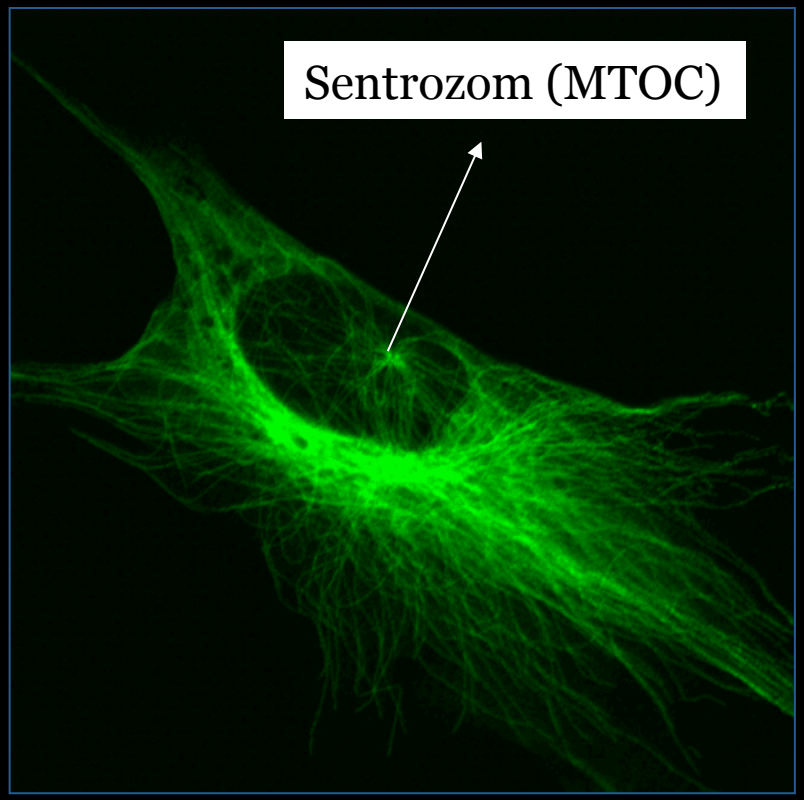
Kardeş kromatidler birbirinden ayrılır



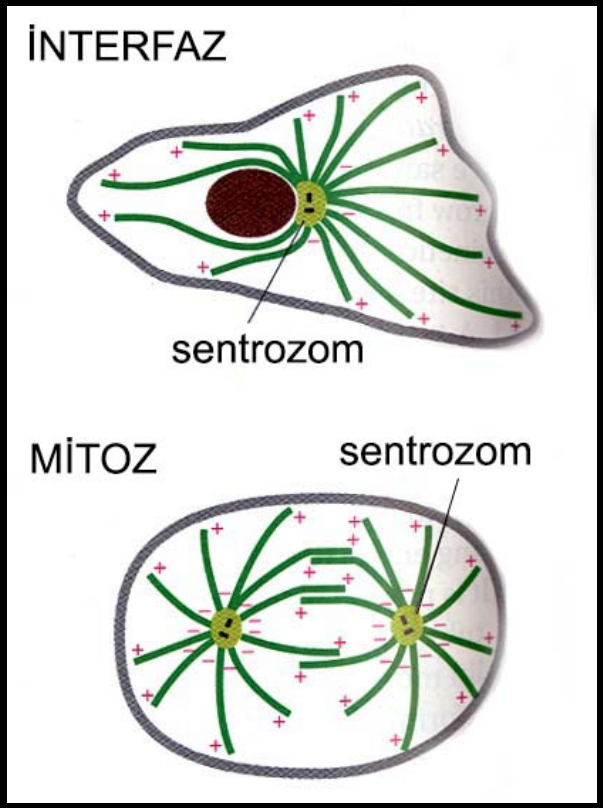
APC, M-CDK kompleksini de parçalayarak mitozun sona ermesini sağlar



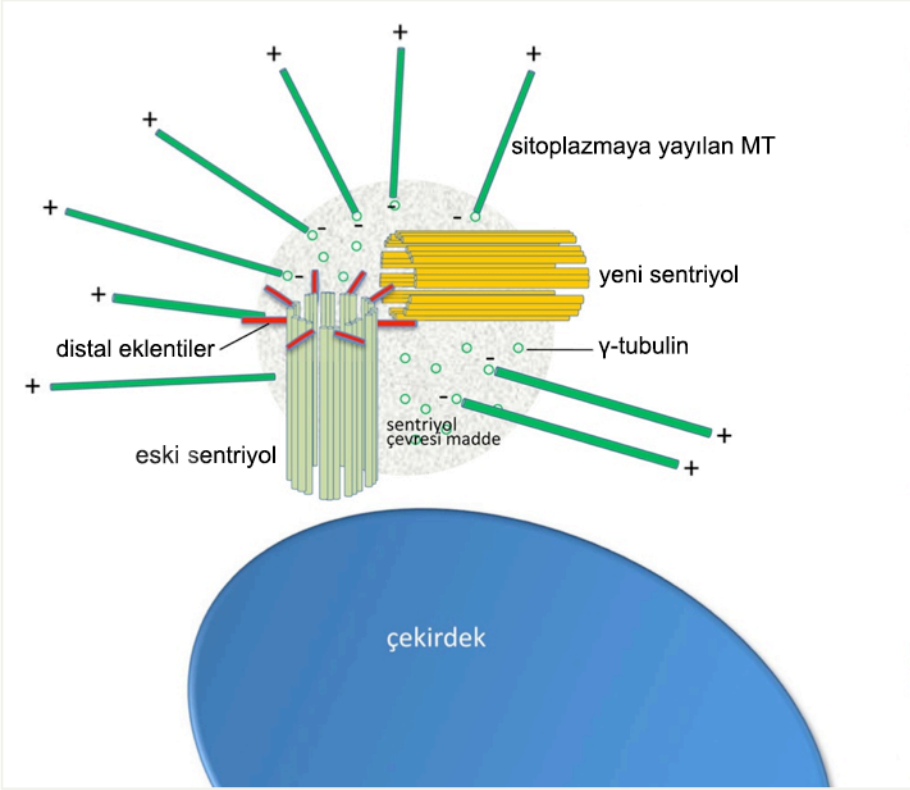
Sentrozom
(Hücre Merkezi)
(Mikrotübülüs Düzenleyici Merkez (MTOC)

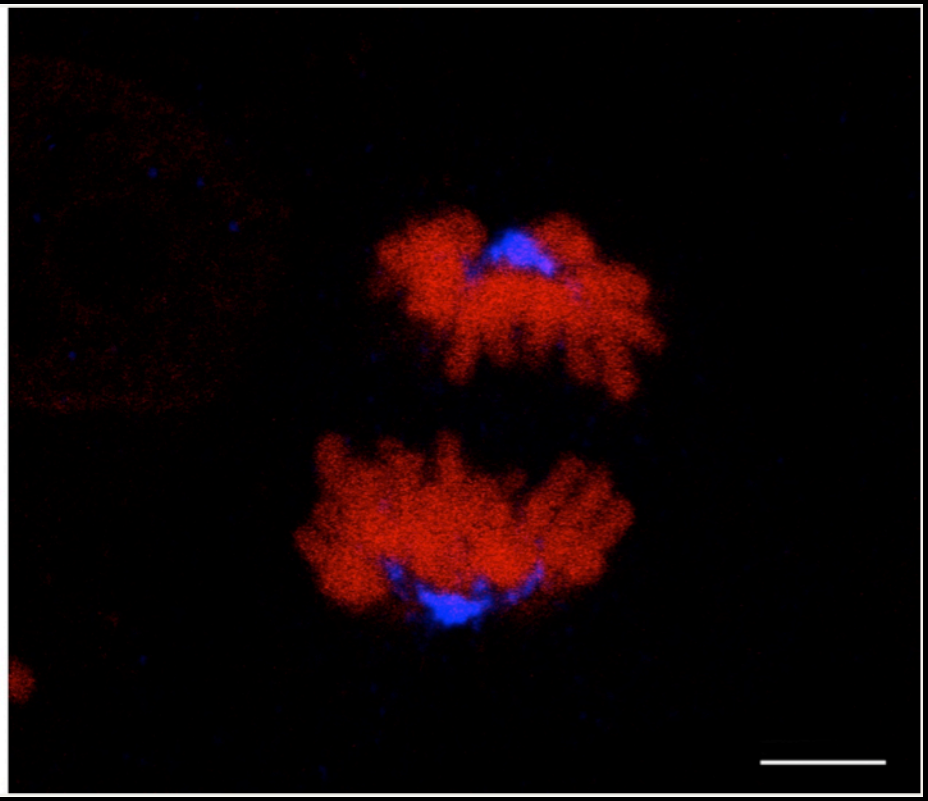


A. Can, 1997



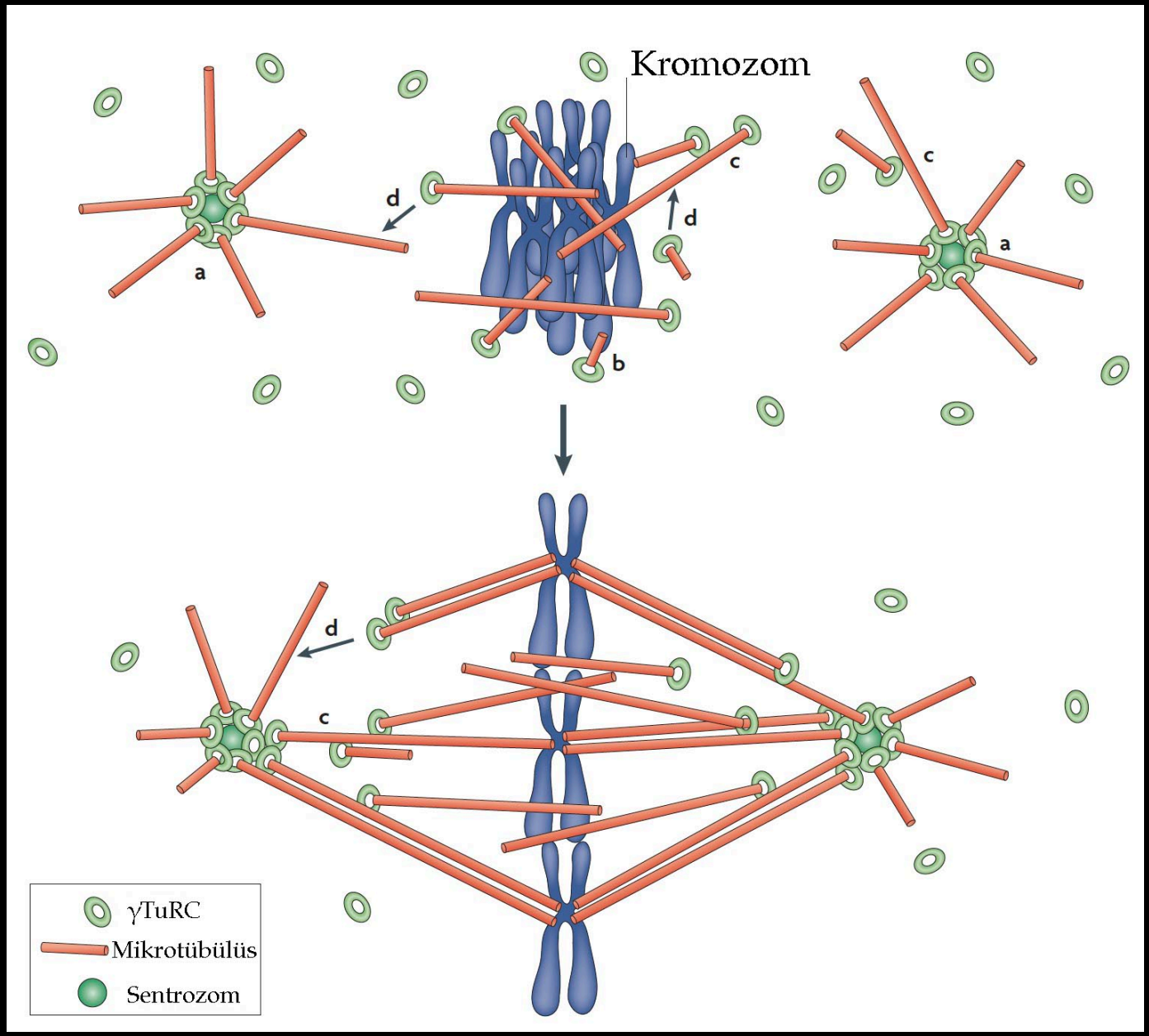
Sentrozom



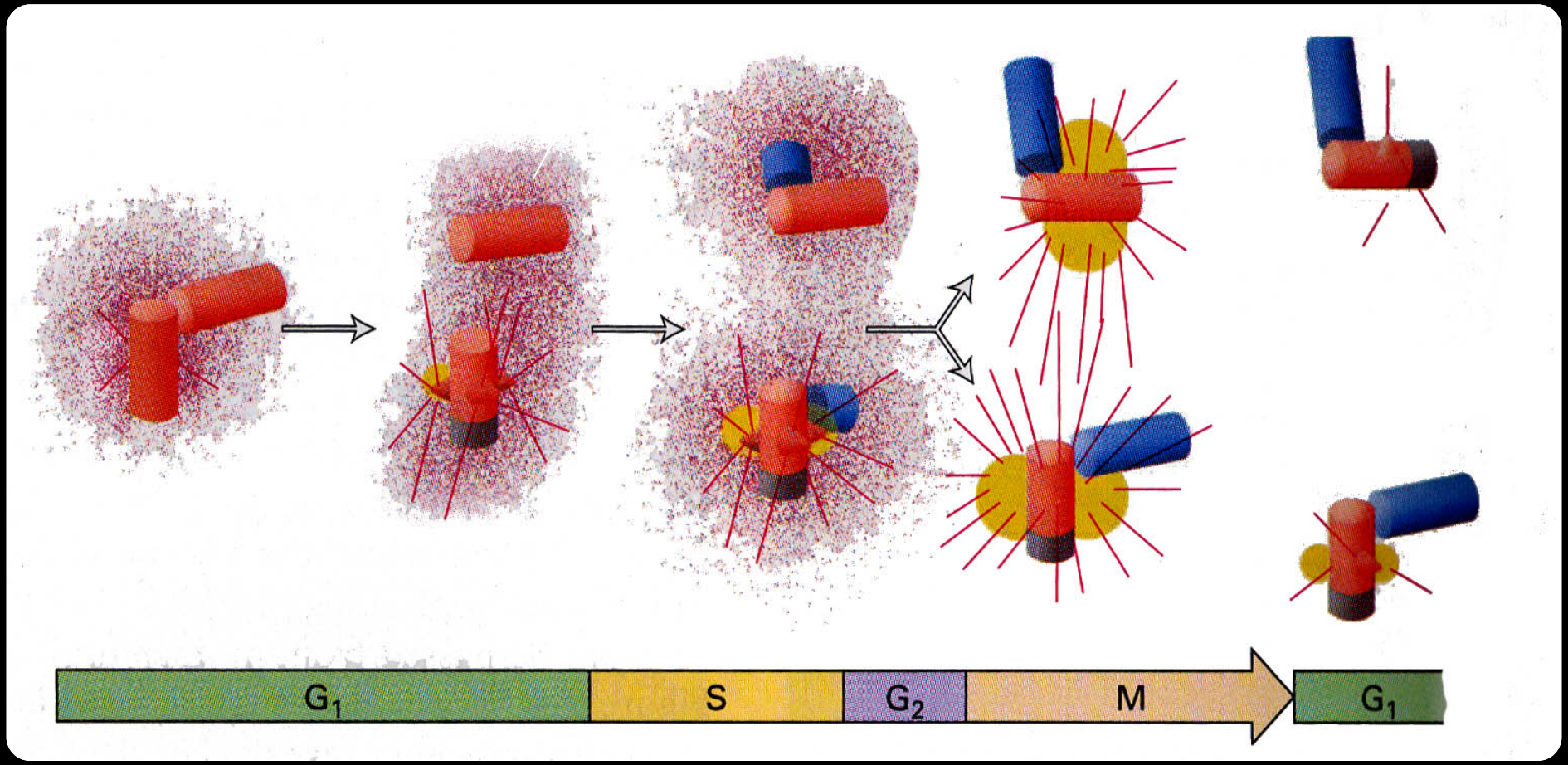


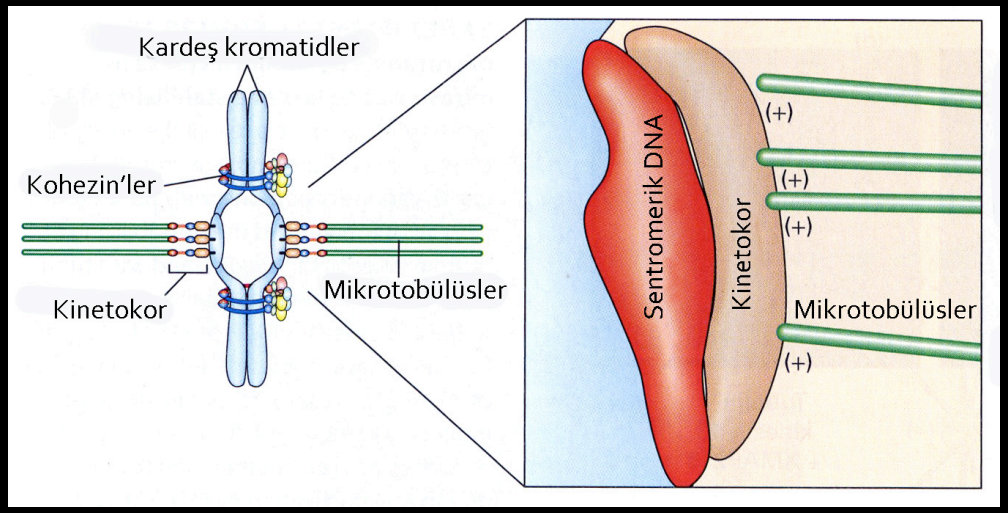
Perisentriyoler Materyal: >120 farklı protein tipi

Can ve Oktar, 2010

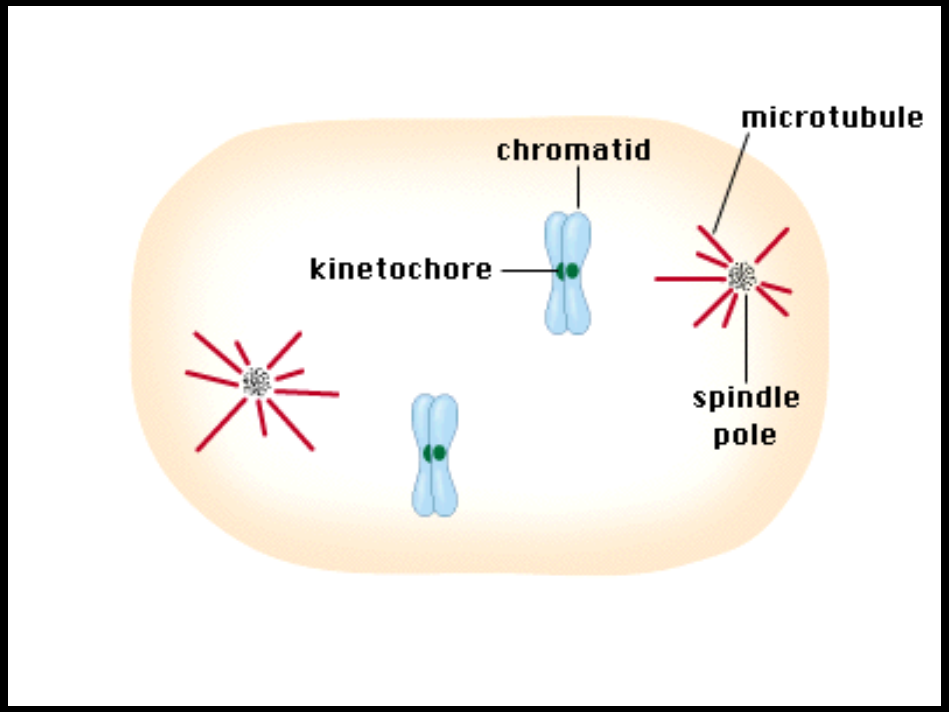

Kromozom
a
d
b
c
d
c
a
d
c
γTuRC
Mikrotübülüs
Sentrozom

Sentrozom eşlemesi tüm döngü boyunca sürer



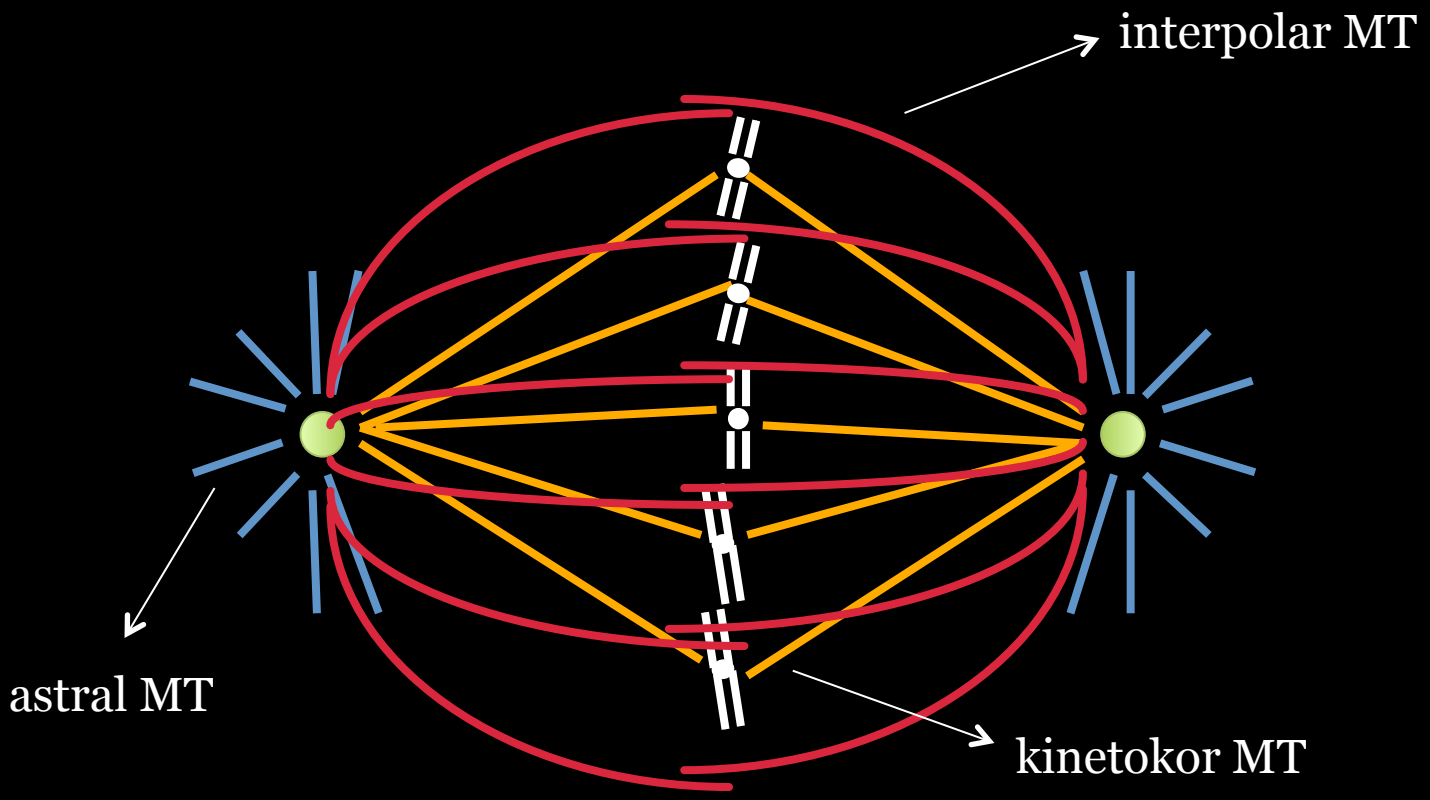


Kinetokor kromozom ilişkisi

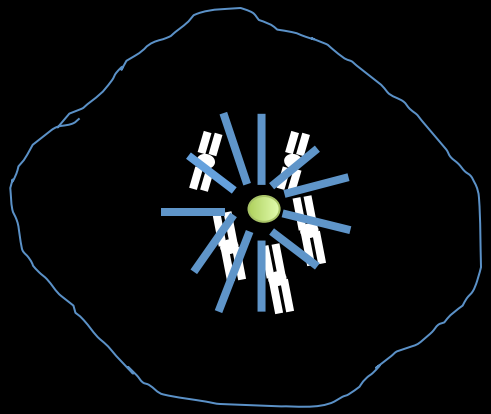


MİTOZ MEKİĞİ

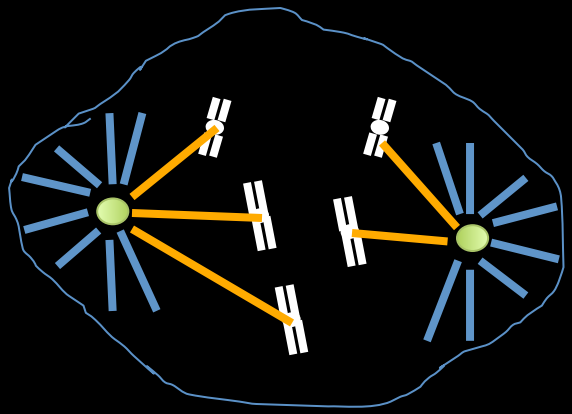
(sentrozomlarca kontrol edilir)



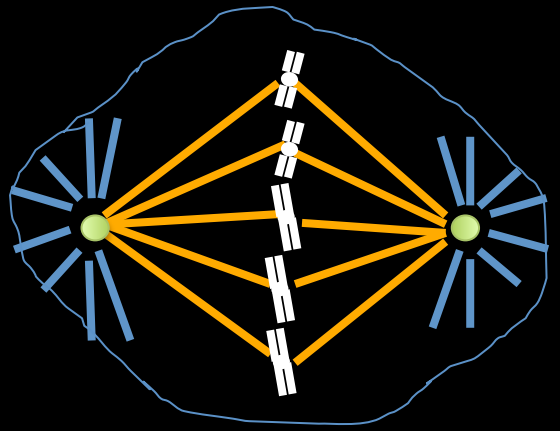
Profaz



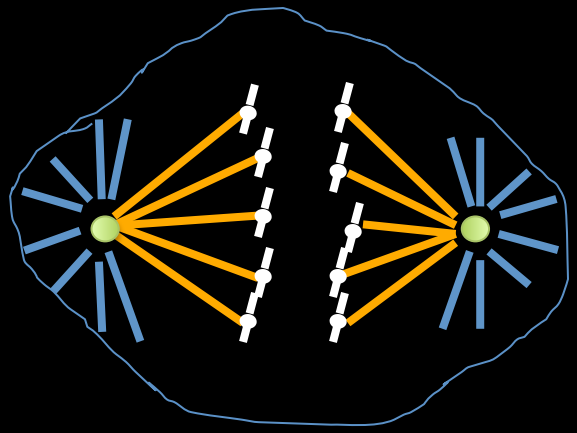
Prometafaz



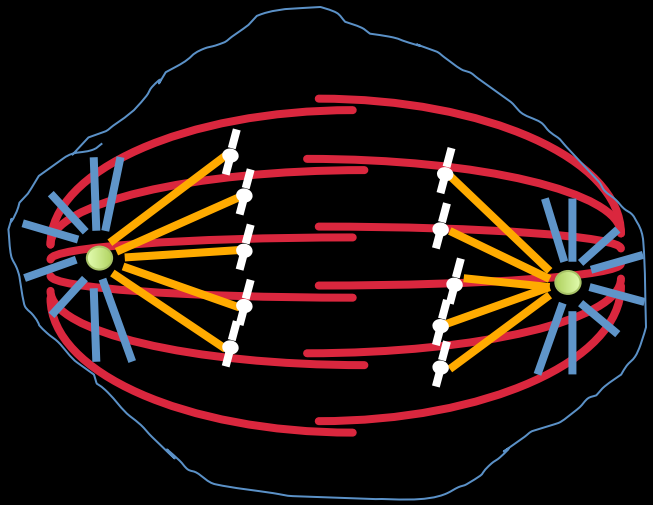
Metafaz



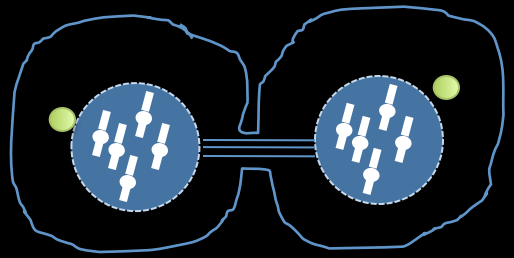
Anafaz-A

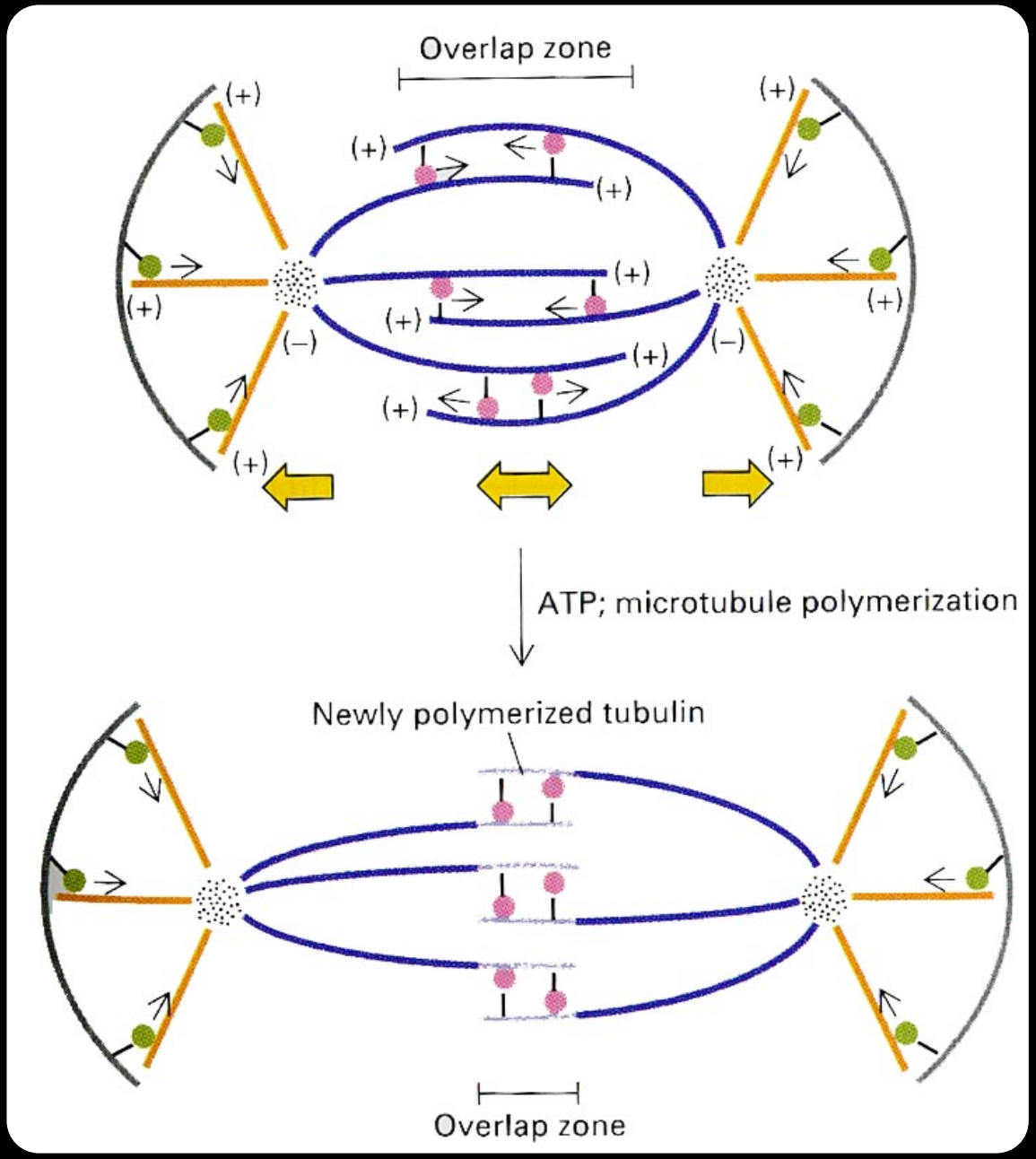


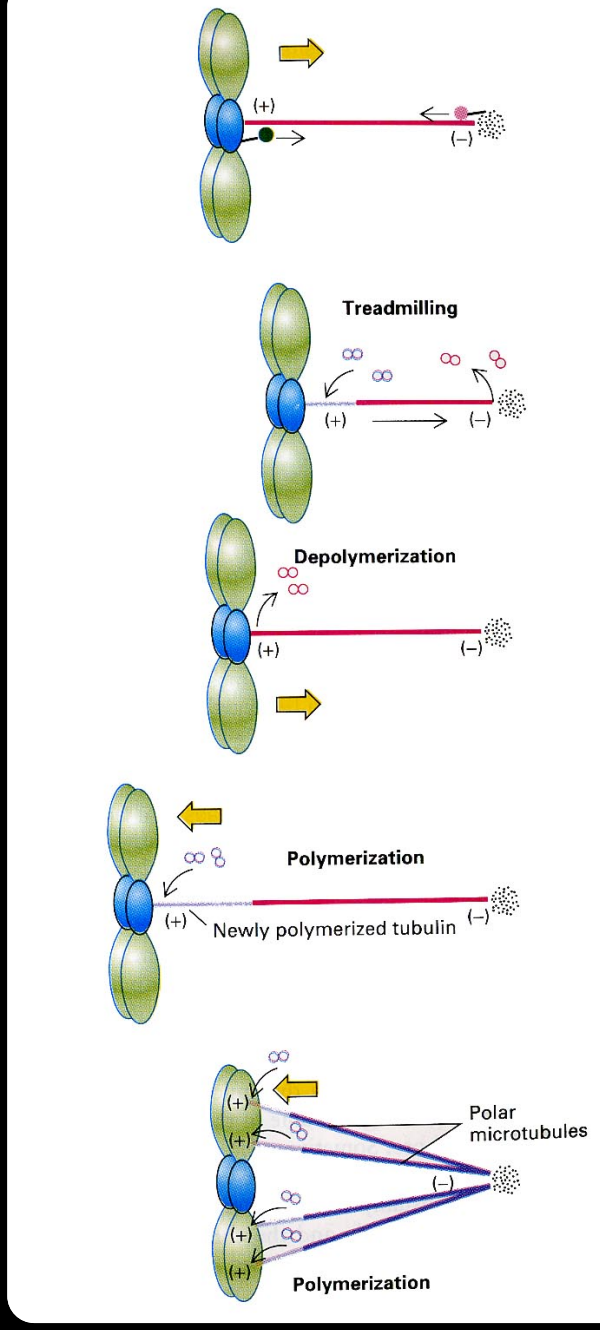
Anafaz-B



Telofaz







Kinesin 5 (CENP-E)
Dynein