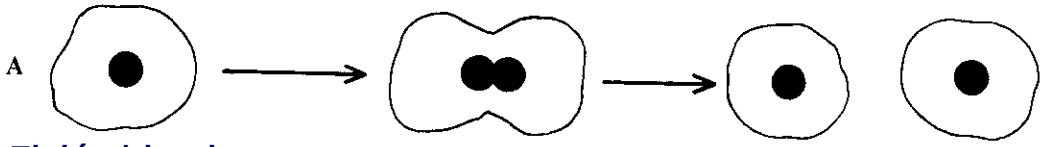
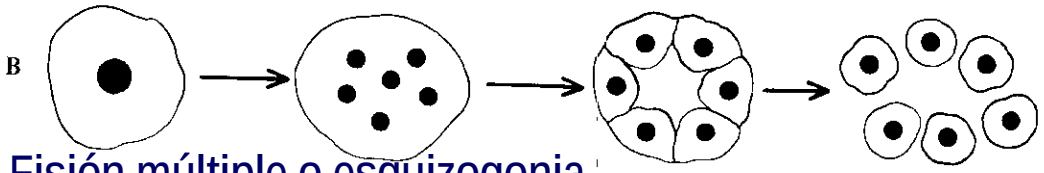
Genética de protozoos

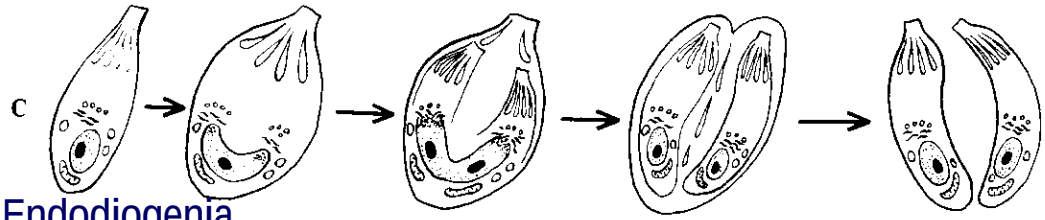
Reproducción asexuada



Fisión binaria

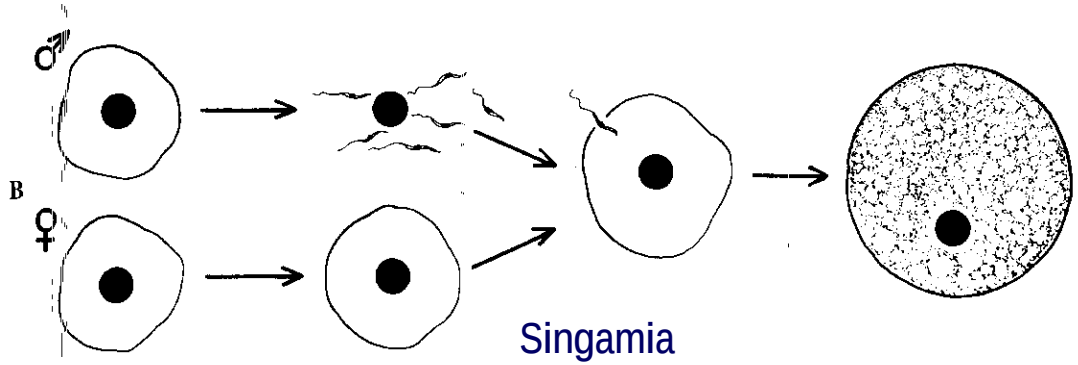


Fisión múltiple o esquizogonia

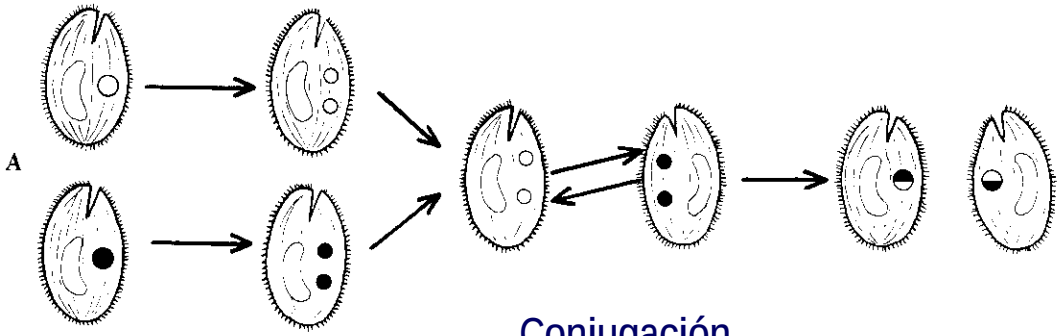


Endodiogenia

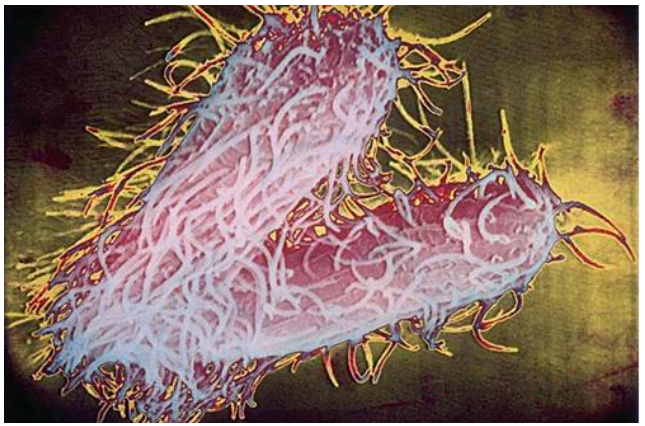
Reproducción sexuada



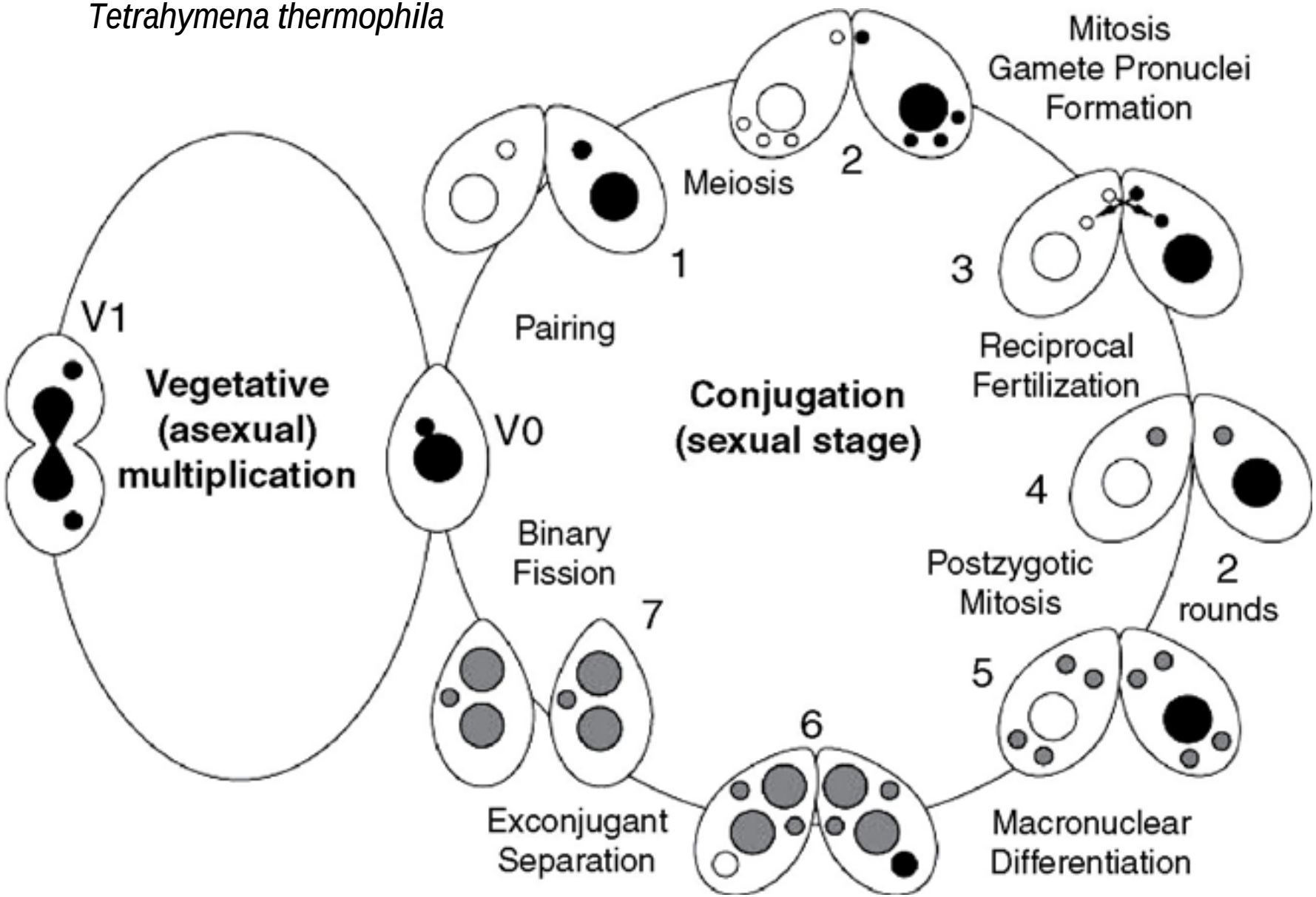
Singamia

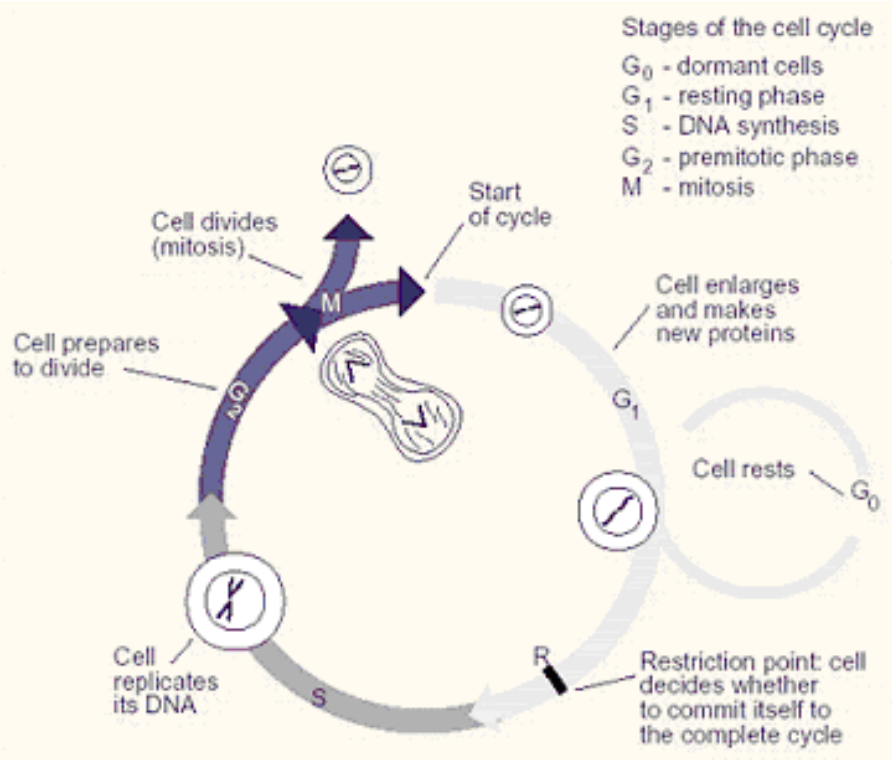


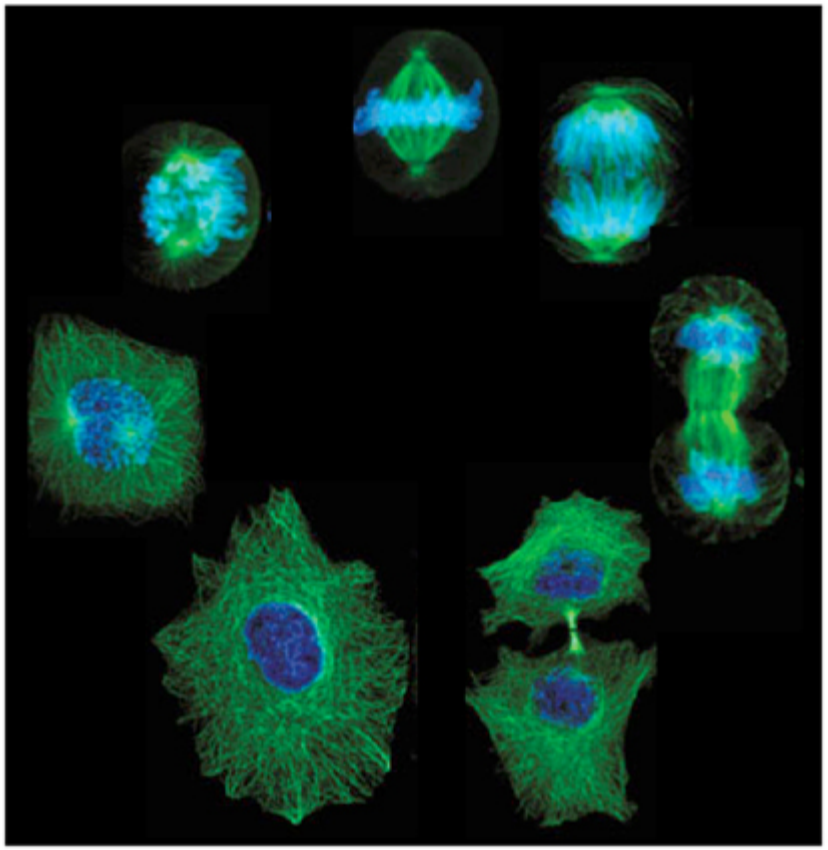
Conjugación

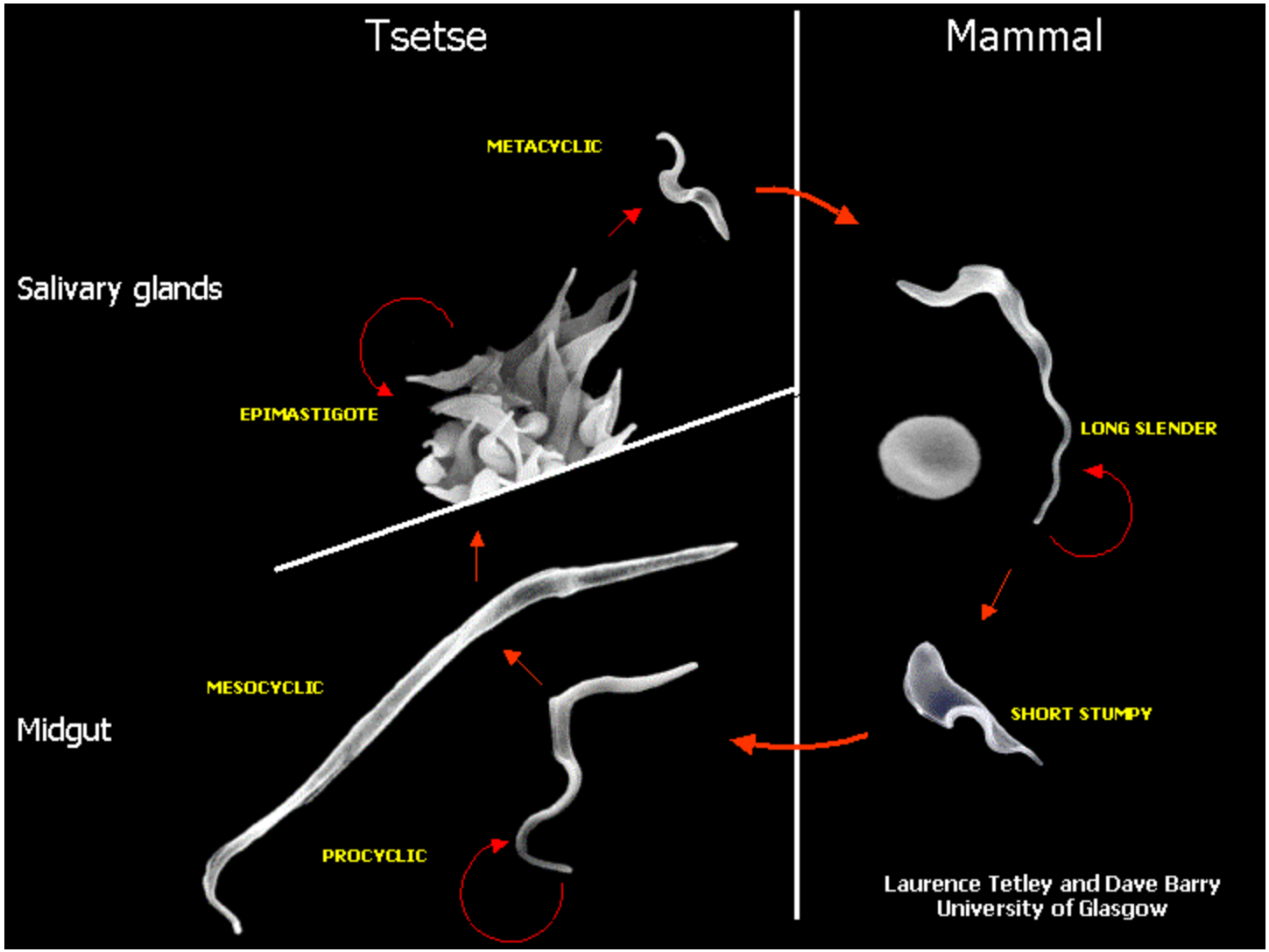


Tetrahymena thermophila

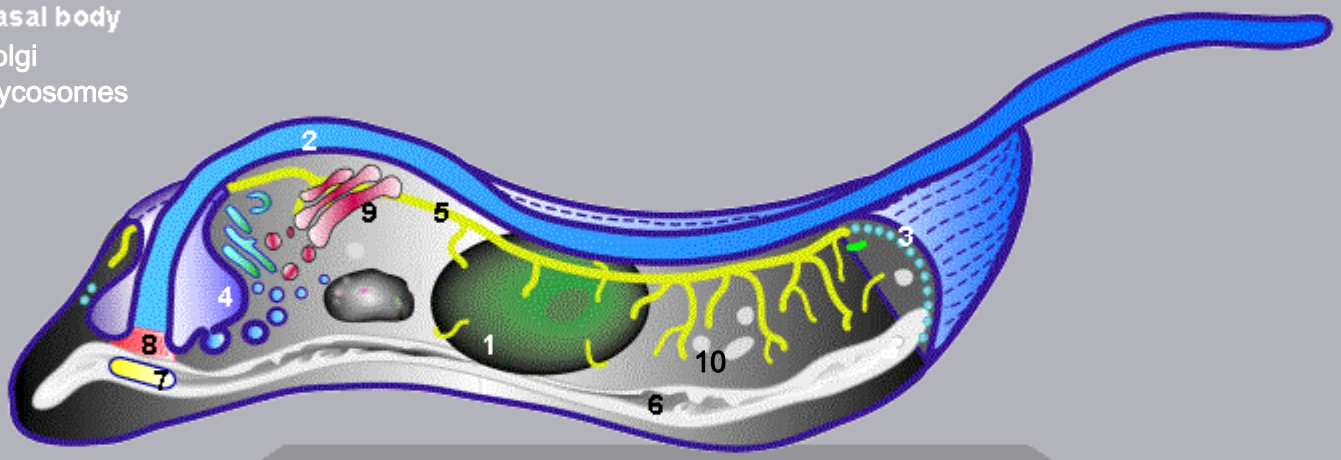



Stages of the cell cycle
G_0 - dormant cells
G_1 - resting phase
S - DNA synthesis
G_2 - premitotic phase
M - mitosis
Start of cycle
Cell divides (mitosis)
Cell enlarges and makes new proteins
Cell prepares to divide
G_1
Cell rests
G_0
Cell replicates its DNA
S
R
Restriction point: cell decides whether to commit itself to the complete cycle

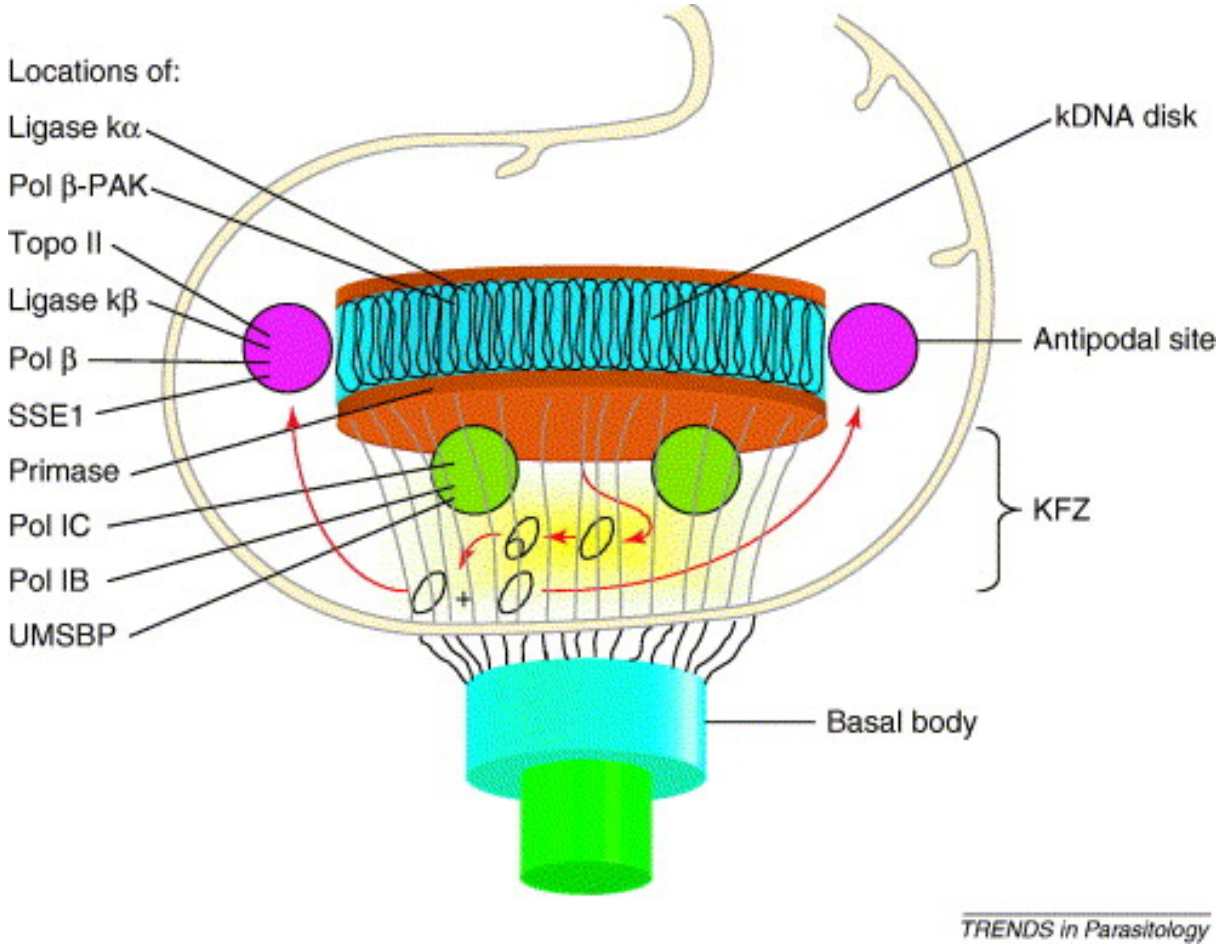



Tsetse
Mammal
METACYCLIC
Salivary glands
EPIMASTIGOTE
LONG SLENDER
MESOCYCLIC
Midgut
SHORT STUMPY
PROCYCLIC
Laurence Tetley and Dave Barry
University of Glasgow

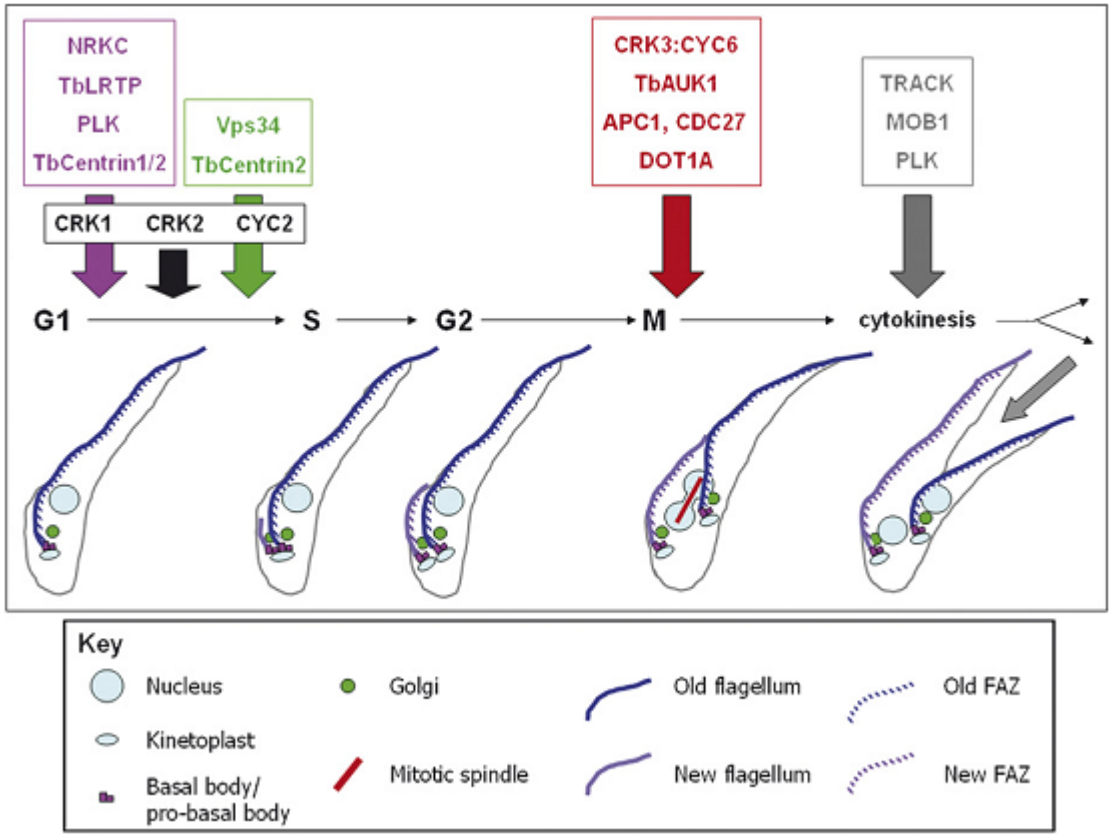
1 nucleus
2 flagellum
3 subpellicular microtubules
4 flagellar pocket
5 endoplasmic reticulum
6 mitochondrion
7 kinetoplast
8 basal body
9 golgi
10 glycosomes



Markus Engstler
Ludwig-Maximilians-Universitaet
Muenchen



TRENDS in Parasitology


NRKC
TbLRTP
PLK
TbCentrin1/2
Vps34
TbCentrin2
CRK3:CYC6
TbAUK1
APC1, CDC27
DOT1A
TRACK
MOB1
PLK
CRK1
CRK2
CYC2
G1
S
G2
M
cytokinesis
Key
Nucleus
Kinetoplast
Basal body/
pro-basal body
Golgi
Mitotic spindle
Old flagellum
New flagellum
Old FAZ
New FAZ

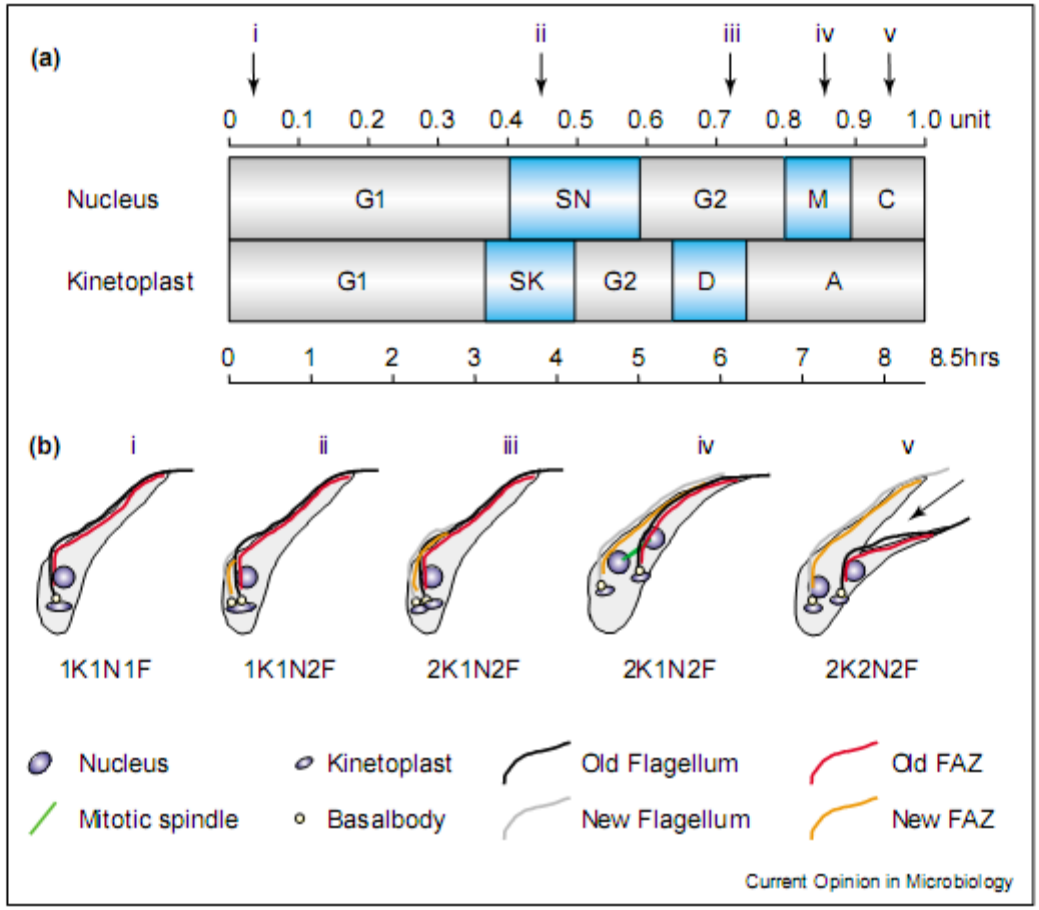
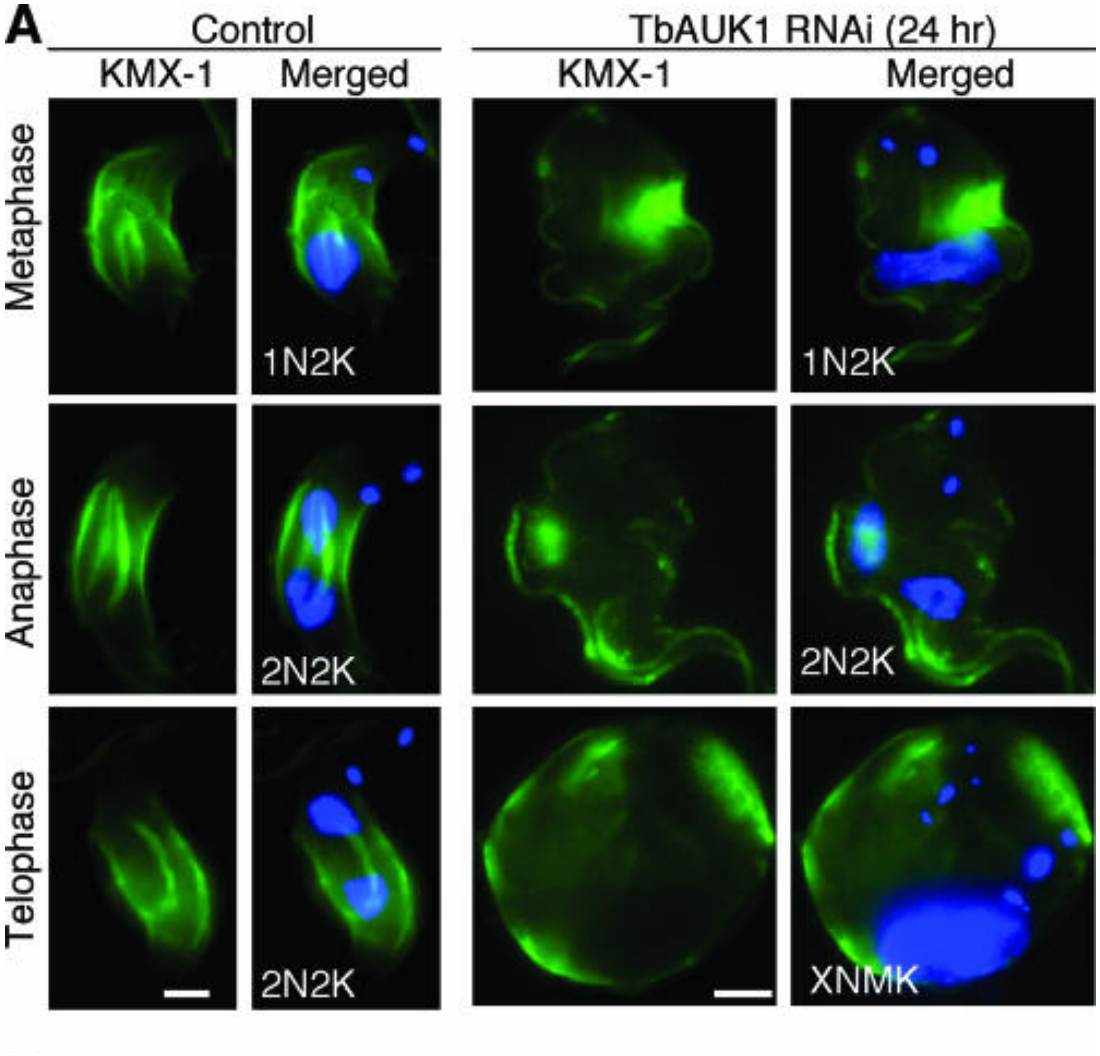
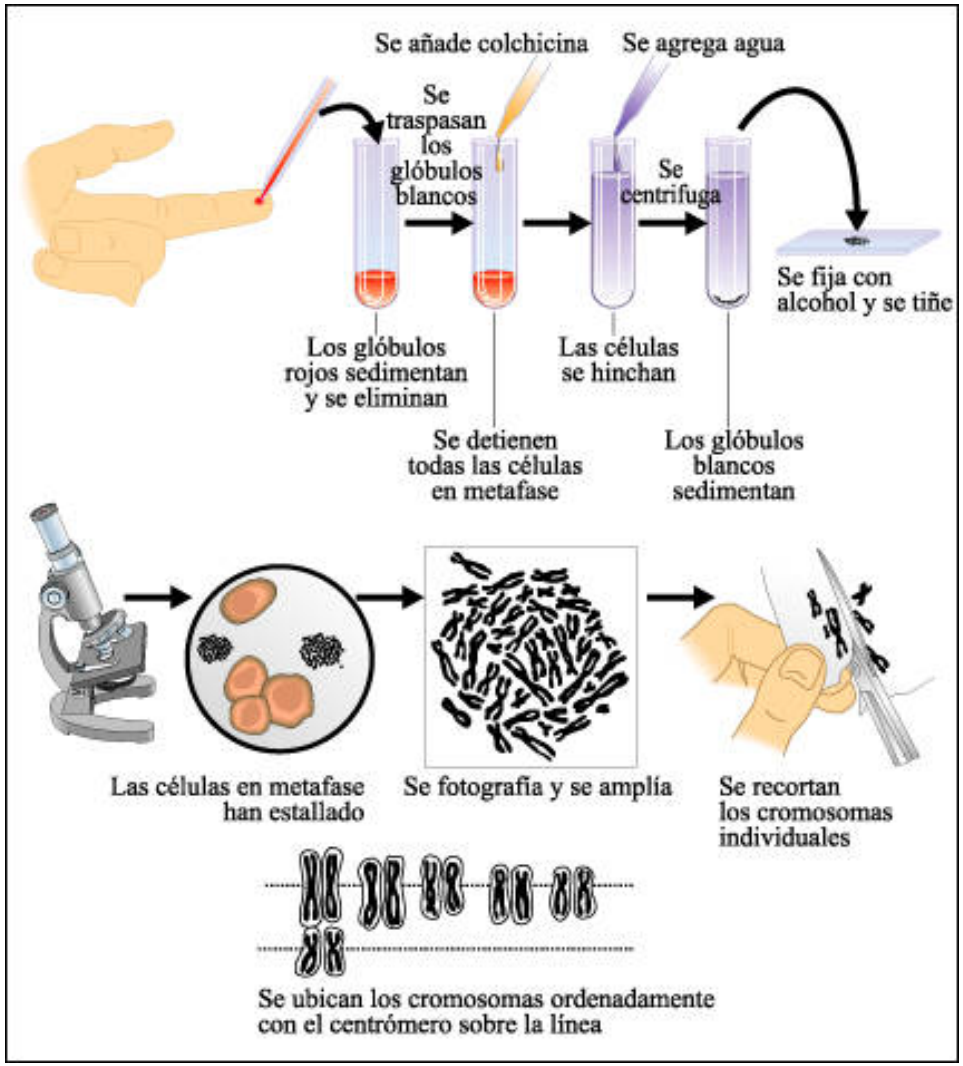


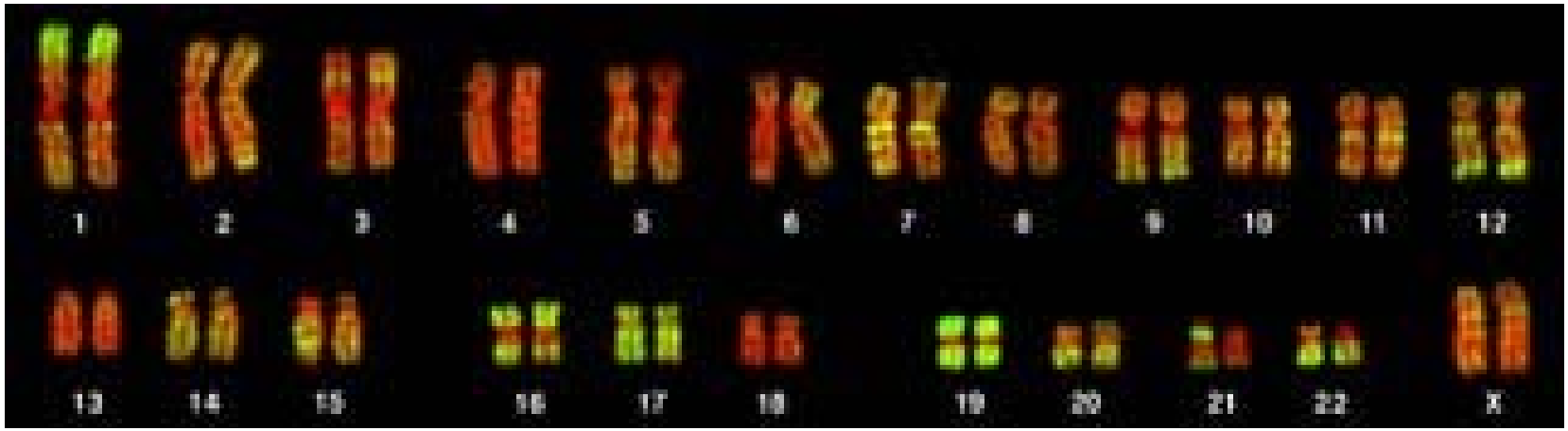
Diagram showing the major morphological events of the procyclic *T. brucei* cell cycle on the basis of data in [11,12] **(a)** The trypanosome cell cycle is separated into nuclear and kinetoplast components. Cell cycle duration for exponentially growing procyclic trypanosomes is 8.5 h. Kinetoplast replication (S) initiates before nuclear S phase, but is considerably shorter and consequently kinetoplast segregation (D) occurs before the onset of nuclear mitosis (M). The phase annotated on the kinetoplast cycle as 'A' refers to the 'apportioning' phase during which basal bodies continue to move apart. **(b)** Schematic representations of trypanosome cells taken from various time points through the cell cycle. The black arrow indicates the direction and position of the cleavage furrow.



Eukaryot Cell. 2006; 5(7): 1026–1035

CARIOTIPO


Se añade colchicina
Se agrega agua
Se traspasan los glóbulos blancos
Se centrifuga
Se fija con alcohol y se tiñe
Los glóbulos rojos sedimentan y se eliminan
Las células se hinchan
Se detienen todas las células en metafase
Los glóbulos blancos sedimentan
Las células en metafase han estallado
Se fotografía y se amplía
Se recortan los cromosomas individuales
Se ubican los cromosomas ordenadamente con el centrómero sobre la línea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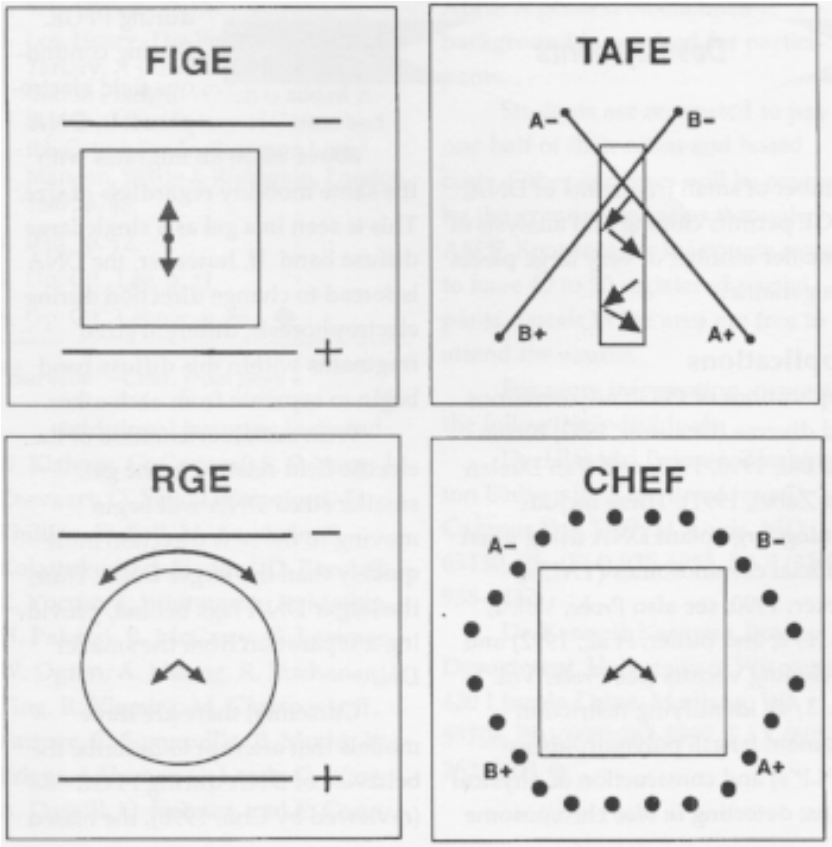
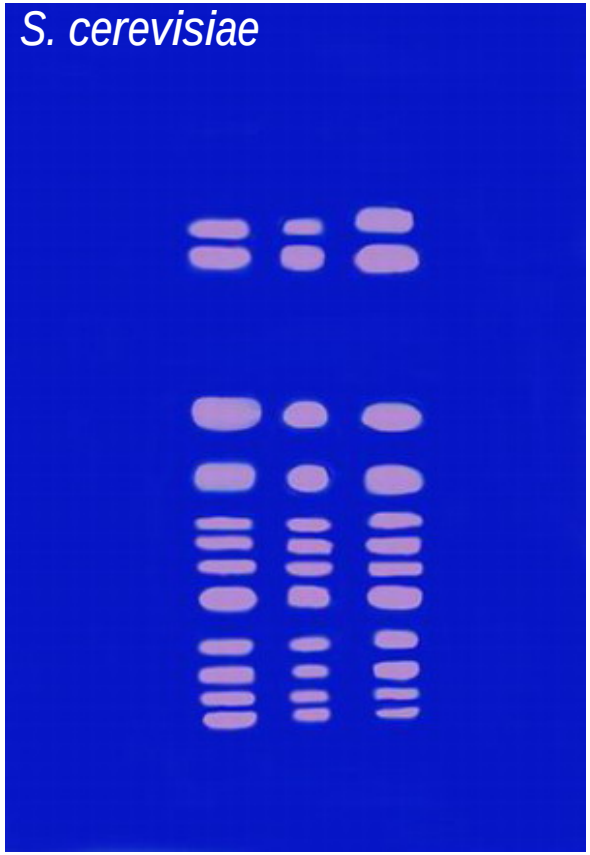
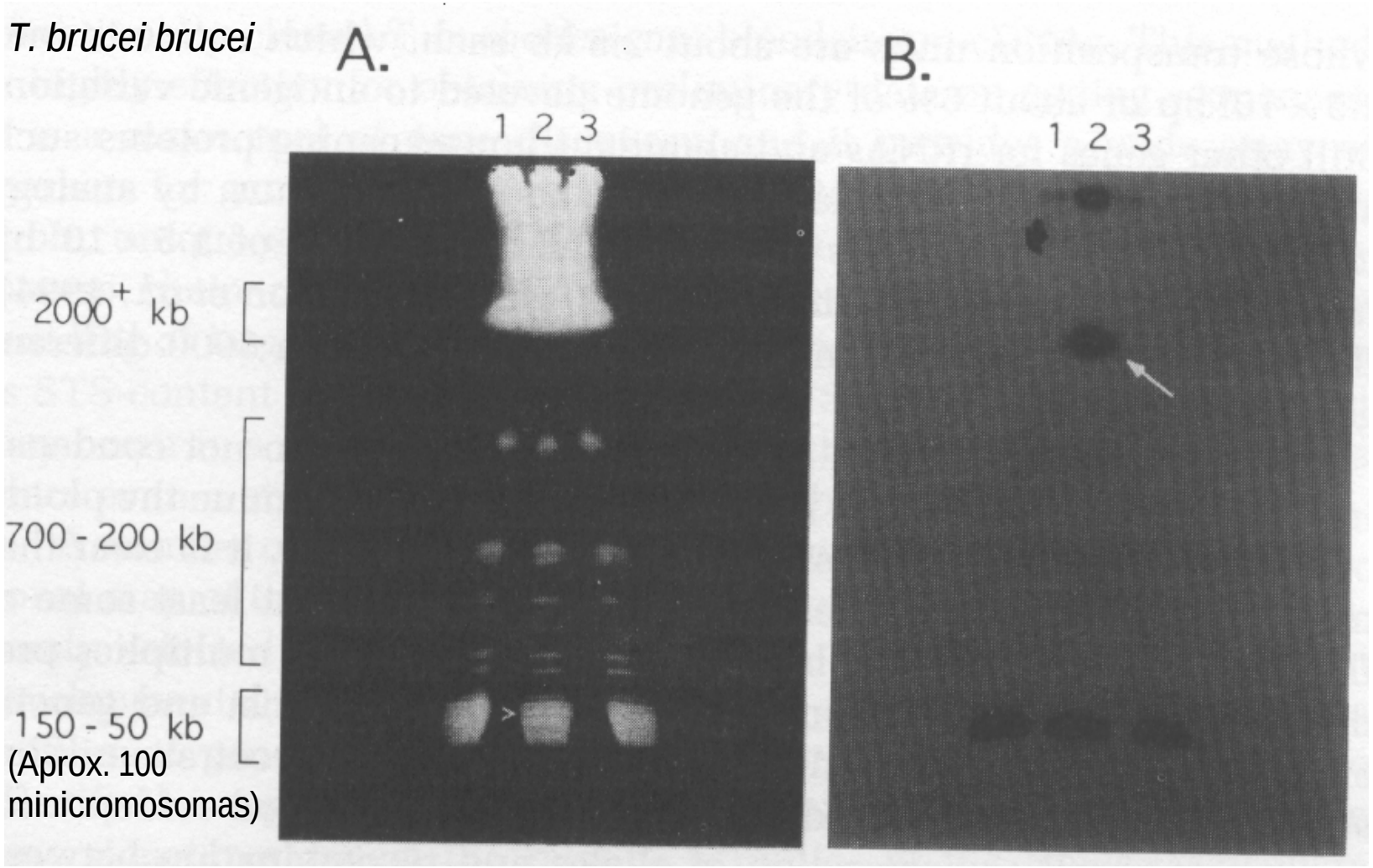
X

CAMPO PULSANTE





T. brucei brucei



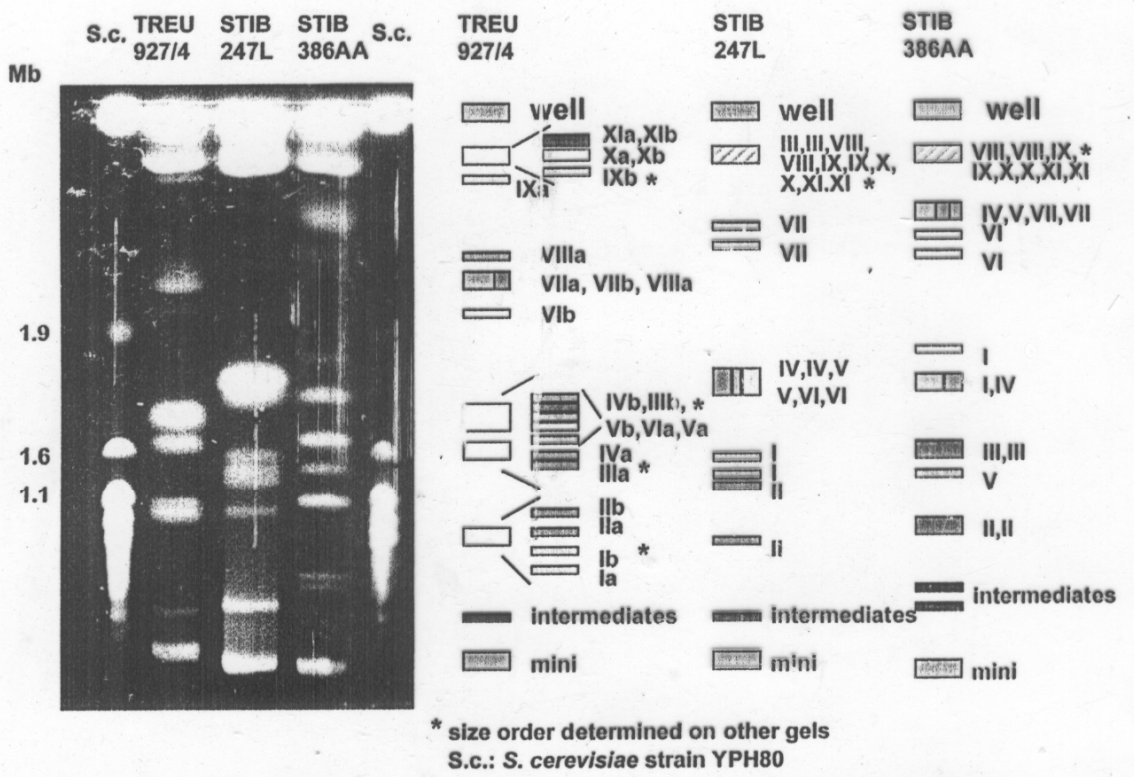


Fig. 3. Molecular karotypes of three *T. brucei* field isolates, TRUE927/4, STIB257/L and STIB 386AA. The left panel shows an ethidium bromide-stained gel of the PFGE-separated chromosomes of the three *T. brucei* field isolates and of *Saccharomyces cerevisiae* (left and right lanes). The sizes of some of the *S. cerevisiae* chromosomes are indicated on the left. The right panel summarises the results of multiple Southern blot hybridisations of similar PFGEs with numerous cDNA probes used to identify the homologues of chromosomes I–VIII (colour-coded). The PFGE was conducted under conditions that are optimal for separating DNA molecules between 1 and 4 Mb. Other electrophoretic conditions are necessary to maximally resolve DNA molecules more than 4 Mb (chromosomes IX–XI) and less than 1 Mb [the intermediate chromosomes (intermed) and minichromosomes (mini)]. In this PFGE the DNA molecules larger than 4 Mb are in the compression zone or the gel well. Note that in TREU927/4 the chromosome III homologues are 1.7–1.8 Mb, whereas in STIB 247/L they are 4 Mb or larger. Adapted from [55] and web site http://parsun1.path.cam.ac.uk/xsom.gif.http://parsun1.path.cam.ac.uk/xsom.gif.

A3.7: Genome Sizes of Selected Parasites, Their Hosts and Some Related Organisms

Organism	Haploid Genome Size (bp)	(G+C) Content (%)	Ref
M13 phage	7×10^3		[5]
Lambda phage	4.8×10^4		
Escherichia coli	4.7×10^6	50%	[6]
Yeast (*S. cerevisiae*)	1.3×10^7	39%	[6]
Amoeba	2×10^7		
Trypanosoma brucei	4×10^7		[7]
Leishmania donovani	4.6×10^7		[8]
Eimeria tenella	7.0×10^7		[9]
Plasmodium falciparum	8×10^7	20%	[10,11]
Dirofilaria immitis	7.9×10^7	27%	[12]
Brugia malayi	8.1×10^7	27%	[13,14]
Caenorhabditis elegans	1×10^8	36%	[15]
Trypanosoma cruzi	1.2×10^8		[16]
Drosophila melanogaster	1.7×10^8	40%	[17]
Schistosoma mansoni	2.7×10^8	34%	[18]
Mosquitoes	$2 \times 10^8 - 1 \times 10^9$		
Ascaris lumbricoides (see *Note 1*)	5.8×10^8		[19]
Mouse	3×10^9	58%	
Human	3×10^9	59%	

Notes :

1. Ascarid nematodes eliminate a high proportion of DNA from all somatic cells; only germ line cells retain the full complement. In *Ascaris lumbricoides* the somatic haploid DNA content is 4.2×10^8 bp.

Proyectos genoma:

Caenorhabditis elegans

Ascaris lumbricoides
Echinococcus granulosus
Echinococcus multilocularis
Fasciola hepatica
Haemonchus contortus
Necator americanus
Onchocerca volvulus
Schistosoma mansoni
S. haematobium
Trichuris muris
Trichinella spiralis
Taenia solium

Blastocystis hominis
Babesia bigemina
Babesia bovis
Crithidia deanei
Dictyostelium discoideum
Eimeria tenella
Entamoeba dispar
Entamoeba histolytica
Entamoeba invadens
Entamoeba moshkovskii
Entamoeba terrapinae
Leishmania braziliensis
Leishmania infantum
Leishmania major (TriTryps)
Leishmania mexicana
Neospora caninum
Plasmodium berghei
Plasmodium chabaudi
Plasmodium falciparum
Plasmodium gallinaceum
Plasmodium knowlesi
Plasmodium reichenowi
Plasmodium vivax
Perkinsus marinus
Theileria annulata
Theileria parva
Toxoplasma gondii
Trichomonas vaginalis
Trypanosoma brucei (TriTryps)
Trypanosoma cruzi (TriTryps
Trypanosoma congolense
Trypanosoma brucei gambiense
Trypanosoma vivax
Tetrahymena thermophila

Table 1. Summary of the *T. brucei* genome. Genome size and chromosome numbers exclude intermediate and mini-chromosomes. Details of contig coverage for each chromosome are described in table S1. Intergenic regions are regions between protein-coding sequences (CDSs). The exact number of spliced leader (sl) RNA copies cannot be resolved in the assembly.

Parameter	Number
The genome	
Size (bp)	26,075,396
G+C content (%)	46.4
Chromosomes	11
Sequence contigs	30
Percent coding	50.5
Protein-coding genes	
Genes	9068
Pseudogenes	904
Mean CDS length (bp)	1592
Median CDS length (bp)	1242
G+C content (%)	50.9
Gene density (genes per Mb)	317
Intergenic regions	
Mean length (bp)	1279
G+C content (%)	41
RNA genes	
transfer RNA	65
ribosomal RNA	56
slRNA	>28
small nuclear RNA	5
small nucleolar RNA	353

Table 1. Summary of the *T. cruzi* annotated genome. For RNA genes, see details in table S3. tRNA, transfer RNA; snRNA, small nuclear RNA; srpRNA, signal recognition particle RNA.

Parameter	Number
The genome	
Size* (bp)	60,372,297
G+C content (%)	51
Sequence scaffolds†	838
Sequence contigs	4,008
Percent coding	58.9
Protein-coding genes	
No. of gene models	23,216
No. of genes‡	22,570
Estimated no. of genes per haploid genome§	~12,000
Pseudogenes	3,590
Mean CDS length‖ (bp)	1,513
Median CDS length‖ (bp)	1,152
G+C content (%)	53.4
Gene density (genes per Mb)	385
Intergenic regions¶	
Mean length (bp)	1,024
G+C content (%)	47
RNA genes	
tRNA	115
rRNA	219
slRNA	192
snRNA	19
snoRNA	1,447
srpRNA	2

Table 1. Summary of the *L. major* genome.

Parameter	Number
The genome	
Size (bp)	32,816,678
G+C content (%)	59.7
Chromosomes	36
Sequence contigs	36
Percent coding	47.9
Protein-coding genes	
Genes	8272
Pseudogenes	39
Mean CDS length (bp)	1901
Median CDS length (bp)	1407
G+C content (%)	62.5
Gene density (genes per Mb)	252
*Intergenic regions**	
Mean length (bp)	2045
G+C content (%)	57.3
RNA genes	
tRNA	83
rRNA†	63
slRNA†	63
snRNA	6
snoRNA	695
srpRNA	1

*Region between protein-coding CDS. †The exact number cannot be determined because of misassembly.

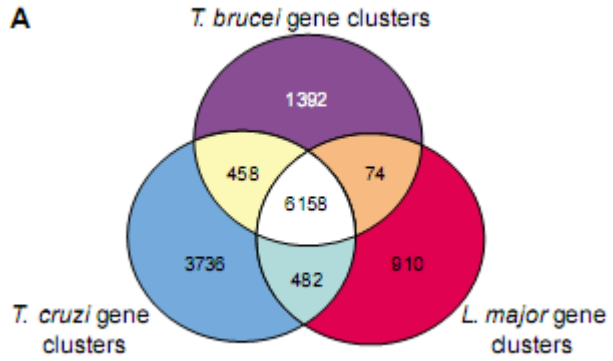


Table 1. General features of the Tritryp genomes. We found 5812 syntenic three-way COGs and 346 nonsyntenic three-way COGs. Mbp, mega–base pairs; NC, not computed.

	T. brucei	*T. cruzi*	*L. major*
Haploid genome size (Mbp)	25*	55	33
No. of chromosomes (per haploid genome)	11*	~28†	36
No. of genes (per haploid genome)	9068‡	~12,000§	8311‖
Total regions with synteny blocks (Mbp)	19.9	NC	30.7
Mean CDS size (bp) in syntenic three-way COGs	1511	1457	1731
Mean inter-CDS size (bp) between syntenic three-way COGs	721	561	1431

*Excluding ~100 mini- and intermediate-sized chromosomes (totaling ~10 Mb). †The exact number is not known and homologs can differ substantially in size. ‡Includes 904 pseudogenes. §The exact number of haploid genes has not been determined in *T. cruzi*. ‖Includes 34 pseudogenes.

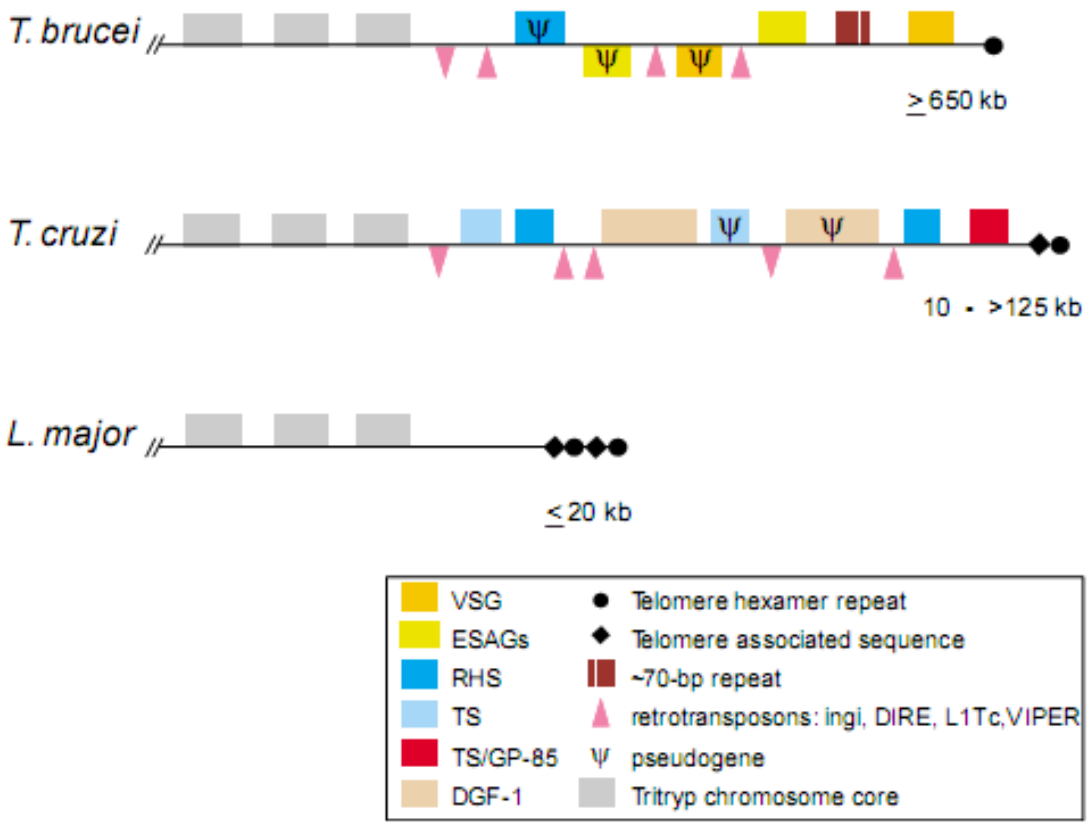


Fig. 3. Prototypes of Tritryp subtelomeric regions. Subtelomeric regions are defined here as the area that extends from the telomeric hexamer repeats to the first nonrepetitive sequence. Boxes indicate genes and/or gene arrays. Genes and/or gene arrays shown above the line are oriented toward the telomeres, whereas those shown below the line are oriented in the opposite direction. The size range of the subtelomeric regions in each genome is indicated on the right. The TS and TS/GP-85 boxes depict the trans-sialidase and GP-85 trans-sialidase superfamilies, respectively.

Table 1 ***Plasmodium falciparum*** **nuclear genome summary and comparison to other organisms**

Feature	Value				
	P. falciparum	*S. pombe*	*S. cerevisiae*	*D. discoideum*	*A. thaliana*
Size (bp)	22,853,764	12,462,637	12,495,682	8,100,000	115,409,949
(G + C) content (%)	19.4	36.0	38.3	22.2	34.9
No. of genes	5,268*	4,929	5,770	2,799	25,498
Mean gene length† (bp)	2,283	1,426	1,424	1,626	1,310
Gene density (bp per gene)	4,338	2,528	2,088	2,600	4,526
Per cent coding	52.6	57.5	70.5	56.3	28.8
Genes with introns (%)	53.9	43	5.0	68	79
Exons					
Number	12,674	ND	ND	6,398	132,982
No. per gene	2.39	ND	NA	2.29	5.18
(G + C) content (%)	23.7	39.6	28.0	28.0	ND
Mean length (bp)	949	ND	ND	711	170
Total length (bp)	12,028,350	ND	ND	4,548,978	33,249,250
Introns					
Number	7,406	4,730	272	3,587	107,784
(G + C) content (%)	13.5	ND	NA	13.0	ND
Mean length (bp)	178.7	81	NA	177	170
Total length (bp)	1,323,509	383,130	ND	643,899	18,055,421
Intergenic regions					
(G + C) content (%)	13.6	ND	ND	14.0	ND
Mean length (bp)	1,694	952	515	786	ND
RNAs					
No. of tRNA genes	43	174	ND	73	ND
No. of 5S rRNA genes	3	30	ND	NA	ND
No. of 5.8S, 18S and 28S rRNA units	7	200–400	ND	NA	700–800

ND, not determined; NA, not applicable. 'No. of genes' for *D. discoideum* are for chromosome 2 (ref. 155) and in some cases represent extrapolations to the entire genome. Sources of data for the other organisms: *S. pombe*[65], *S. cerevisiae*[156], *D. discoideum*[155] and *A. thaliana*[157].

*70% of these genes matched expressed sequence tags or encoded proteins detected by proteomics analyses[14,15].

†Excluding introns.

Cromosomas	14	3	16	6	5

Table 1

Summary of the *T. vaginalis* genome sequence data. Assembly size (bp, base pairs) includes all contigs and differs from estimated genome size of ~160 Mb (4). The scaffold size is the minimum scaffold length, such that more than half the genome is contained in scaffolds of at least that length. The number of predicted genes may include low-complexity repeats or novel transposable elements rather than true *T. vaginalis* genes, but in the absence of decisive evidence these remain in the gene set. The number of evidence-supported genes includes those with either similarity to a known protein ($E < 1 \times 10^{-10}$, >25% length of protein) or similarity to an expressed sequence tag (>95% identity over >90% length of the gene). A total of 763 rDNA fragments (258 copies of 28S, 254 copies of 18S, and 251 copies of 5.8S) were identified.

Feature	Value
Genome	
Size of assembly (bp)	176,441,227
G+C content (%)	32.7
No. of scaffolds	17,290
N_{50} scaffold size (bp)	68,338
Protein-coding genes	
No. of predicted genes	59,681
No. of evidence-supported genes	25,949
No. of genes with introns	65
Mean gene length (bp)	928.6
Gene G+C content (%)	35.5
Gene density (bp)	2956
Mean length of intergenic regions (bp)	1165.4
Intergenic G+C content (%)	28.8
Non–protein-coding genes	
Predicted tRNA genes	479
Predicted 5.8S, 18S, and 28S rDNA units	~250

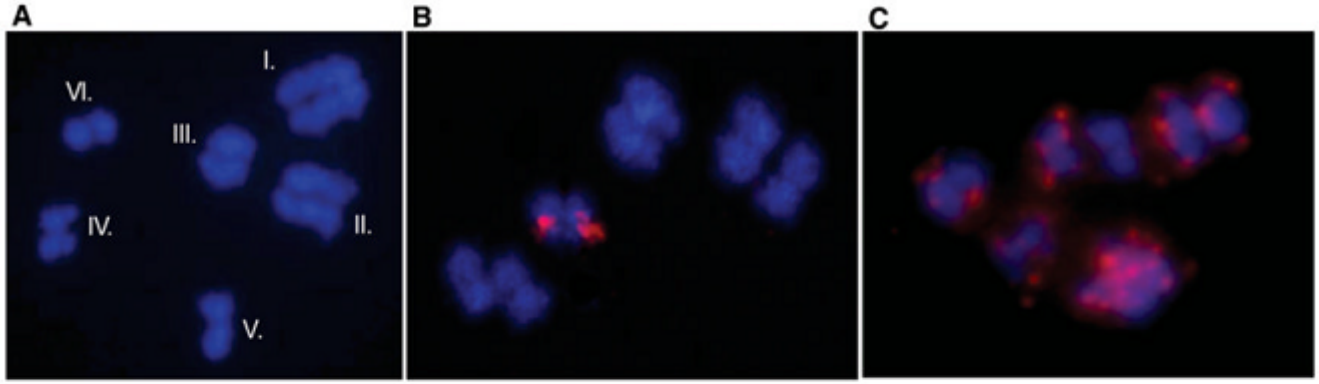


Fig. 1.
Karyotype and fluorescent in situ hybridization (FISH) analysis of *T. vaginalis* chromosomes. (**A**) Metaphase chromosome squashes of *T. vaginalis* reveal six chromosomes (I to VI). (**B**) FISH analysis using an 18S rDNA probe shows that all ~250 rDNA units localize to a single chromosome. (**C**) In contrast, the *Tvmar1* transposable element (8) is dispersed throughout the genome.

Science 315, 207-212 (2007)

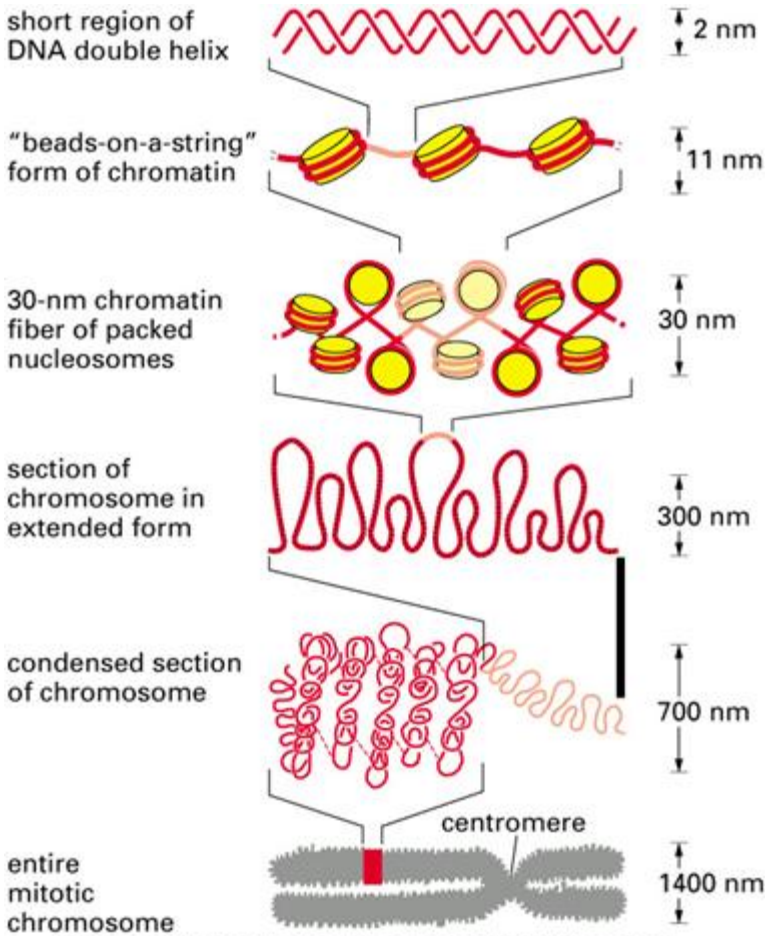
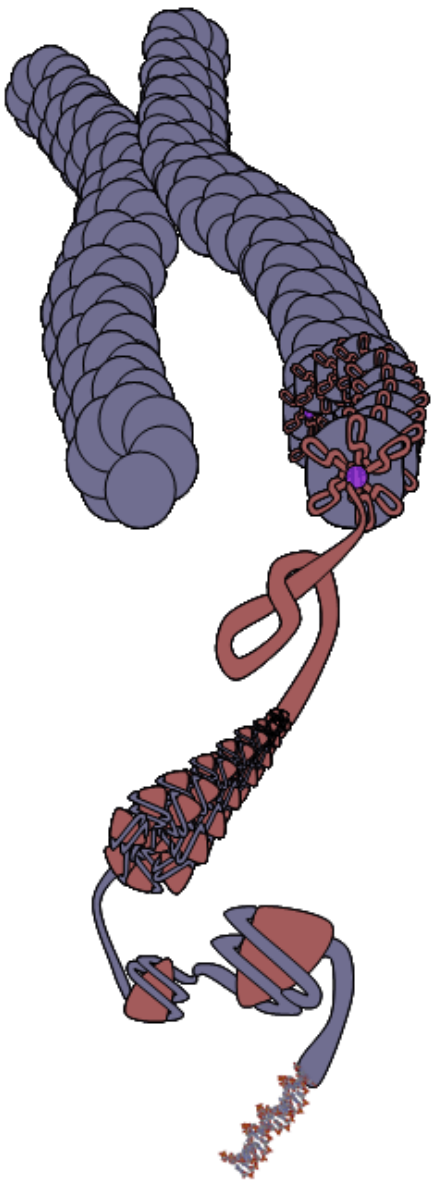


Figure 4–55. Molecular Biology of the Cell, 4th Edition.



Chromatids (10 coils long)

One coil (30 rosettes)

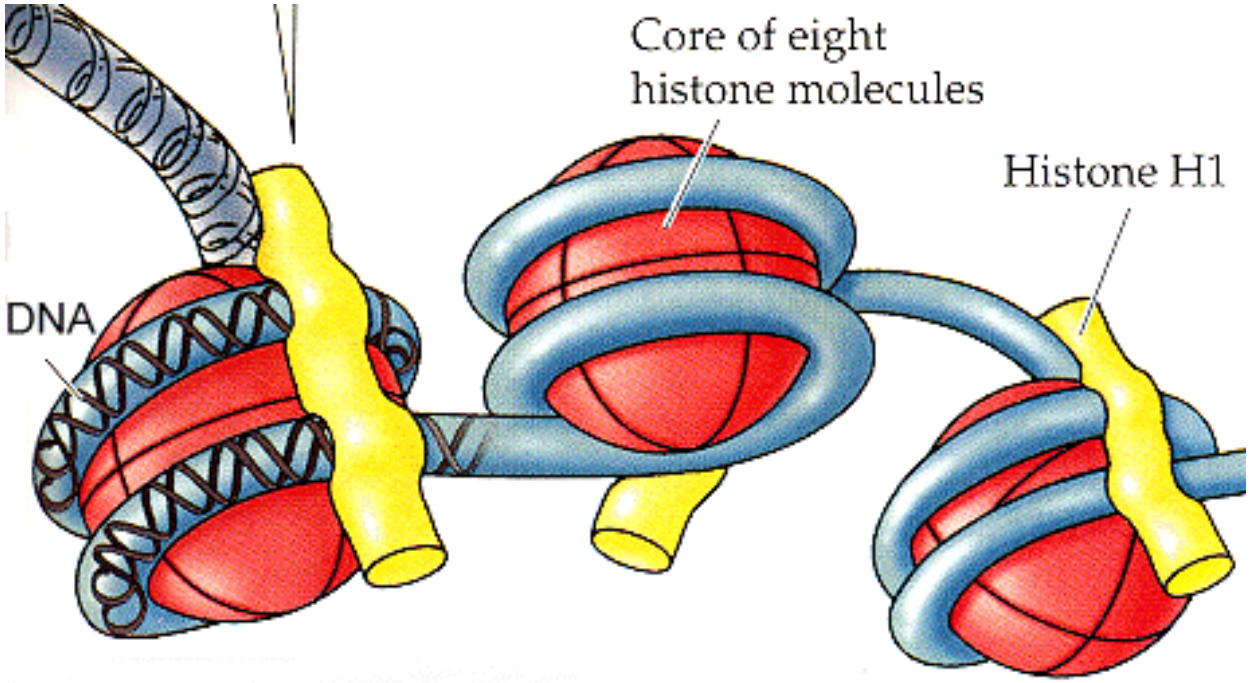
One rosette (6 loops) around nuclear scaffold

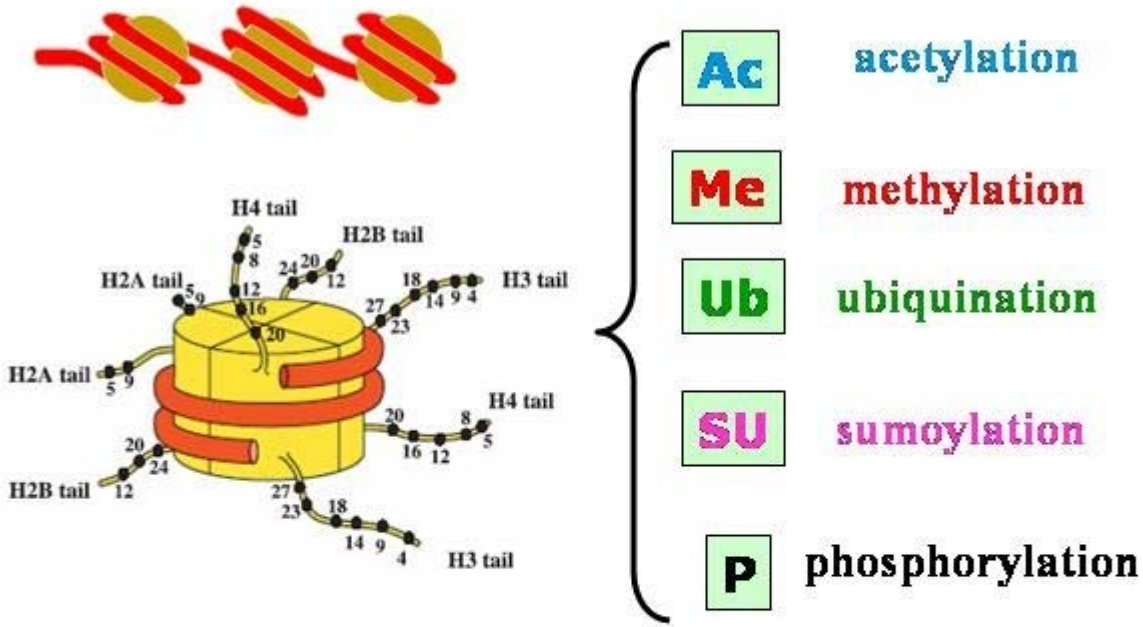
One loop (75 kbp)

30 nm chromatin fibre

Beads-on-a-string chromatin fibre wrapped around histones

DNA

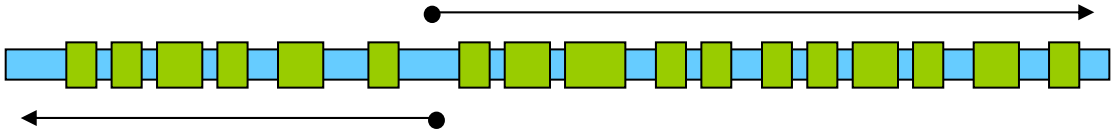

Core of eight
histone molecules
Histone H1
DNA



The figure illustrates nucleosome models and major posttranslational modifications which play essential roles in gene expression regulation and disease processes

Modelo de cromosoma en tripanosomátidos

(Tomando como referencia el crom. 1 de *L. major*)



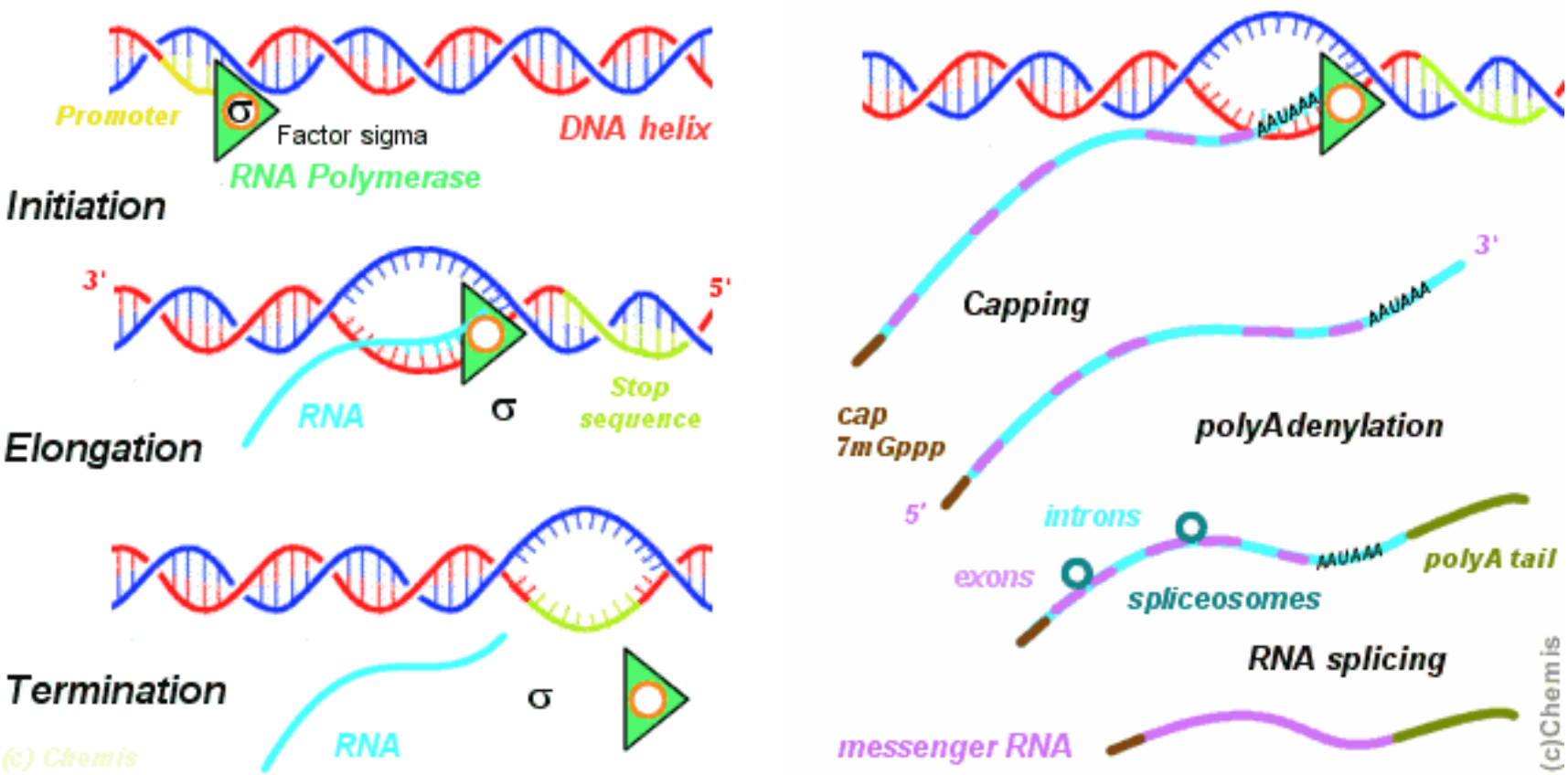
RNA polimerasas:

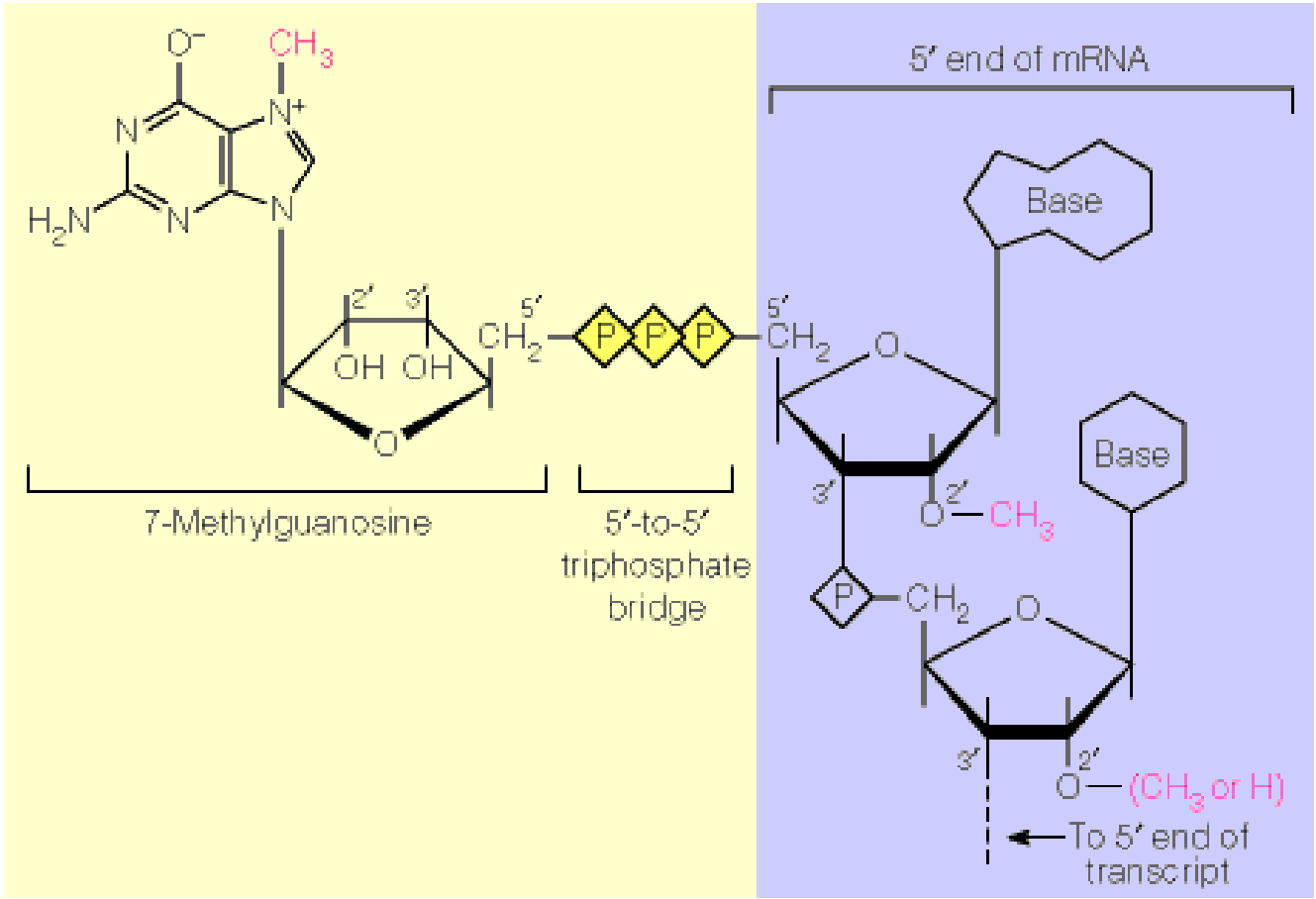
Procariotas: RNApol única

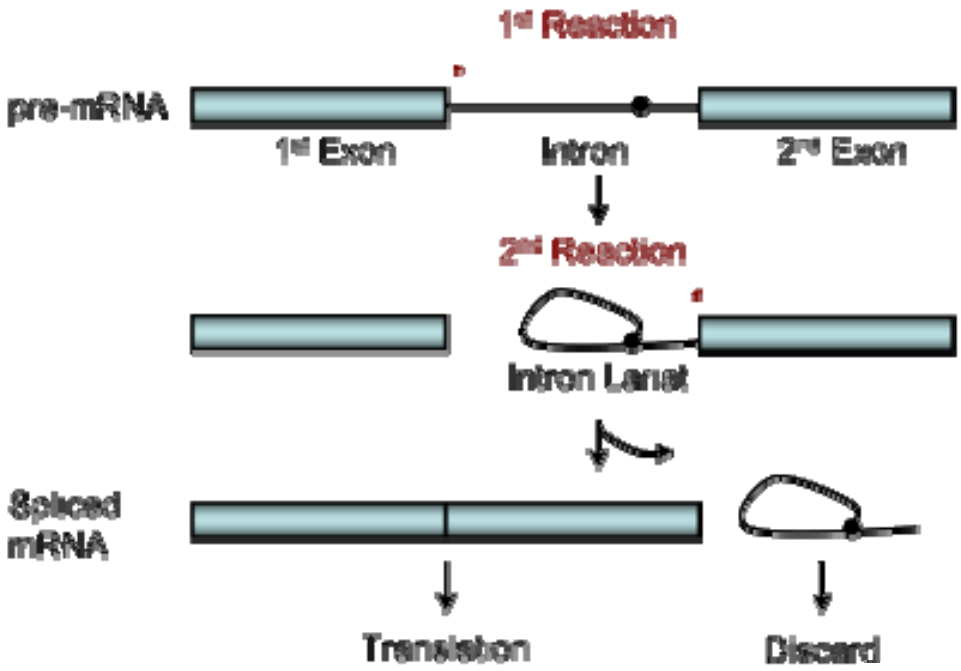
Regulación de la transcripción mediada por estructura secundaria de mRNA y factores proteicos

Eucariotas: tres tipos de RNApol

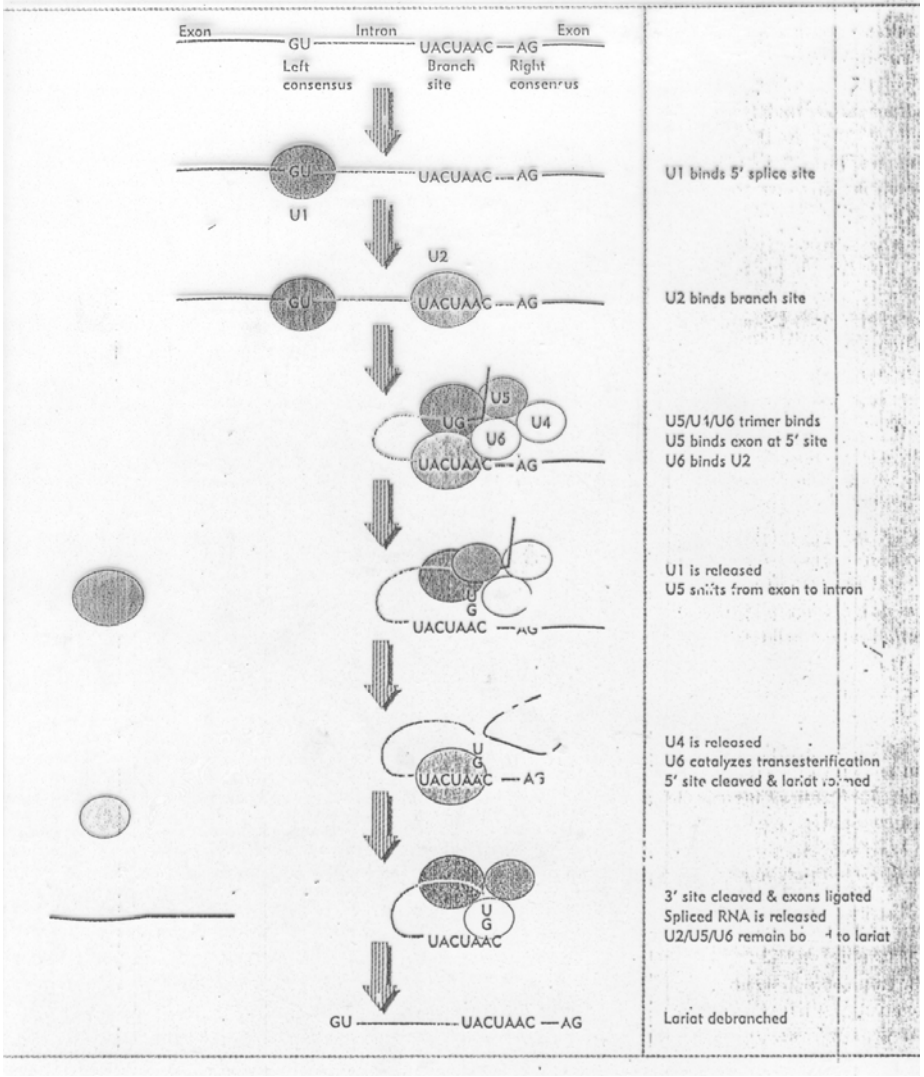
	RNApol I	RNApol II	RNApol III
Vertebrados:	rRNA	mRNA y snRNA	tRNA y snRNA
Tripanosomátidos:	rRNA y mRNA tel.	SL-RNA y mRNA	SL-RNA y snRNA
Resistencia a α-amanitina:	R	S	variable

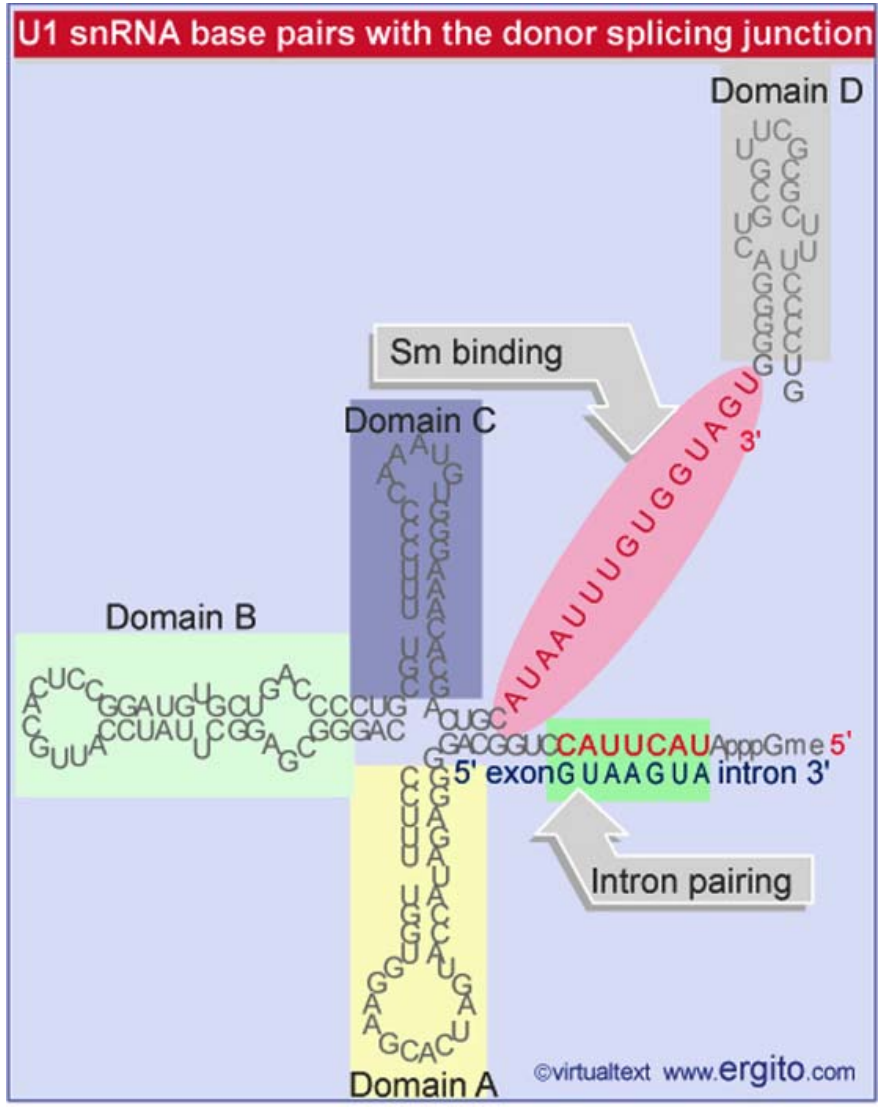

Promoter
σ
Factor sigma
DNA helix
RNA Polymerase
Initiation
3'
5'
RNA
σ
Stop
sequence
Elongation
Termination
RNA
σ
(c) Chemis
AAUAAA
Capping
3'
AAUAAA
cap
7mGppp
polyAdenylation
5'
introns
exons
AAUAAA
polyA tail
spliceosomes
RNA splicing
messenger RNA
(c)Chemis


5′ end of mRNA
Base
Base
7-Methylguanosine
5′-to-5′
triphosphate
bridge
To 5′ end of
transcript


1st Reaction
pre-mRNA
1st Exon
Intron
2nd Exon
2nd Reaction
Intron Lariat
Spliced mRNA
Translation
Discard

The splicing reaction proceeds through discrete stages in which spliceosome formation involves the interaction of components that recognize the consensus sequences.




U1 snRNA base pairs with the donor splicing junction
Domain D
Sm binding
Domain C
3'
Domain B
AUAAUUUGUGGUAGU
CAUUCAUApppGme 5'
5' exonGUAAGUA intron 3'
Intron pairing
Domain A
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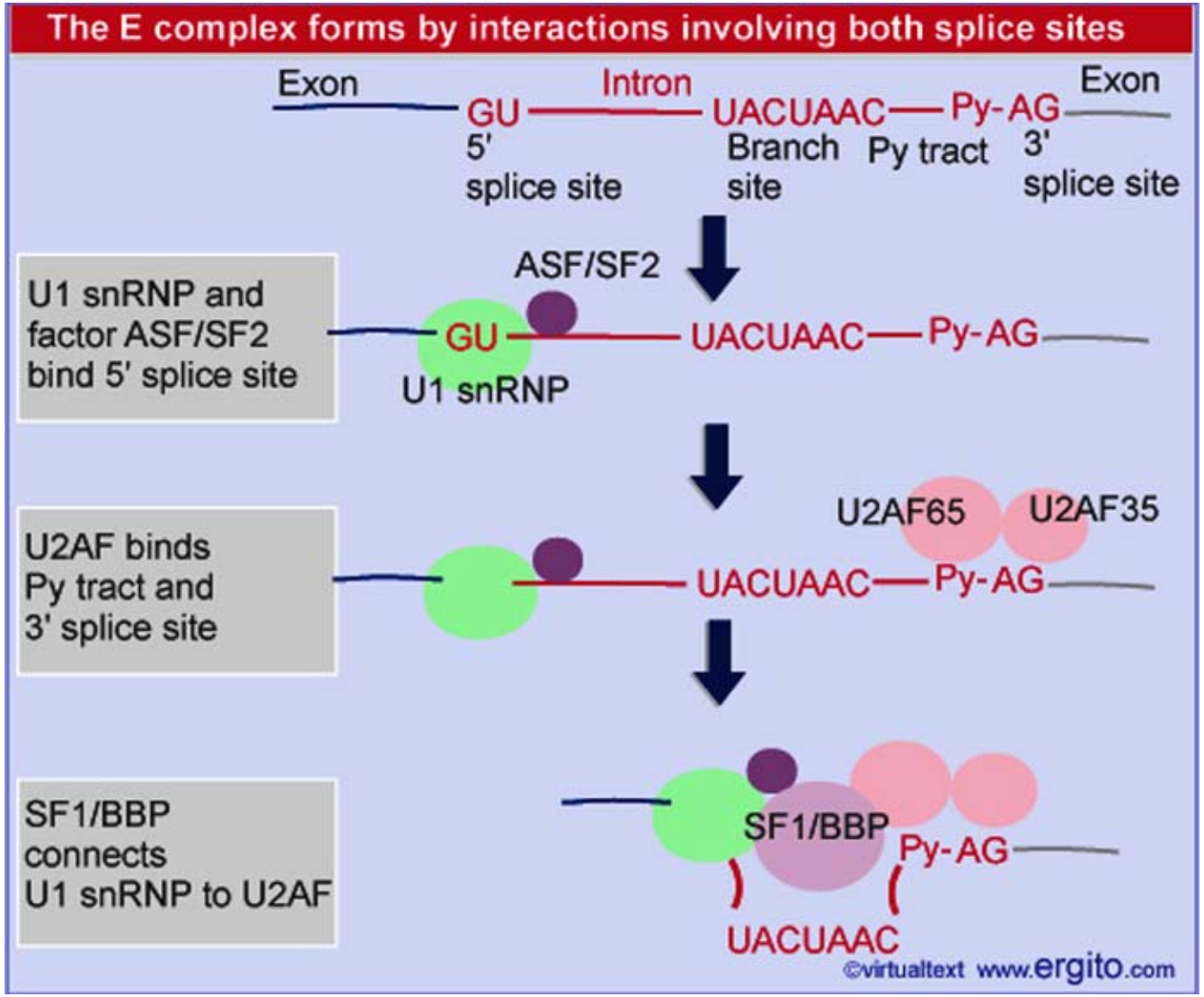
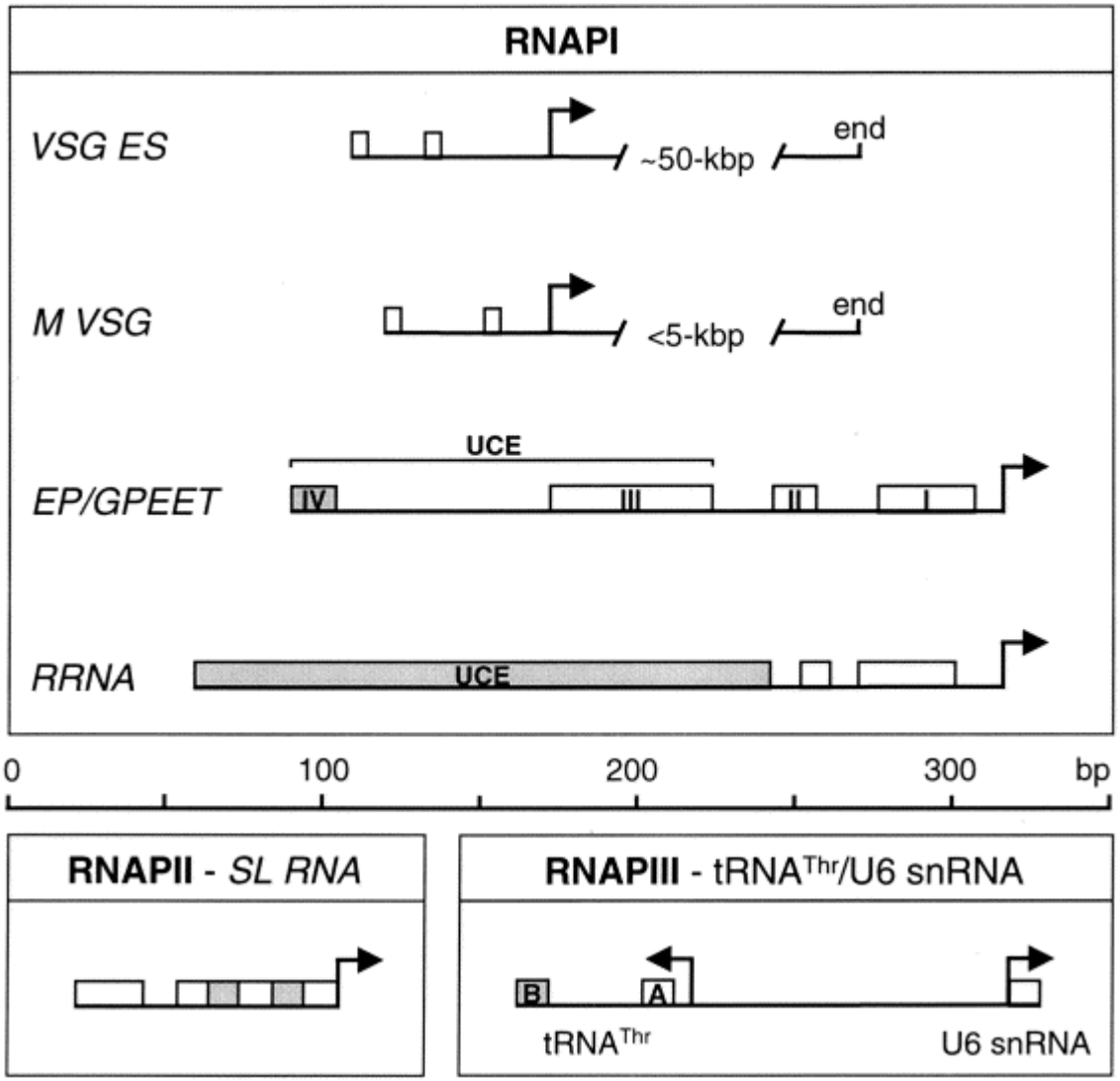

The E complex forms by interactions involving both splice sites
Exon
Intron
Exon
GU
UACUAAC
Py-AG
5'
splice site
Branch
site
Py tract
3'
splice site
ASF/SF2
U1 snRNP and
factor ASF/SF2
bind 5' splice site
GU
UACUAAC
Py-AG
U1 snRNP
U2AF65
U2AF35
U2AF binds
Py tract and
3' splice site
UACUAAC
Py-AG
SF1/BBP
connects
U1 snRNP to U2AF
SF1/BBP
Py-AG
UACUAAC
©virtualtext www.ergito.com


RNAPI
VSG ES
~50-kbp
end
M VSG
<5-kbp
end
UCE
EP/GPEET
IV
III
II
I
RRNA
UCE
0
100
200
300
bp
RNAPII - SL RNA
RNAPIII - tRNAThr/U6 snRNA
B
A
tRNAThr
U6 snRNA

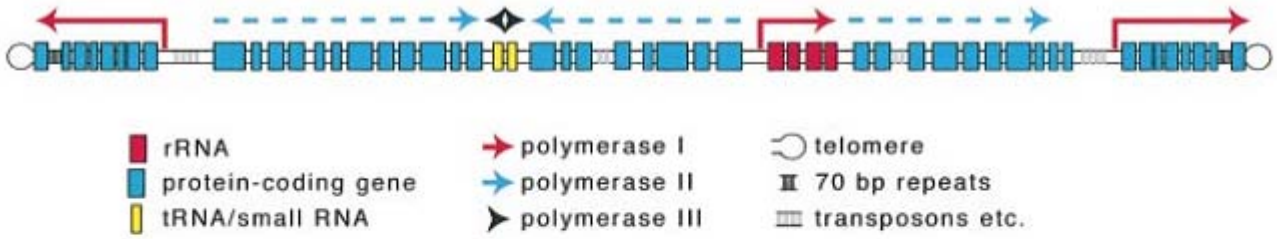


Fig. 1. Schematic diagram of a generic *T.brucei* chromosome. The diagram is meant only to show typical features. It does not illustrate a particular chromosome and is not to scale. Information is taken from Myler *et al*. (1999), personal communications, other references in the text and the websites listed below. Trypanosomes and leishmanias are diploid. Although homologous chromosomes can differ considerably in size, this is mostly due to variations in the numbers of tandemly repeated genes or non-coding repeated sequences, particularly sub-temomeric repeats. Haploid genome sizes range from 30 to 40 Mb with ~10 000 genes, and most chromosomes are 0.3–10 Mb long. *Trypanosoma brucei* also has many smaller 'intermediate' and 'minichromosomes' that have repetitive regions, rRNA genes and VSG genes; at the end of some of the large *T.brucei* chromosomes there are VSG expression sites transcribed by RNA polymerase I. Current relevant websites are http://www.cbs.dtu.dk/services/GenomeAtlas/Eukaryotes/Leishmania/major/Friedlin/Lmajor_Friedlin_1.structureatlas.lin.html; http://www.sanger.ac.uk/Projects/L_major/; http://www.tigr.org/tdb/mdb/tbdb/index.shtml; http://www.tigr.org/tdb/; http://parsun1.path.cam.ac.uk/; http://www.sanger.ac.uk/Projects/T_brucei/; http://www.ebi.ac.uk/parasites/paratable.html#cruzi.

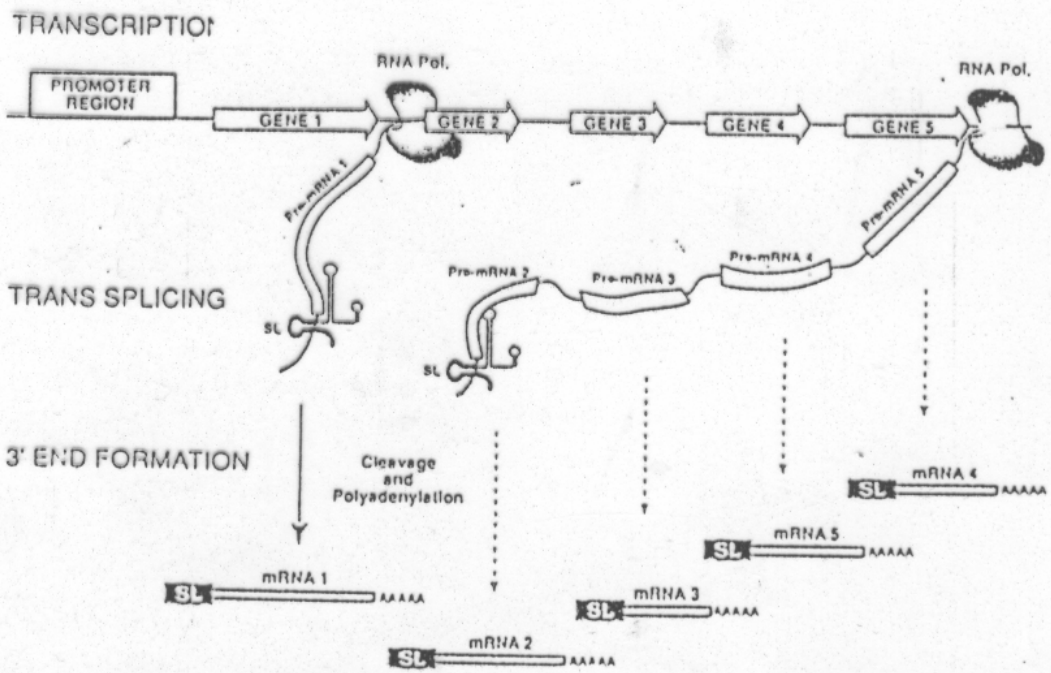


FIG. 1.1 Biogenesis of trypanosomatid mRNA. A schematic view of trypanosome gene expression. Mature mRNAs are generated from polycistronic pre-mRNAs via two RNA processing reactions, *trans*-splicing and polyadenylation. For details, see text.

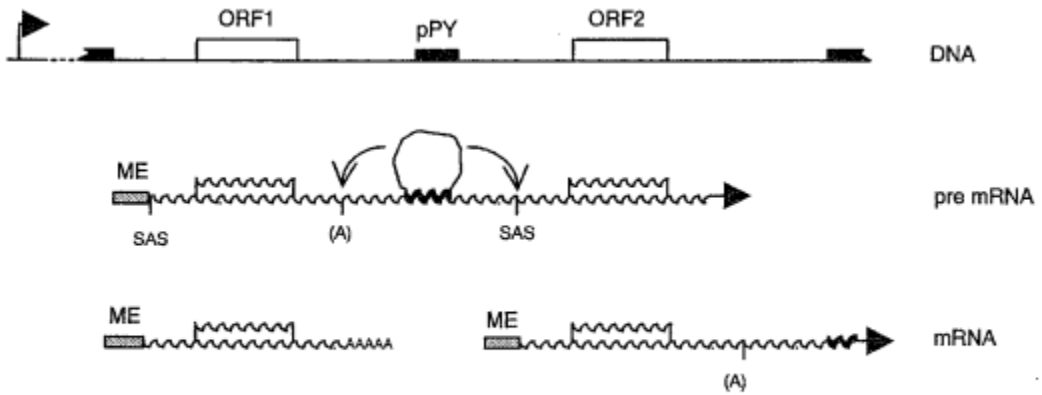


FIG. 2. Coupling between *trans* splicing and polyadenylation. Probably as soon as they are synthesized, intergenic transcripts of the polycistronic units are cleaved and processed by *trans* splicing and polyadenylation. These two events are coupled, probably through the binding of the processing machinery to intergenic polypyrimidine tracts (pPY). ORF, open reading frame; SAS, splice acceptor site; (A), polyadenylation site; ME, miniexon. The arrow in the DNA map denotes the transcription promoter.

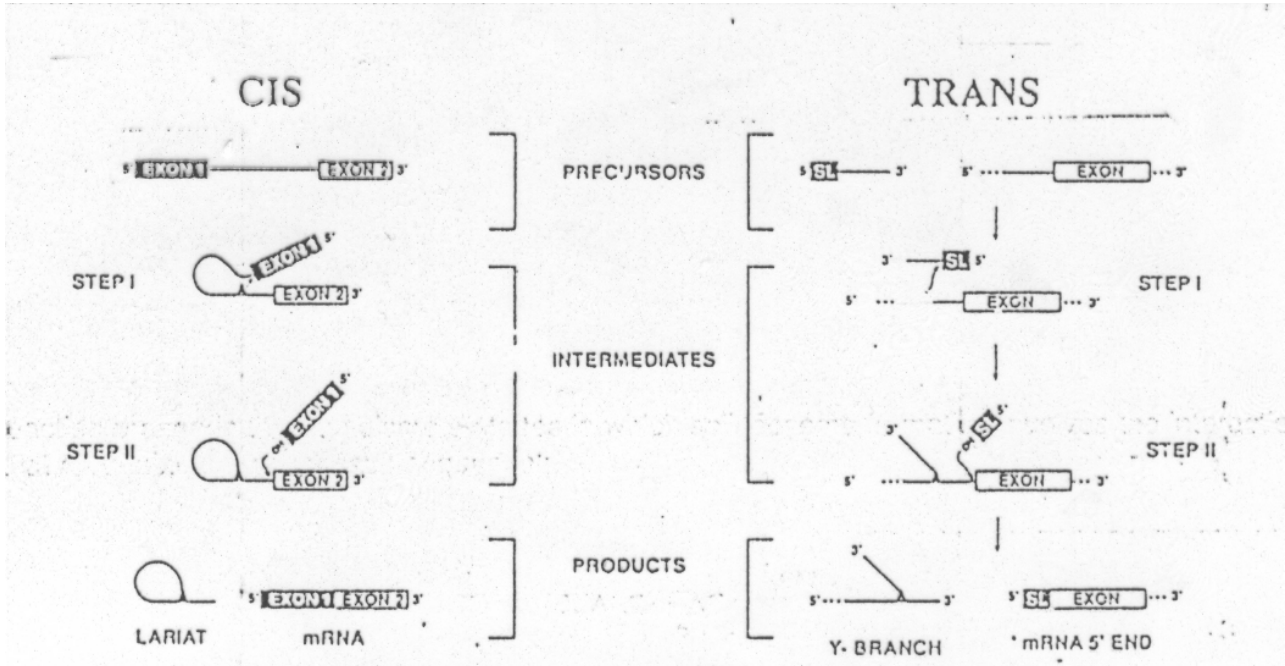


FIG. 1.2 *Cis* and *trans*-splicing proceed through analogous two-step reaction pathways. A schematic illustration of the similarities between *cis* and *trans*-splicing. See text for details.

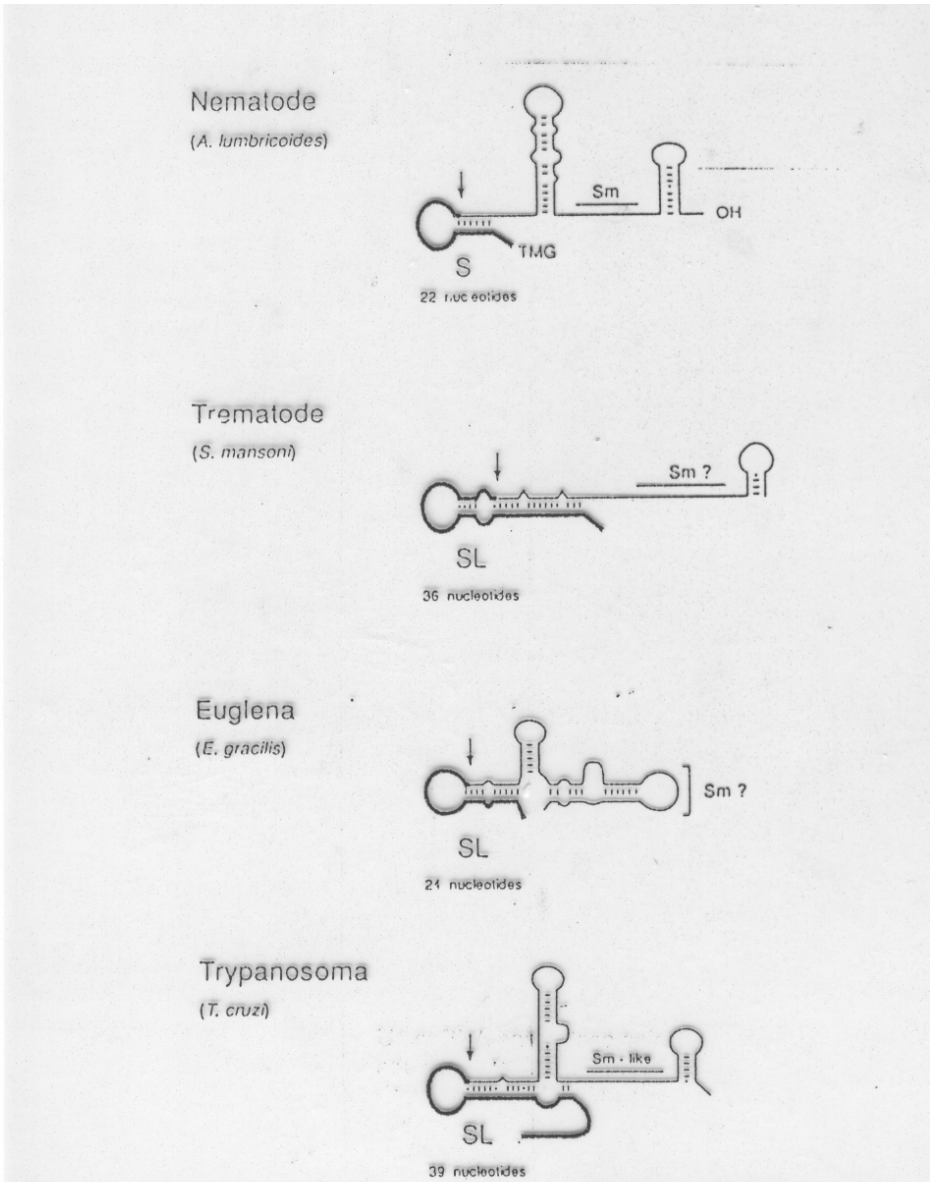
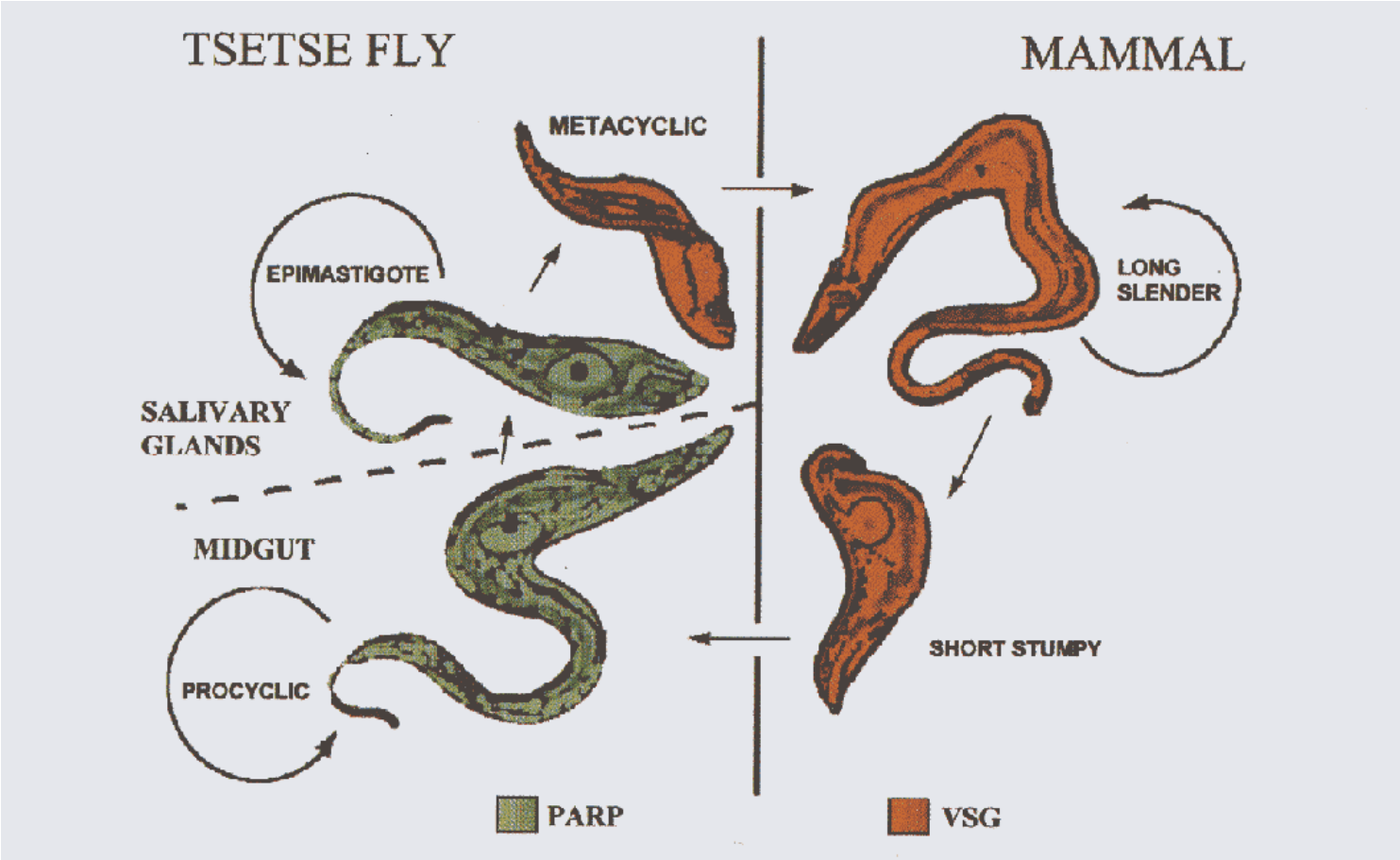


FIG. 1.3 SL RNAs have similar structures and resemble U snRNAs. Schematic representation of secondary structures of SL RNAs from organisms known to carry out *trans*-splicing. See text for details.

Ciclo de vide de *T. brucei*



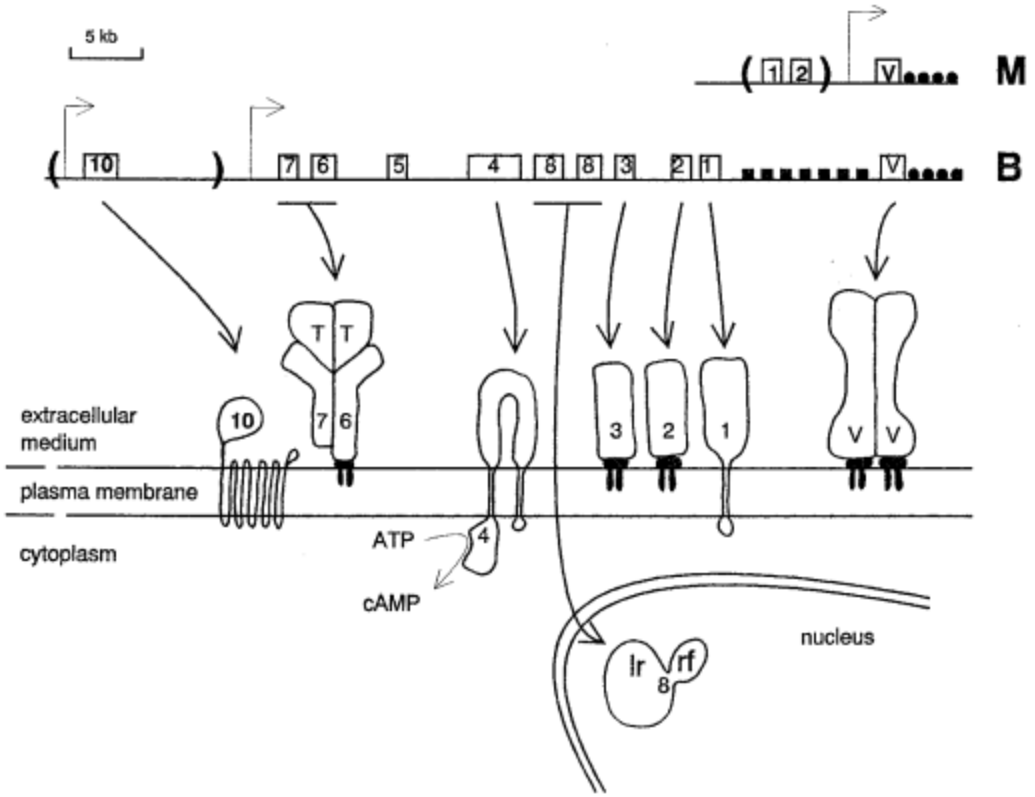


FIG. 4. Anatomy of the VSG gene transcription units. The bloodstream (B) and metacyclic (M) VSG transcription units are both telomeric. While the metacyclic units contain only the VSG gene, the bloodstream units also harbor a collection of ESAGs, numbered in this map of the AnTat 1.3A VSG expression site (7, 110, 146, 152). ESAG 7 and 6 encode the subunits of a heterodimeric transferrin receptor, ESAG 4 encodes a receptor-like transmembrane adenylate cyclase, ESAG 8 encodes a nuclear factor with a ring finger (rf) and a leucine repeat domain (lr), and ESAG 3, 2, and 1 are minor surface proteins of unknown function. A 13-kb region provided with another copy of the VSG promoter characterizes the 5' extremity of approximately half of the expression sites. This region contains ESAG 10 as well as a transposable element. The small squares and circles represent the arrays of 76-bp repeats and telomeric repeats, respectively. T, transferrin; V, VSG.

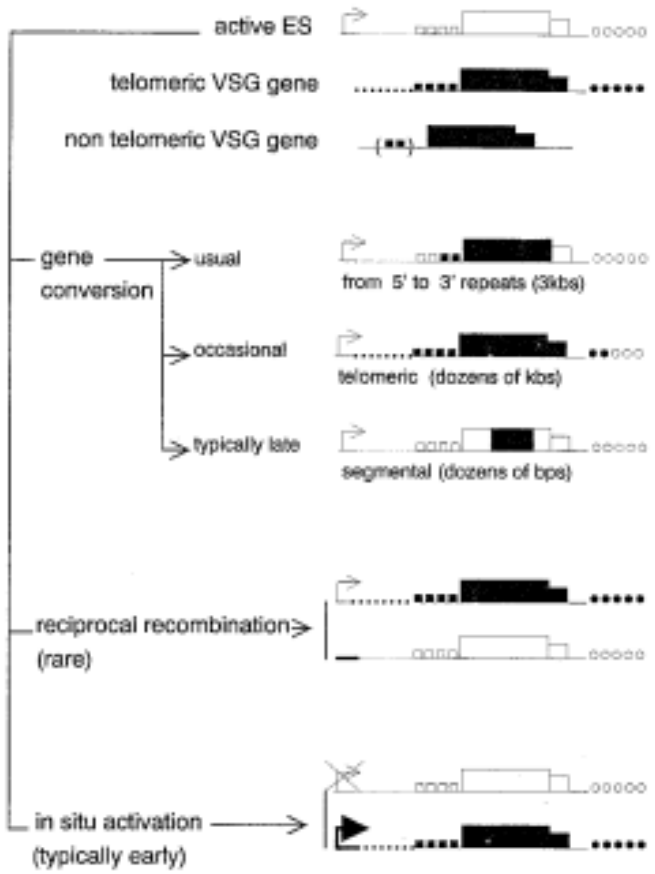
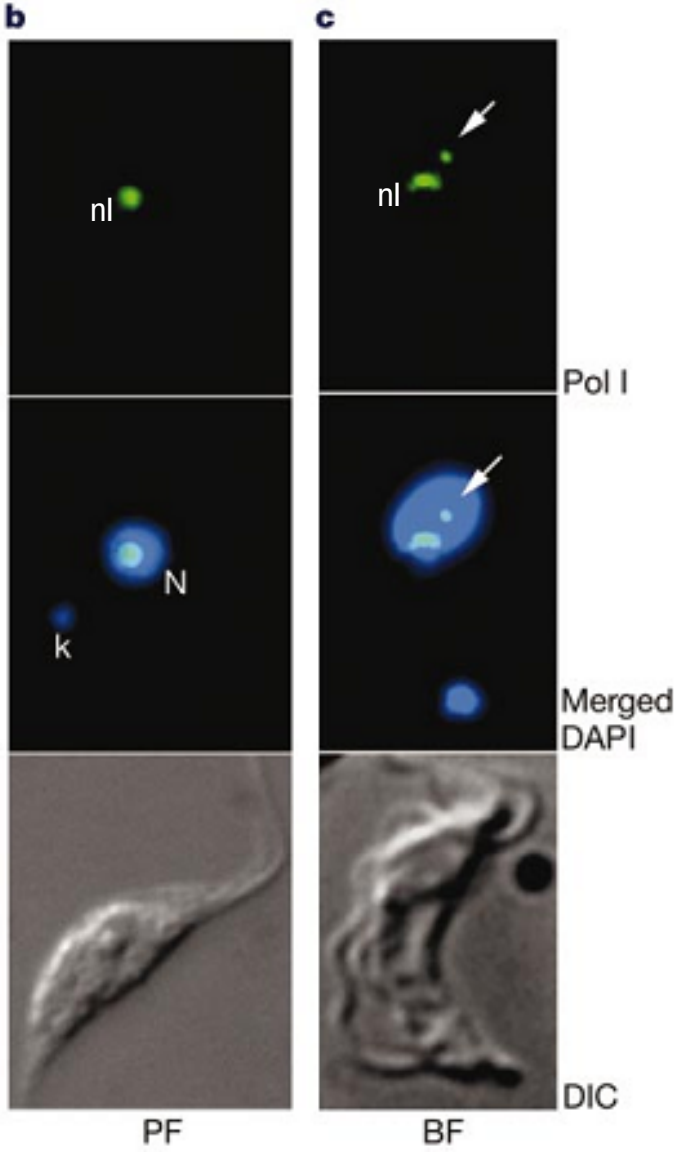


FIG. 5. The mechanisms of antigenic variation in *T. brucei*. The VSG genes (large boxes) are either telomeric or nontelomeric, but the active VSG gene in the expression site (ES) is always telomeric. Telomeric VSG genes are flanked by large arrays of repeats, downstream telomeric repeats (circles) and upstream 76-bp repeats (squares). Nontelomeric VSG genes may be preceded by limited numbers of 76-bp repeats. The change of active VSG gene in the ES may be achieved by gene conversion, often extending from the 76-bp repeats to the conserved 3' terminus of the gene (small box). Larger and smaller conversions can occur, depending on the location and extent of homologies between the target and donor sequences. Intragenic segmental conversions characterize genes expressed late in infection. Reciprocal recombination between telomeres has been observed in only a few cases. Finally, the different ESs can alternatively (in)activate in situ, by a mechanism which remains to be determined and which is frequent early in infection.



Centros de actividad RNApol I en *T. brucei:*

- Síntesis de rRNA (Nucleolo, nl)

-Síntesis de VSG (ESB, flecha)

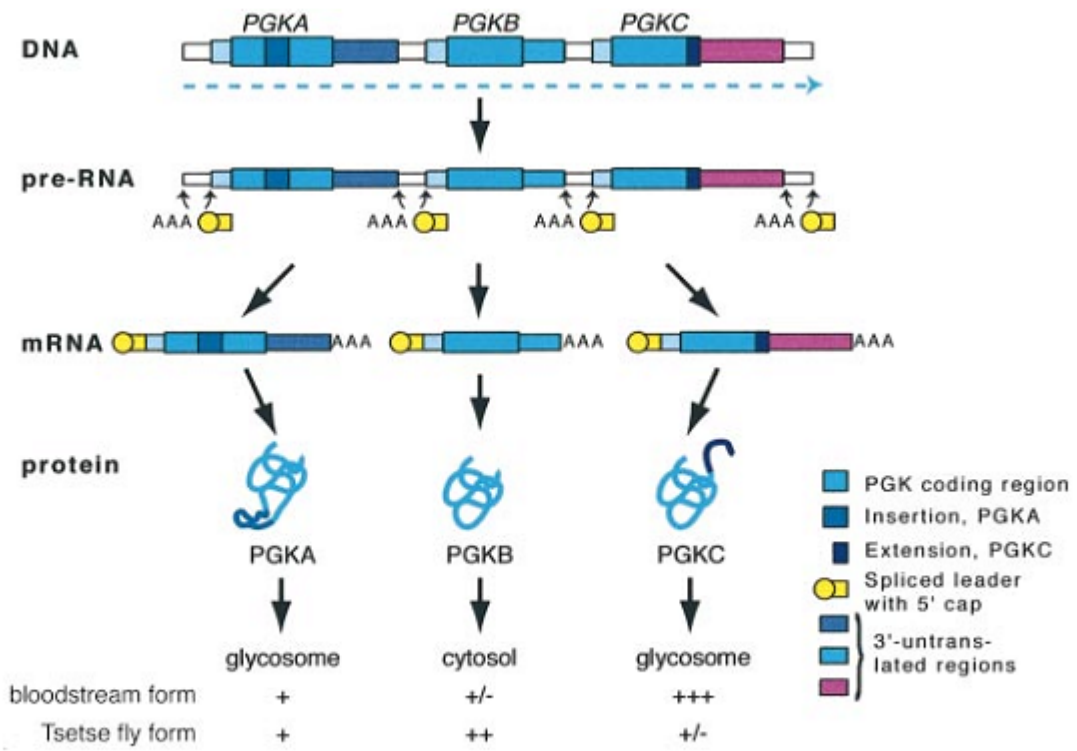


Fig. 2. The *PGK* locus of *T.brucei*, showing patterns of transcription, processing, translation and protein targeting in bloodstream forms and procyclic (tsetse fly) forms.

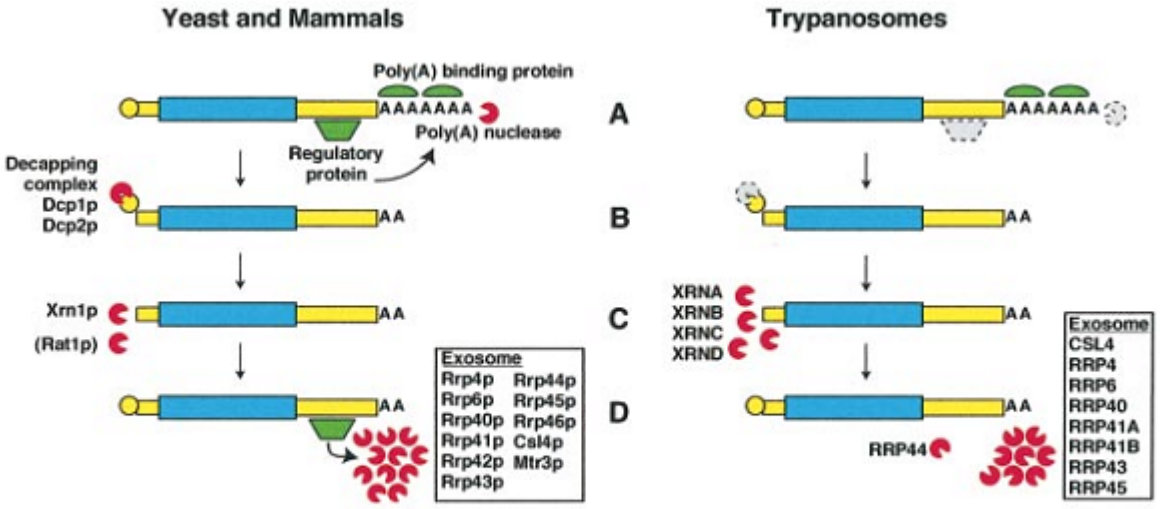
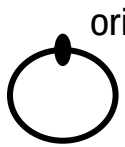


Fig. 3. mRNA degradation in mammals and trypanosomes. Some of the known *Saccharomyces cerevisiae* participants are shown to the left; corresponding *T.brucei* proteins are on the right. Red pacmen are exonucleases. Where clear homologues are not yet established, the protein is illustrated in grey with a dotted border. Processes are: (**A**) deadenylation reducing the poly(A) tail to oligo(A); (**B**) decapping; (**C**) 5′→3′ degradation; (**D**) 3′→5′ degradation. For references, see the text.

Kinetoplasto

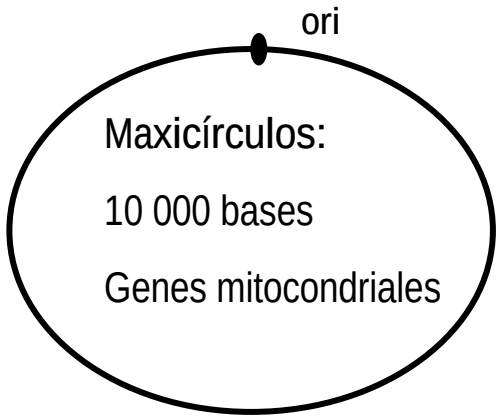


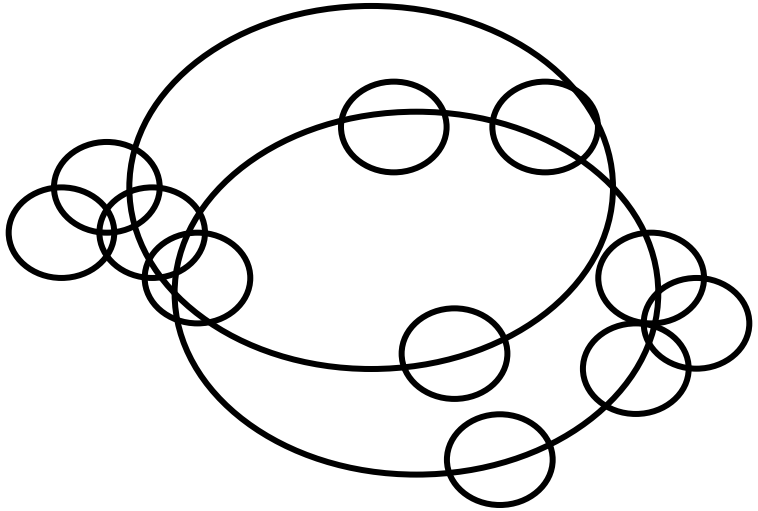
Minicírculos:

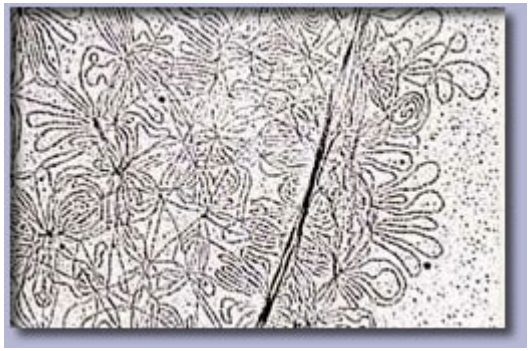
1000-2500 bases

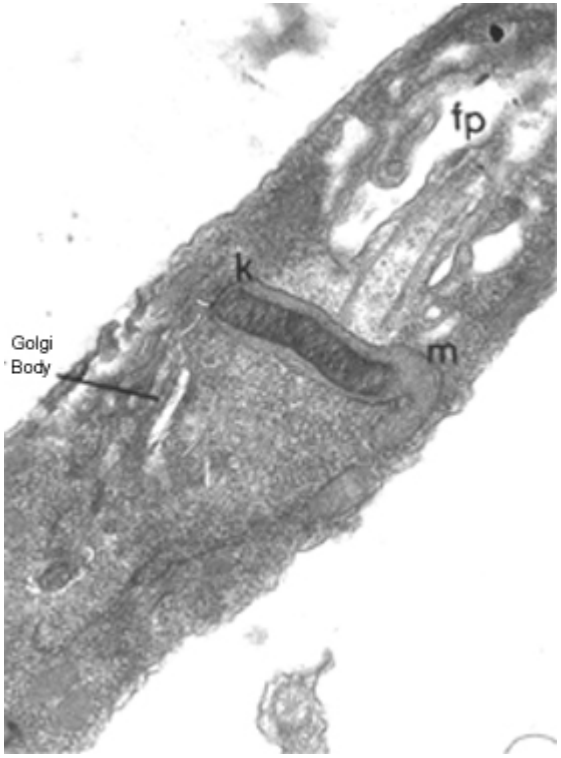
gRNA (guías)

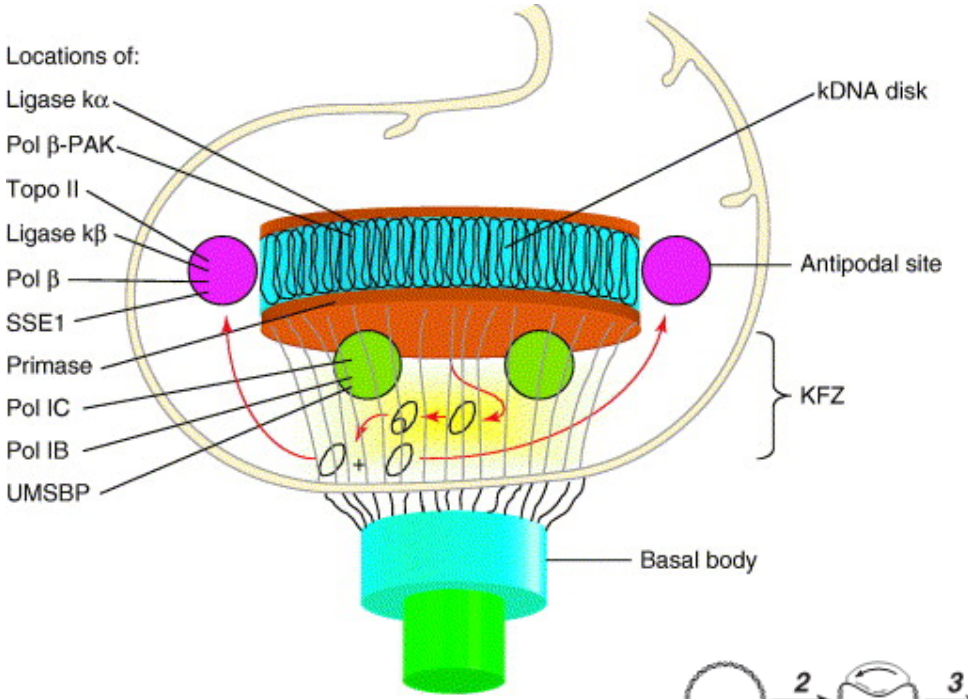
gRNA:











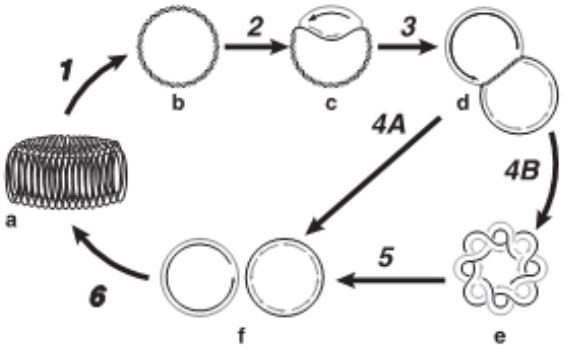
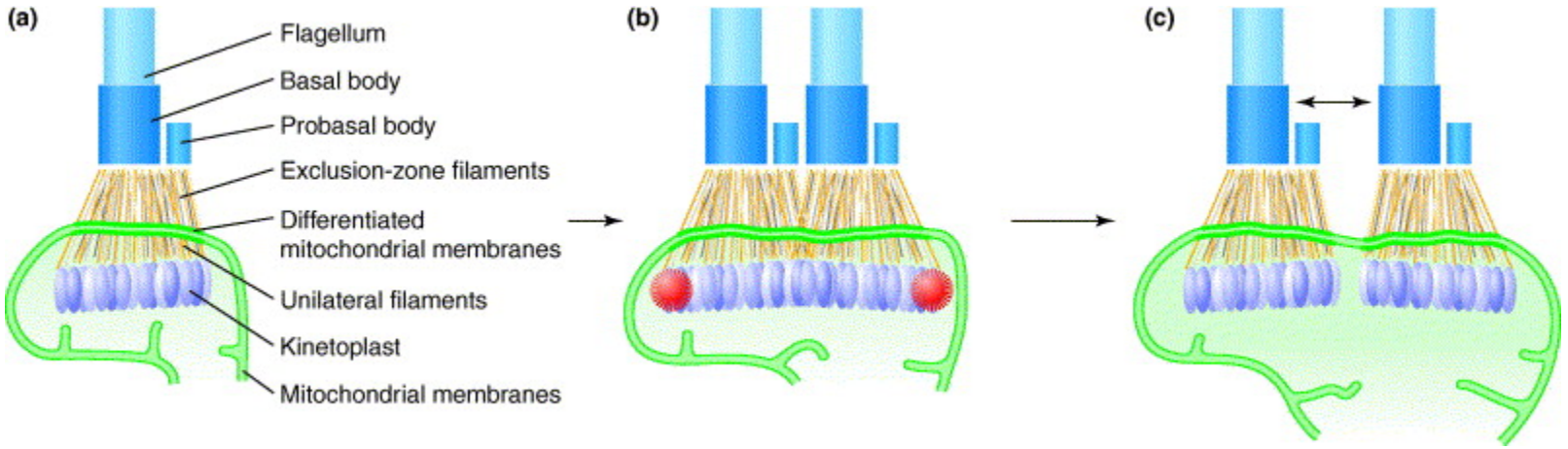
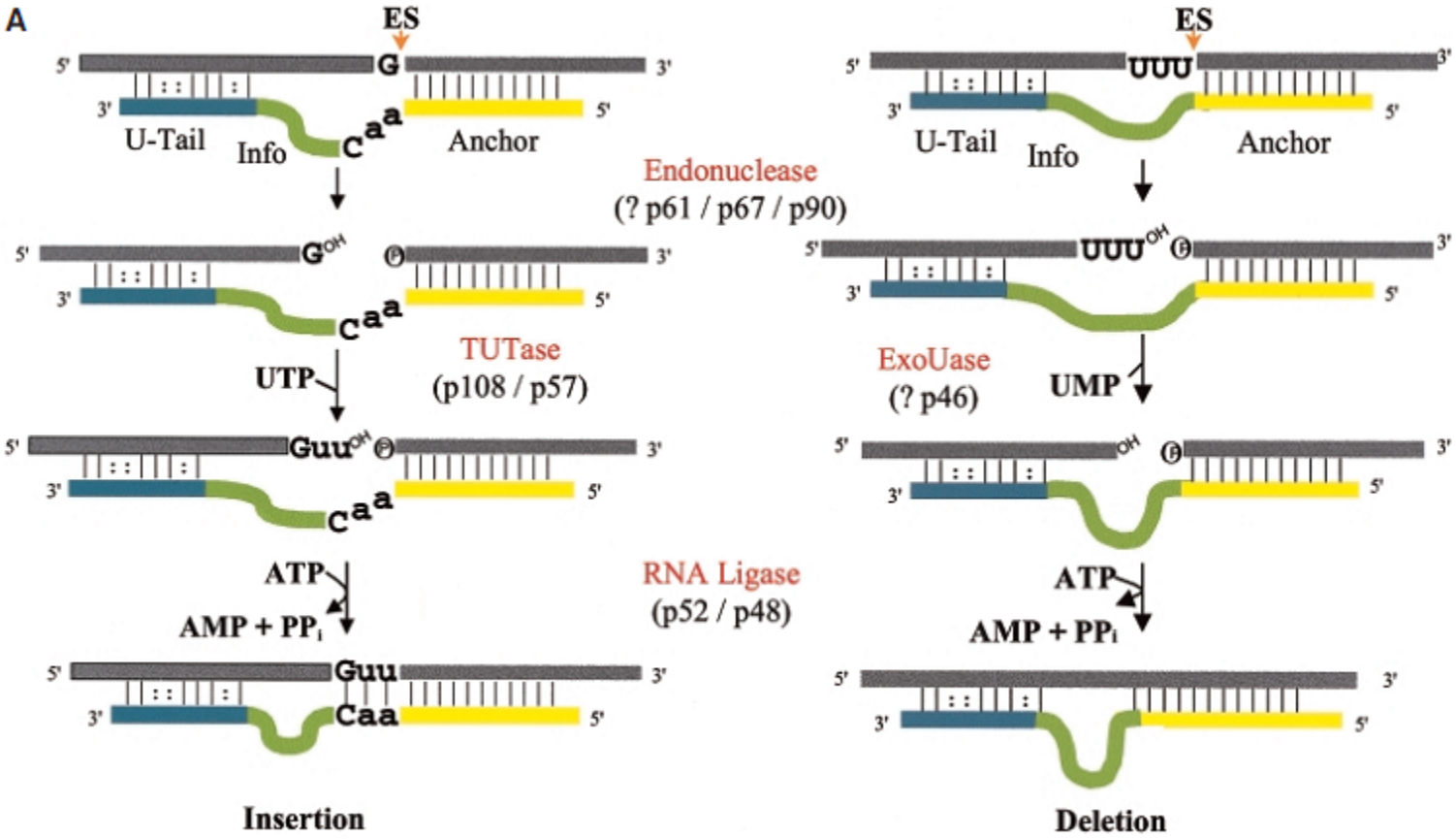
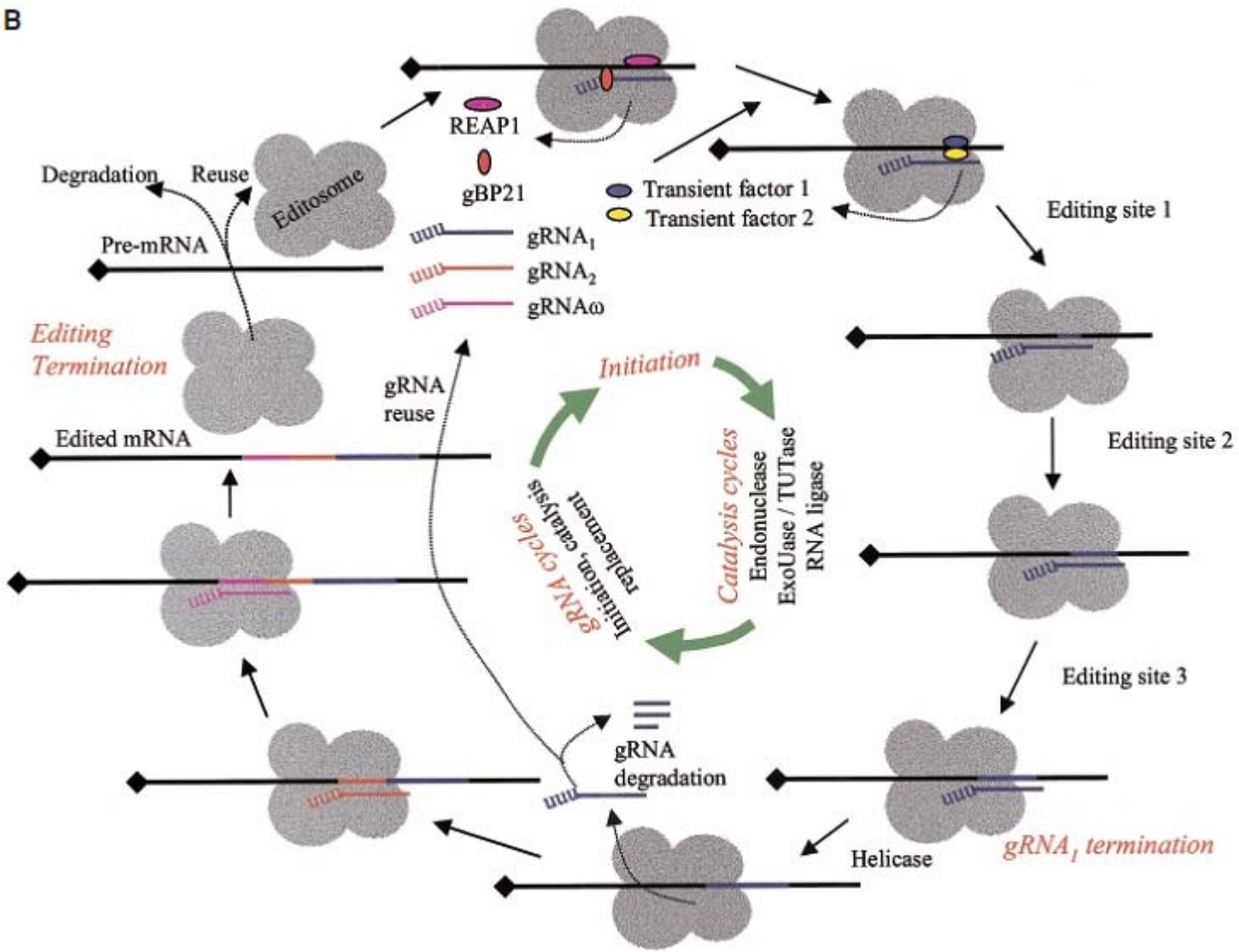


Fig. 1. Replication of kDNA minicircles occurs free of the network matrix. In a non-synchronized population of cells most minicircles are catenated within the network (a) and only a small percentage are in the pool of free minicircle replication intermediates (b–f). Replication begins with the decatenation of covalently closed monomer minicircles (b), followed by RNA-primed unidirectional DNA synthesis via theta structure intermediates (c and d), segregation of daughter circles (path 4A, and/or paths 4B plus 5) and reattachment of individual daughters (f) to the network. The newly synthesized DNA retains nicks or gaps that are not repaired until all minicircles have replicated and the double size network is ready to divide.


(a)
Flagellum
Basal body
Probasal body
Exclusion-zone filaments
Differentiated mitochondrial membranes
Unilateral filaments
Kinetoplast
Mitochondrial membranes
(b)
(c)


A
ES
5'
G
3'
3'
U-Tail
Info
C a a
Anchor
5'
Endonuclease
(? p61 / p67 / p90)
G OH
P
TUTase
(p108 / p57)
UTP
Guu OH
ATP
AMP + PPi
RNA Ligase
(p52 / p48)
Guu
Caa
Insertion
UUU
ExoUase
(? p46)
UMP
Deletion


B
REAP1
gBP21
Transient factor 1
Transient factor 2
Editosome
Degradation
Reuse
Pre-mRNA
gRNA1
gRNA2
gRNAω
Editing site 1
Editing site 2
Editing site 3
Editing Termination
Edited mRNA
gRNA reuse
Initiation
Catalysis cycles
Endonuclease
ExoUase / TUTase
RNA ligase
gRNA cycles
Initiation, catalysis
replacement
gRNA degradation
Helicase
gRNA1 termination

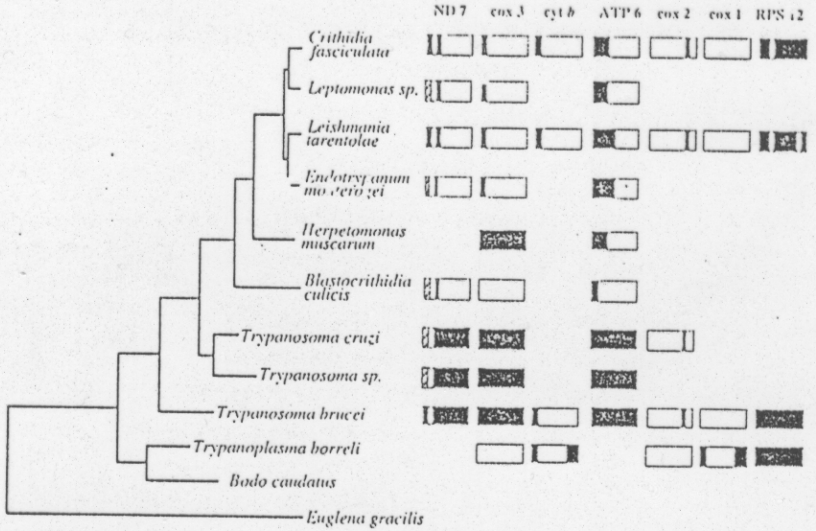


Figure 3. *Phylogeny of RNA editing in kinetoplastids*
A phylogenetic tree of kinetoplastids is given, adapted from [250] which was based on 18S rRNA sequences. On the right-hand side, editing patterns of seven mRNAs are shown (not drawn to scale) as far as known for each species. The boxes indicate (the regions of) the transcripts that are edited (black) or unedited (white). A hatched box indicates that the editing status of the corresponding RNA segment is not known. Adapted from [13].

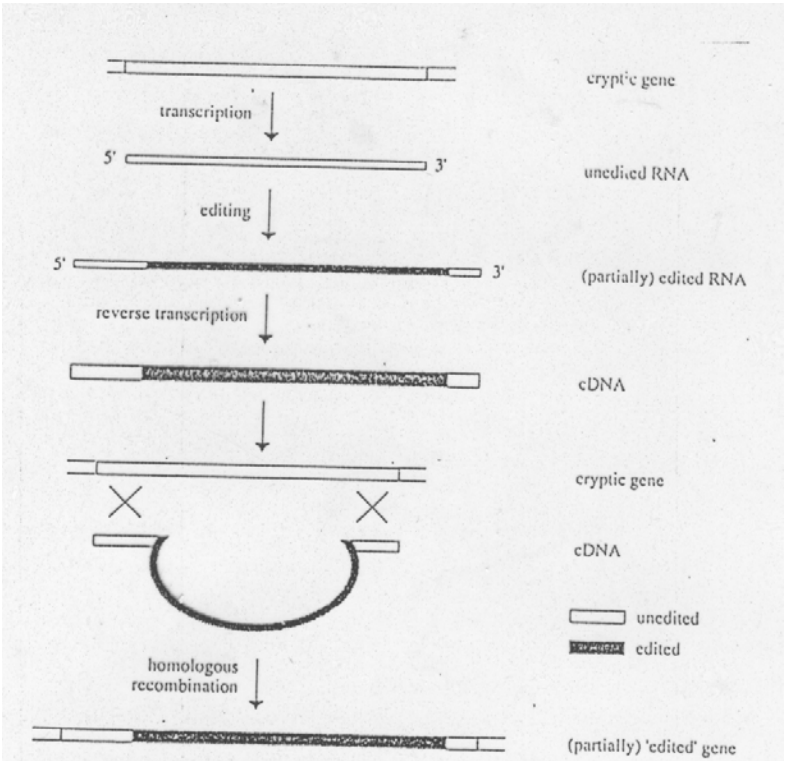


Figure 11. *Model explaining the loss of RNA editing via recombination*
In this example, a cryptic gene is converted into a (partially) 'edited' gene via homologous recombination with a (partially) 'edited' cDNA. The transcript of the new gene no longer requires extensive editing. For details see text. Taken from [13].

Table II. Different types of conversion RNA editing

Type	Organism (Genetic system)	RNA	*Cis*-acting elements	*Trans*-acting factors	Mechanism	Refs
C to U	*Physarum polycephalum* (mt)	cox1 mRNA	?	?	?	[18]
	higher plants (mt, cp)	many mRNAs, also tRNA, rRNA	flanking sequence?	?	C deamination	[24,25,78-80,252-254]
	mammals (n)	apoB, NF1 mRNAs	3' mooring sequence, efficiency and AU rich element	C deaminase (APOBEC-1), other factors	C deamination	[28,31,34, 50-57,255-257]
	mammals (n)	tRNA	?	?	?	[26]
	marsupials (mt)	tRNA	?	?	?	[27]
U to C	mammals (n)	WT1 mRNA also tRNA	?	?	?	[26,35]
	higher plants (mt,cp)	some mRNAs	flanking sequence?	?	?	[24,25]
A to I	mammals (n)	GluR-B, 5, 6 and 5-HT$_{2c}$R mRNAs	dsRNA structure	dsRAD/RED1 (?), other factors	dsRNA-dependent A-deamination	[28,38-40,70,72]
	squids (n)	Kv2 K$^+$ channel mRNA	dsRNA structure	dsRAD/RED1 (?), other factors	dsRNA-dependent A-deamination	[41]
	Drosophila melanogaster (n)	*4f-rnp* mRNA	dsRNA structure	dsRAD/RED1 (?), other factors	dsRNA-dependent A-deamination	[42]
	human hepatitis δ virus (v)	δ protein	dsRNA structure	dsRAD(?)	dsRNA-dependent A-deamination	[37,258,29]
G to A	mice (n)	GPT mRNA	?	?	base replacement?	[44]
U to A	humans (n)	α galactosidase mRNA	?	?	base replacement?	[43]
A to C, U to C, U to A	platypus (mt)	tRNA	?	internal guide sequence?	base-replacement?	[48]
C to A, A to G, U to G, U to A	*Acantamoeba castellani* (mt), fungi(mt)	tRNA	?	internal guide sequence?	base-replacement?	[45-47]

Abbreviations: apo B, apolipoprotein B; cox1, cytochrome c oxidase subunit 1; cp, chloroplast; ds, double stranded; dsRAD, dsRNA A-deaminase; GPT, GlcNac-1-phosphate transferase; GluR, glutamate receptor; 5-HT$_{2c}$R, serotonin 2C receptor; mt, mitochondrial; n, nuclear; NF1, neurofibromatosis type 1 gene; RED1, dsRNA-specific editase 1; v, viral; WT1, Wilms' tumor susceptibility gene 1. Adapted from [13].

Table I. Different types of insertion/deletion RNA editing

Type	Organism (Genetic system)	RNA	*Cis*-acting elements	*Trans*-acting factors	Mechanism	Refs
U insertion/deletion	kinetoplastids (mt)	many mRNAs	anchoring sequence	gRNAs, TUTase, RNA ligase, endonuclease, other factors	cleavage/ligation	[3,10-14]
mostly C insertion, also U, AA, CU, GU, GC	*Physarum polycephalum* (mt)	many mRNAs also tRNA, rRNA	?	?	?	[15-20]
G insertion	paramyxoviruses (v)	P mRNA	slippery sequence	viral polymerase	pseudo-templated transcription	[8,9]
A insertion	ebolaviruses (v)	GP mRNA	slippery sequence	viral polymerase	pseudo-templated transcription	[21]
3' terminal A addition	vertebrates (mt)	many mRNAs	flanking tRNA structure	endonuclease, TATase	cleavage/ TATase action	[6,7]
3' terminal A addition	land snails, squids (n	tRNA	flanking tRNA structure?	endonuclease, TATase	cleavage/ TATase action	[22,23]

Abbreviations: GP, glycoprotein; mt, mitochondrial; TATase, terminal adenylyltransferase; TUTase, terminal uridylyltransferase; v, viral. Adapted from [13].