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import datetime, itertools, logging, os, sys, msatools, sqlite3, re, glob
import numpy as np
import random as rnd
APPLOGGER=logging.getLogger("ngsphy-refselector")
class NRSException(Exception):
def init(self, expression, message, time):
self.expression = expression
self.message = message
self.time= time
class ReferenceSelection:
startTime=None
endTime=None
path=""
projectName=""
output=""
inputprefix=""
outputprefix=""
seqDescriptionFile=""
method=0
nsize=-1
numLociPerReplicate=[]
numLociPerReplicateDigits=[]
numReplicates=0
numReplicatesDigits=0
ploidy=1
db="" # Path of the SimPhy DB
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# Checking correctness of the given paths
   if (args.simphy_path[-1]=="/"):
       self.projectName=os.path.basename(args.simphy_path[0:-1])
   else:
       self.projectName=os.path.basename(args.simphy_path)
   self.path=os.path.abspath(args.simphy_path)
   output=os.path.abspath(args.output)
   outputFolderName=""
   if (args.output[-1]=="/"):
       outputFolderName=os.path.basename(args.output[0:-1])
   else:
       outputFolderName=os.path.basename(output)
   if (os.path.exists(output)):
       listdir=os.listdir("{}".format(os.path.dirname(output)))
       counter=0
       for item in listdir:
           if outputFolderName in item:
               counter+=1
       if not counter == 0: outputFolderName+="_{0}".format(counter+1)
   self.output=os.path.join(os.path.dirname(output),outputFolderName)
   if args.ploidy in [1,2]:
       self.ploidy=args.ploidy
   else:
       parserMessageWrong="\n\t{0}\n\t{1}\n\t{2}".format(\
           "Ploidy value is out of range.",\
           "Value must be in [1,2].",\
           "Please verify. Exiting."
       raise NRSException(False, message, datetime.datetime.now()-self.startTime)
   # Generation of the output folder
   try:
       os.mkdir(self.output)
       APPLOGGER.info("Generating output folder:\t{}".format(self.output))
   except:
       APPLOGGER.info("Output folder ({0}) exists. ".format(self.output))
   if self.nsize > -1:
           os.mkdir(os.path.join(self.output, "bed"))
           APPLOGGER.info("Generating output folder:\t{}".format(os.path.join(self
       except:
           APPLOGGER.info("Output folder ({0}) exists. ".format(os.path.join(self.c
def checkArgs(self):
   APPLOGGER.info("Checking arguments...")
   APPLOGGER.info("\tSimPhy...")
   simphydir=os.path.exists(self.path)
   if simphydir:
       APPLOGGER.info("SimPhy folder exists:\t{0}".format(simphydir))
   else:
       exc_type, exc_obj, exc_tb = sys.exc_info()
       fname = os.path.split(exc_tb.tb_frame.f_code.co_filename)[1]
       ex="SimPhy folder does not exist."
       message="\{1\} \mid File: \{2\} - Line: \{3\} \setminus \{0\}".format(\
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ex,exc_type,fname, exc_tb.tb_lineno,\
      "Please verify. Exiting.")
   raise NRSException(False, message, datetime.datetime.now()-self.startTime)
fileList=os.listdir(os.path.abspath(self.path))
for index in range(0,len(fileList)):
   fileList[index]=os.path.abspath(os.path.join(self.path,fileList[index]))
self.db = os.path.join(self.path,"{0}.db".format(self.projectName))
if not self.db in fileList:
   ex="SimPhy required file do not exist."
   exc_type, exc_obj, exc_tb = sys.exc_info()
   fname = os.path.split(exc_tb.tb_frame.f_code.co_filename)[1]
   message="\{1\} \mid File: \{2\} - Line: \{3\} \setminus \{0\}".format(\
      ex,exc_type,fname, exc_tb.tb_lineno,\
      "Please verify. Exiting."\
   raise NRSException(False, message, datetime.datetime.now()-self.startTime)
APPLOGGER.info("SimPhy data base exist:\t{0} ({1})".format(\
   os.path.basename(self.db), self.db in fileList)
APPLOGGER.info("\tIdentifying replicates...")
# check how many of them are dirs
for item in fileList:
   baseitem=os.path.basename(item)
   if (os.path.isdir(os.path.abspath(item)) and baseitem.isdigit()):
      self.numReplicates=self.numReplicates+1
self.numReplicatesDigits=len(str(self.numReplicates))
# check if at least one
if not (self.numReplicates>0):
   ex="Number of replicates/folders:\t{0} [Required at least 1]".format(self.nu
   exc_type, exc_obj, exc_tb = sys.exc_info()
   fname = os.path.split(exc_tb.tb_frame.f_code.co_filename)[1]
   message="{1} | File: {2} - Line:{3}\n\t{0}\".format(\
      ex,exc_type,fname, exc_tb.tb_lineno,\
      "Please verify. Exiting."\
   raise NRSException(False, message, datetime.datetime.now()-self.startTime)
APPLOGGER.info("\tDone!")
APPLOGGER.info("Number of replicates:\t{0}".format(self.numReplicates))
if self.nsize > -1:
   APPLOGGER.info("Reference sequences will be concatenated.")
if self.method==1:
   if not (os.path.exists(self.seqDescriptionFile) and os.path.isfile(self.seqDescriptionFile)
      message="{0}\\n{t{1}}".format(
          "Sequence description file does not exist.",\
          "Please verify. Exiting."
      raise NRSException(False, message, datetime.datetime.now()-self.startTime.now()
self.getNumLociPerReplicate()
# sequence list initialization
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replicateIndexes=[self.numLociPerReplicate[item]*[item+1] for item in range(0, :
    replicateIndexes=[item for sublist in replicateIndexes for item in sublist]
    lociIndexes=[range(1, self.numLociPerReplicate[item]+1) for item in range(0, self.
   lociIndexes=[item for sublist in lociIndexes for item in sublist]
    seqs=["1_0_0"]*len(lociIndexes)
   self.sequenceList=[ (replicateIndexes[index], lociIndexes[index], seqs[index]) 1
def getNumLociPerReplicate(self):
   query="select N_Loci from Species_Trees"
   con = sqlite3.connect(self.db)
   res=con.execute(query).fetchall()
   con.close()
   self.numLociPerReplicate=[item for sublist in res for item in sublist]
   for item in range(0,len(self.numLociPerReplicate)):
        self.numLociPerReplicateDigits+=[len(str(self.numLociPerReplicate[item]))]
def getBEDfile(self, index):
   repID=index+1
   control=os.path.join(\
        self.path, \
        "{0:0{1}d}".format(repID, self.numReplicatesDigits),\
        "control.txt"\
    )
    f=open(control, "r")
   lines=f.readlines()
   f.close()
   sizes=[ int(line.replace("[","").replace("]","").strip().split()[4]) for line in
   startpos=0
   bedfile=os.path.join(\
       self.output, \
        "bed", \
        "{0}_{1:0{2}d}.bed".format(\
            self.outputprefix,\
            repID, self.numReplicatesDigits\
   outfile=open(bedfile, 'a')
    totalConcatSize=len(str(sum(sizes)+(self.nsize*len(sizes))))
    sequenceListIndex=sum(self.numLociPerReplicate[0:repID-1])
   if repID==1: sequenceListIndex=0
   for locID in range(1, self.numLociPerReplicate[repID-1]+1):
        endpos=startpos+sizes[locID-1]
        chromField="{chrom:{align}0{fillChrom}d}".format(\
            align="<",\
            chrom=repID, \
            fillChrom=self.numReplicatesDigits)
        positions="{startPOS:{align}{posSIZE}}\t{endPOS:{align}{posSIZE}}".format(\
            align=">", \
            startPOS=startpos, \
            endPOS=(endpos-1), \
            posSIZE=int(str(totalConcatSize))\
        )
        nameField="{name:0{fillName}d}.{seqDescription}".format(\
            name=locID, \
            fillName=self.numLociPerReplicateDigits[repID-1], \
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seqDescription=self.sequenceList[sequenceListIndex][2]
       )
       outfile.write("Replicate{0}\t{1}\tLocus{2}\n".format(\
           chromField, \
           positions, \
           nameField\
       ))
       startpos=endpos+(self.nsize-1)
       sequenceListIndex+=1
   outfile.close()
def filterReplicatesMatchingIndPerSpeciesAndPloidy(self, ploidy):
   Identifies and filters the species tree replicates that SimPhy
   database.
   Returns: a list with the number of loci per species tree replicate
   query="select SID from Species_Trees"
   if not (ploidy == 1):
       query="select SID from Species_Trees WHERE Ind_per_sp % {0} = 0".format(plo:
   con = sqlite3.connect(self.db)
   res=con.execute(query).fetchall()
   con.close()
   res=[item for sublist in res for item in sublist]
   return res
def iterateOverReplicate(self):
   APPLOGGER.debug("IterateOverReplicate")
   filtered=self.filterReplicatesMatchingIndPerSpeciesAndPloidy(self.ploidy)
   for index in range(0, self.numReplicates):
       repID=index+1
       if repID in filtered:
           APPLOGGER.debug("Replicate {0}/{1} ".format(repID, self.numReplicates))
           curReplicatePath=os.path.join(\
              self.path, \
               "{0:0{1}d}".format(repID, self.numReplicatesDigits),\
           )
           fileList=glob.glob("{0}/{1}_*.fasta".format(curReplicatePath, self.input)
           prefixLoci=len(fileList)
           APPLOGGER.info("Method chosen: {0}".format(self.method))
           print (self.numLociPerReplicateDigits)
           if self.method==0:
              self.methodOutgroup(index)
           if self.method==1:
              if not self.seqDescriptionFile == "":
                  self.seqPerLocus(index)
              else:
                  message="{0}\n\t{1}".format(\
                      "Required file for method 1.",\
                      "Please verify. Exiting."
                  )
                  raise NRSException(False, message, datetime.datetime.now()-self
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if self.method==2:
              self.methodRandomIngroup(index)
          if self.method==3:
              self.methodConsensusRandomSpecies(index)
          if self.method==4:
              self.methodConsensusAll(index)
          if (self.nsize>-1): # only way I know sequences are concatenated
              self.getBEDfile(index)
def writeLocus(self, index,locID,description,sequence):
   APPLOGGER.debug("Write Loci()")
   if self.nsize > -1:
       APPLOGGER.debug("CONCAT")
       self.concatSelectedLoci(index,locID,description,sequence)
   else:
       APPLOGGER.debug("SEPARATE SEQUENCE")
       self.writeSelectedLoci(index, locID, description, sequence)
def methodOutgroup(self,index):
   Method 0 for the selection of reference loci.
   This method selects the outgroup as a reference locus.
   attributes: repID: Index of the species tree that is being used.
   returns: Nothing
   APPLOGGER.debug("method outgroup")
   description="0_0_0"
   repID=index+1
   sequenceListIndex=sum(self.numLociPerReplicate[0:index])
   if index==0: sequenceListIndex=0
   for locID in range(1, self.numLociPerReplicate[index]+1):
       APPLOGGER.info("Locus {0}/{1} | Table Index: {2}".format(locID, self.numLocil
       mytuple=list(self.sequenceList[sequenceListIndex])
       mytuple[2]=description
       self.sequenceList[sequenceListIndex]=tuple(mytuple)
       fastapath=os.path.join(\
          self.path, \
          "{0:0{1}d}".format(repID, self.numReplicatesDigits),\
          "{0}_{1:0{2}d}.fasta".format(self.inputprefix,locID, self.numLociPerRep.
       lociData=msatools.parseMSAFileWithDescriptions(fastapath)
       selectedSequence=lociData[description]
       self.writeLocus(index,locID,description,selectedSequence)
       sequenceListIndex+=1
   APPLOGGER.info("Done outgroup sequence")
def seqPerLocus(self,index):
   Method 1 for the selection of reference loci.
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This method selects a sequence per locus as indicated in the seq_desc_file.
   Args: repID: Index of the species tree that is being used.
   Returns: Nothing
    0.00
   entries=self.parseReferenceLociFile(self.seqDescriptionFile)
   for entry in entries:
        repID=entry[0]
       locID=entry[1]
        seqID=entry[2]
        APPLOGGER.info("Locus {0}/{1}".format(locID, self.numLociPerReplicate[index]
        fastapath=os.path.join(
            self.path, \
            "{0:0{1}d}".format(repID, self.numReplicatesDigits),\
            "{0}_{1:0{2}d}_TRUE.fasta".format(self.inputprefix,locID,self.numLociPe
        fastaFile=msatools.parseMSAFileWithDescriptions(fastapath)
        sequence=""
        try:
            sequence=fastaFile[seqID]
        except:
            message="{0}\n\t{1}".format(\
                "One of the selected sequences (description) has not been found on
                "Please verify. Exiting"
            )
            raise NRSException(False, message, datetime.datetime.now()-self.startTime.
        self.writeLocus(index,locID,seqID,sequence)
   APPLOGGER.info("Done Seq Per locus")
def methodRandomIngroup(self,index):
   11 11 11
   Method 1 for the selection of reference loci.
   This method selects a random sequence from the ingroup species as
   a reference and from all the loci.
   Args: repID: Index of the species tree that is being used.
   Returns: Nothing
   0.000
   repID=index+1
   sequenceListIndex=sum(self.numLociPerReplicate[0:index])
   if index==0: sequenceListIndex=0
   for locID in range(1, self.numLociPerReplicate[index]+1):
       APPLOGGER.info("Locus {0}/{1} | Table Index: {2}".format(locID, self.numLocil
        fastapath=os.path.join(\
            self.path, \
            "{0:0{1}d}".format(repID, self.numReplicatesDigits),\
            "{0}_{1:0{2}d}.fasta".format(self.inputprefix,locID, self.numLociPerRep.
        )
        lociData=msatools.parseMSAFile(fastapath)
        keys=lociData.keys()
        rndKey1="0"; rndKey2="0"
        try:
            rndKey1=rnd.sample(set(keys)-set("0_0"),1)[0]
        except:
            rndKey1="0"
        subkeys=lociData[rndKey1]
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try:
            rndKey2=rnd.sample(len(subkeys),1)[0]
        except:
            rndKey2="0"
        selected=lociData[rndKey1][rndKey2]
        # print(self.sequenceList[sequenceListIndex])
       mytuple=list(self.sequenceList[sequenceListIndex])
        mytuple[2]="\{0\}_{\{1\}}".format(rndKey1,rndKey2)
        self.sequenceList[sequenceListIndex]=tuple(mytuple)
        self.writeLocus(index,locID, selected["description"], selected["sequence"])
        sequenceListIndex+=1
   APPLOGGER.info("Done random ingroup sequence")
def methodConsensusRandomSpecies(self,index):
   Method 2 for the selection of reference loci.
   This method selects a consensus sequence, obtained from the random selection
   of a species, and then computing a consensus from all the sequences
   within the selected species.
   Args: repID: Index of the species tree that is being used.
   Returns: Nothing
   0.000
   repID=index+1
   sequenceListIndex=sum(self.numLociPerReplicate[0:index])
   if repID==1: sequenceListIndex=0
   for locID in range(1, self.numLociPerReplicate[index]+1):
       APPLOGGER.info("Locus {0}/{1} | Table Index: {2}".format(locID, self.numLociI
        fastapath=os.path.join(\
            self.path, \
            "{0:0{1}d}".format(repID, self.numReplicatesDigits),\
            "{0}_{1:0{2}d}.fasta".format(self.inputprefix,locID, self.numLociPerRep.
        lociData=msatools.parseMSAFile(fastapath)
        keys=lociData.keys()
        rndKey1=0; rndKey2=0
        try:
            rndKey1=rnd.sample(set(keys)-set("0_0"),1)[0]
        except:
            rndKey1=0
        subkeys=lociData[rndKey1]
        sequences=[]
        self.sequenceList[sequenceListIndex]
        for sk in subkeys:
            sequences+=[lociData[rndKey1][sk]["sequence"]]
        mytuple=list(self.sequenceList[sequenceListIndex])
       mytuple[2]="{0}_CONSENSUS_RND_SP".format(rndKey1)
        self.sequenceList[sequenceListIndex]=tuple(mytuple)
        selected=self.computeConsensus(sequences)
        selectedDes=">consensus_sp_{0}".format(rndKey1)
        self.writeLocus(index, locID, selectedDes, selected)
        sequenceListIndex+=1
   APPLOGGER.info("Done random ingroup consensus")
def methodConsensusAll(self,index):
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Method 3 for the selection of reference loci.
   Computes the consensus from all the sequences of a gene tree file,
   and uses this sequence as reference loci.
   Args: repID: Index of the species tree that is being used.
   Returns: Nothing
   H \oplus H
   repID=index+1
    sequenceListIndex=sum(self.numLociPerReplicate[0:index])
   if repID==1: sequenceListIndex=0
   for locID in range(1, self.numLociPerReplicate[index]+1):
        APPLOGGER.info("Locus {0}/{1} | Table Index: {2}".format(locID, self.numLocil
        fastapath=os.path.join(\
            self.path,\
            "{0:0{1}d}".format(repID, self.numReplicatesDigits),\
            "{0}_{1:0{2}d}.fasta".format(self.inputprefix,locID, self.numLociPerRep.
        lociData=msatools.parseMSAFileWithDescriptions(fastapath)
        keys=set(lociData.keys())
        sequences=[]
        for mk in keys:
            sequences+=[lociData[mk]]
        selected=self.computeConsensus(sequences)
        self.writeLocus(index, locID, ">consensus_all", selected)
        mytuple=list(self.sequenceList[sequenceListIndex])
        mytuple[2]="{0}_CONSENSUS_ALL".format(rndKey1)
        self.sequenceList[sequenceListIndex]=tuple(mytuple)
        sequenceListIndex+=1
   APPLOGGER.info("Done all ingroups consensus")
def computeConsensus(self, sequences):
   Method for the computation of a consensus sequence from a set
   of sequences.
   Args: sequences: list of the sequences
   Returns: Single consensus sequence
   H \oplus H
   conseq=""
   # Assume that all the sequences in a file have the same length
   seqSize=len(sequences[0])
   # Need to know how many sequences I have
   numSeqs=len(sequences)
   # Segs for all nucleotides
   A=np.zeros(seqSize);
   C=np.zeros(seqSize);
   G=np.zeros(seqSize);
   T=np.zeros(seqSize);
   N=np.zeros(seqSize);
   for indexCol in range(0, seqSize):
        for indexRow in range(0, numSeqs):
            if sequences[indexRow][indexCol]=="A": A[indexCol]+=1
            if sequences[indexRow][indexCol]=="C": C[indexCol]+=1
            if sequences[indexRow][indexCol]=="G": G[indexCol]+=1
            if sequences[indexRow][indexCol]=="T": T[indexCol]+=1
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if sequences[indexRow][indexCol]=="N": N[indexCol]+=1
   for indexCol in range(0, seqSize):
        if A[indexCol] > C[indexCol] and A[indexCol] > G[indexCol] and A[indexCol] :
            conseq+="A"
       elif C[indexCol] > A[indexCol] and C[indexCol] > G[indexCol] and C[indexCol]
            conseq+="C"
        elif G[indexCol] > A[indexCol] and G[indexCol] > C[indexCol] and G[indexCol]
           conseq+="G"
        elif T[indexCol] > A[indexCol] and T[indexCol] > C[indexCol] and T[indexCol]
            conseq+="T"
       else: conseq+="N"
   APPLOGGER.info("Consensus computed")
   return conseq
def writeSelectedLociMultipleSpecies(self,index,locID,seqs):
   Writes multiple sequences in a single file.
   Args:
   - repID: Index of the species tree that is being used.
    - locID: Index of the locus being used.
    - seqs: sequence of the locus to be written.
   Returns: Nothing
   Generates a file for all the selected loci.
   repID=index+1
   # seqs=[(description, seq), ..., (description, seq)]
   APPLOGGER.info("Writing selected loci {1} from ST: {0}", repID,locID)
   outname=os.path.join(\
        self.output,\
        "{0}_{1:0{2}d}_{3:0{4}d}.fasta".format(\
            self.outputprefix, \
            repID, self.numReplicatesDigits,\
            locID, self.numLociPerReplicateDigits[index]\
        )\
   outfile=open(outname, 'a')
    for item in range(0,len(seqs)):
        des=seqs[item][0]
        nucSeq=seqs[item][1]
        newDes=">{0}:{1:0{2}d}:REF:{7}:{6}:{3:0{4}d}:{5}".format(\
            self.projectName, \
            repID, \
            self.numReplicatesDigits,\
            locID, \
            self.numLociPerReplicateDigits[index],\
            des[1:len(des)],\
            self.inputprefix, \
            self.outputprefix
        )
        outfile.write("{0}\n{1}\n".format(newDes, nucSeq))
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outfile.close()
def parseReferenceLociFile(self, filename):
   Used to parse sequenceList, file with format: STID, LOCID, TIPLABEL
   Parameters:
    - filename: path of the sequenceList file.
   There's only ONE file with the relation of the ref_alleles
   If "None" inputted (file is missing) then reference by default is 1_0_0
   for all species tree replicates.
   Returns:
    - output: list. each element of the list is a triplet
            (REPLICATEID, sequence_tip_label )
                                       sequence_description_locus
            replicate_ID
                            locus_ID
    0.00
   APPLOGGER.info("Retrieving identifiers of the reference alleles...")
   filepath=os.path.abspath(filename)
    if os.path.exists(filepath):
        # There's a file
       lines=None
        with open(filepath) as f:
            lines=[line.strip().split() for line in f if (not line.strip()=="") and
        lines=sorted(lines, key=lambda x:(x[1],x[2]))
        skipped=False
        message="Parsing reference list. "+\
            "A default reference has been introduced.\n"+\
            "Replicate index:"
        for i in range(0,len(self.sequenceList)):
            for j in range(0,len(lines)):
                if (not lines[j][0] == "") and \setminus
                    (not lines[j][1] == "") and \
                    (not lines[j][2] == "") and \setminus
                    (lines[i][0] == self.sequenceList[j][0] \ and \ lines[i][1] == self.sequenceList[j][0]
                    bool(re.match(^{([1-9]+[0-9]+[0-9]+[1]}, lines[i][3])):
                    self.sequenceList[j][3]=lines[i][3]
    return self.sequenceList
def concatSelectedLoci(self,index,locID,description,sequence):
   BEDFILE: replicateID startPOS endPOS locID
    repID=index+1
   APPLOGGER.info("Writing selected loci {1} from ST: {0}".format(repID,locID))
   outname=os.path.join(\
        self.output,\
        "{0}_{1:0{2}d}.fasta".format(\
            self.outputprefix, \
            repID, self.numReplicatesDigits
        )
    )
   newDes=">{0}:{1}:{2:0{3}d}".format(\
        self.projectName,\
        self.outputprefix, \
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repID, self.numReplicatesDigits
    )
    nsequence="".join("N" for item in range(0, self.nsize))
    # I'm assuming that if the file does not exist it will be created
    fullseq="{0}{1}".format(sequence, str(nsequence))
    if os.path.exists(outname):
        with open(outname, 'a+') as f:
            f.seek(-1,2)
            if locID == self.numLociPerReplicate[repID-1]:
                f.write('\n'.encode())
            else:
                f.write(fullseq.encode())
    else:
        f=open(outname, "a+")
        f.write(">{0}\n{1}".format(description, fullseq))
        f.close()
def writeSelectedLoci(self, index, locID, des, seq):
    Writes a single sequence per file.
    Input:
        - repID: Index of the species tree that is being used.
        - locID: Index of the locus being used.
        - des: description of the sequence to be written.
        - seq: sequence of the locus to be written.
    Returns: Nothing
        - Generates a file per selected locus.
    repID=index+1
    APPLOGGER.info("Writing selected loci {1} from ST: {0}", repID, locID)
    outname=os.path.join(\
        self.output,\
        \{0\}_{1:0\{2\}d\}_{3:0\{4\}d\}}. fasta format(\
            self.outputprefix, \
            repID, self.numReplicatesDigits,\
            locID, self.numLociPerReplicateDigits[repID-1]
    )
    newDes=">{0}:{1:0{2}d}:REF:{7}:{6}:{3:0{4}d}:{5}".format(\
        self.projectName,\
        repID,∖
        self.numReplicatesDigits,\
        locID, \
        self.numLociPerReplicateDigits[repID-1],\
        des[1:len(des)], \
        self.inputprefix, \
        self.outputprefix
    # I'm assuming that if the file does not exist it will be created
    outfile=open(outname, 'a')
    outfile.write("{0}\n{1}\n".format(newDes, seq))
    outfile.close()
def run(self):
```

```
Run process of the program.
"""

self.checkArgs()
self.iterateOverReplicate()
raise NRSException(True,"", datetime.datetime.now()-self.startTime)
```